National Institute for Health and Care Excellence

Draft for consultation

Depression in adults

[Supplement B3] Forest plots for first-line treatment of more severe depression

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Evidence review supplement

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This evidence review supplement was developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists



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Forest plots for first-line treatment of more severe depression

3 Appendix E – Forest plots

4 More severe: Behavioural activation (BA) individual versus

5 no treatment

6 Figure 1: Remission (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Patel 2017/Weobong 2017	147	247	91	248	100.0%	1.62 [1.34, 1.97]	
Total (95% CI)		247		248	100.0%	1.62 [1.34, 1.97]	•
Total events	147		91				
Heterogeneity: Not applicable							0.01 0.1 1 10 100
Test for overall effect: Z = 4.9	1 (P < 0.00	001)					Favours no treatment Favours BA

8 Figure 2: Discontinuation (any reason)

	Experimental			Control Risk Ratio				Risk Ratio			
Study or Subgroup	Events Total		Events Total V		Weight	M-H, Fixed, 95% CI	M	M-H, Fixed, 95% CI			
Patel 2017/Weobong 2017	17	247	12	248	100.0%	1.42 [0.69, 2.92]		_			
Total (95% CI)		247		248	100.0%	1.42 [0.69, 2.92]		-			
Total events Heterogeneity: Not applicable			12				0.01 0.1	1	10 100		
Test for overall effect: Z = 0.96	0 (P = 0.34)	,					Favo	urs BA Favours	no treatment		

10 Figure 3: Depression symptomatology at 9-month follow-up

	Expe	erimen	tal	C	ontrol			Std. Mean Difference		Std. Mean	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed	, 95% CI		
Patel 2017/Weobong 2017	8.16	6.96	245	10.46	7.54	248	100.0%	-0.32 [-0.49, -0.14]					
Total (95% CI)			245			248	100.0%	-0.32 [-0.49, -0.14]					
Heterogeneity: Not applicable Test for overall effect: Z = 3.49		0005)							-10	-5 (Favours BA	Favours no	treatme	10 nt

12 Figure 4: Remission at 9-month follow-up (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
Patel 2017/Weobong 2017	155	247	117	248	100.0%	1.33 [1.13, 1.57]		
Total (95% CI)		247		248	100.0%	1.33 [1.13, 1.57]	◆	
Total events	155		117					
Heterogeneity: Not applicable							0.01 0.1 1 10	100
Test for overall effect: Z = 3.4:	3 (P = 0.00	06)					Favours no treatment Favours BA	

13

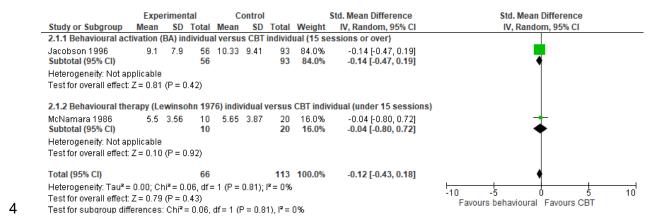
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9

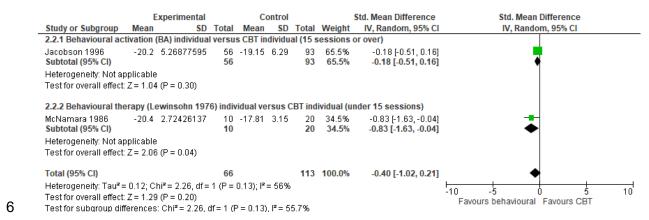
11

More severe: Behavioural therapies individual versus cognitive and cognitive behavioural therapies individual

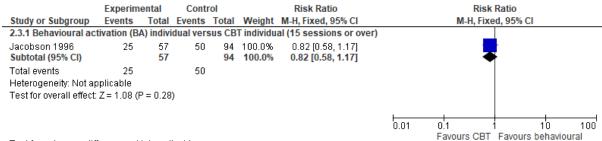
3 Figure 5: Depression symptomatology endpoint



5 Figure 6: Depression symptomatology change score

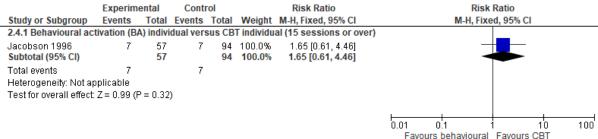


7 Figure 7: Remission (ITT)



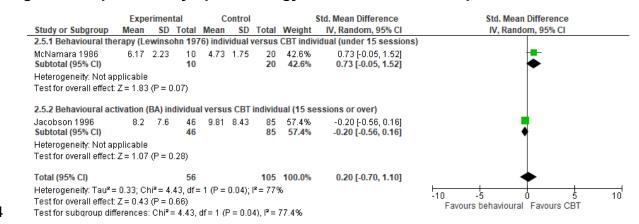
8 Test for subgroup differences: Not applicable

1 Figure 8: Discontinuation (any reason)

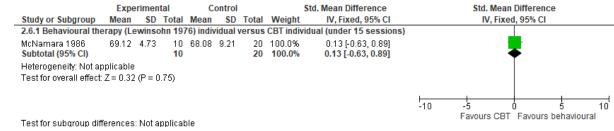


2 Test for subgroup differences: Not applicable

3 Figure 9: Depression symptomatology at 2-6 month follow-up



5 Figure 10: Interpersonal functioning endpoint



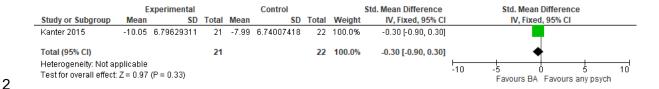
6

8 More severe: Behavioural activation (BA) individual versus any psychotherapy

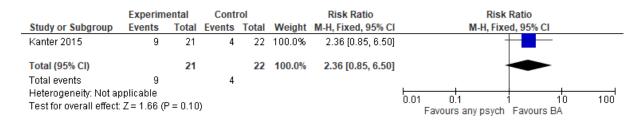
10 Figure 11: Depression symptomatology endpoint



1 Figure 12: Depression symptomatology change score



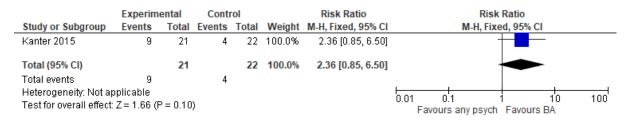
3 Figure 13: Remission (ITT)



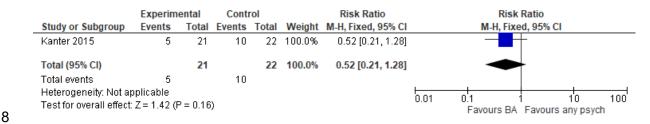
5 Figure 14: Response (ITT)

4

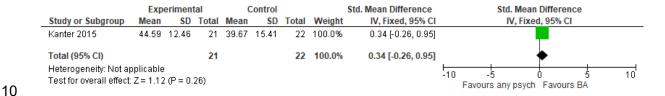
6



7 Figure 15: Discontinuation (any reason)



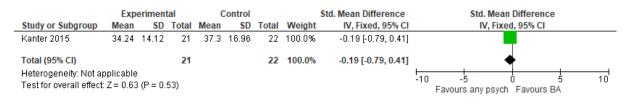
9 Figure 16: Quality of life endpoint



11 Figure 17: Quality of life physical health component endpoint

	Exp	eriment	tal	Control			Std. Mean Difference	Std. Mean Difference					
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fix	ed, 95	% CI	
Kanter 2015	45.41	12.63	21	41.6	9.24	22	100.0%	0.34 [-0.26, 0.94]					
Total (95% CI)			21			22	100.0%	0.34 [-0.26, 0.94]			•		
Heterogeneity: Not as Test for overall effect:			27)						-10	-5 Favours any psycl	o n Fav	5 ours BA	10

1 Figure 18: Quality of life mental health component endpoint



2

7

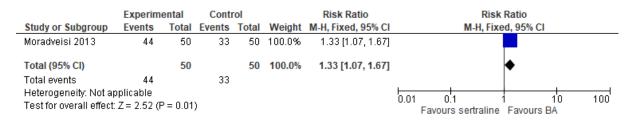
9

4 More severe: Behavioural activation (BA) individual versus 5 sertraline

6 Figure 19: Remission (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixe	ed, 95% CI	
Moradveisi 2013	41	50	24	50	100.0%	1.71 [1.25, 2.34]		-	
Total (95% CI)		50		50	100.0%	1.71 [1.25, 2.34]		*	
Total events	41		24						
Heterogeneity: Not ap Test for overall effect:	•	P = 0.00	09)				0.01 0.1 Favours sertraline	1 10 Favours BA	100

8 Figure 20: Response (ITT)



10 Figure 21: Discontinuation (any)

	Experim	ental	Conti	rol		Risk Ratio		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% CI		
Moradveisi 2013	10	50	30	50	100.0%	0.33 [0.18, 0.61]		-			
Total (95% CI)		50		50	100.0%	0.33 [0.18, 0.61]		•			
Total events	10		30								
Heterogeneity: Not applicable Test for overall effect: Z = 3.60 (P = 0.0003)							0.01	0.1 1 Favours BA	1 Favours se	0 rtraline	100

11

12 Figure 22: Remission at 8-month follow-up (ITT)

	Experim	mental Control			Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Moradveisi 2013	29	50	12	50	100.0%	2.42 [1.40, 4.18]	-
Total (95% CI)		50		50	100.0%	2.42 [1.40, 4.18]	•
Total events	29		12				
Heterogeneity: Not ap Test for overall effect:		P = 0.00	2)				0.01 0.1 1 10 100 Favours sertraline Favours BA

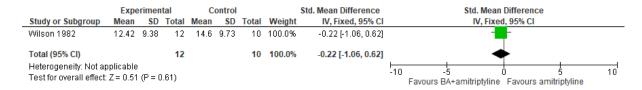
1 Figure 23: Response at 8-month follow-up (ITT)

	Experimental Control			Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed	, 95% CI	
Moradveisi 2013	39	50	20	50	100.0%	1.95 [1.35, 2.82]			
Total (95% CI)		50		50	100.0%	1.95 [1.35, 2.82]		*	
Total events	39		20						
Heterogeneity: Not ap Test for overall effect:	•	P = 0.00	04)				0.01 0.1 1 Favours sertraline	10 avours BA	100

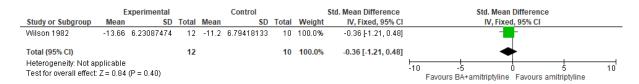
3 More severe: Behavioural activation (BA) individual +

4 amitriptyline versus amitriptyline

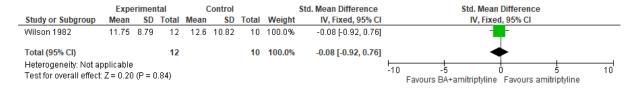
5 Figure 24: Depression symptomatology endpoint



7 Figure 25: Depression symptomatology change score



9 Figure 26: Depression symptomatology at 6-month follow-up



10

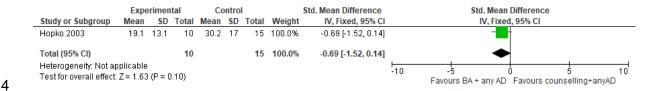
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6

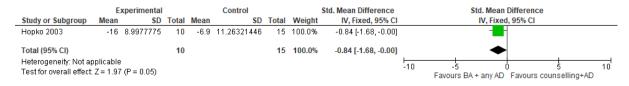
1 More severe: Behavioural activation (BA) individual + any AD

versus counselling + any AD

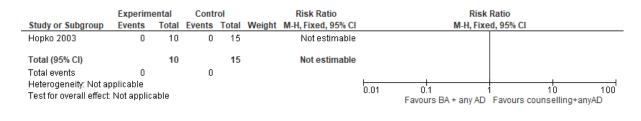
3 Figure 27: Depression symptomatology endpoint



5 Figure 28: Depression symptomatology change score



7 Figure 29: Discontinuation (any reason)



10 More severe: Behavioural activation (BA) individual +

11 amitriptyline versus progressive muscle relaxation +

12 amitriptyline

6

8 9

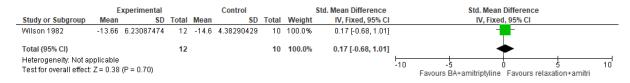
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16

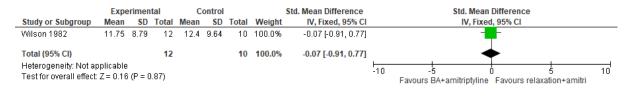
13 Figure 30: Depression symptomatology endpoint



15 Figure 31: Depression symptomatology change score



1 Figure 32: Depression symptomatology at 6-month follow-up



4 More severe: Coping with Depression course (group) versus5 waitlist

6 Figure 33: Discontinuation (any reason)

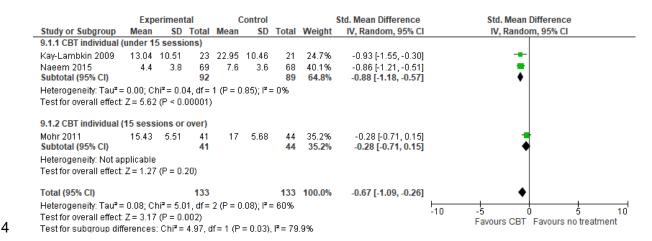
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3

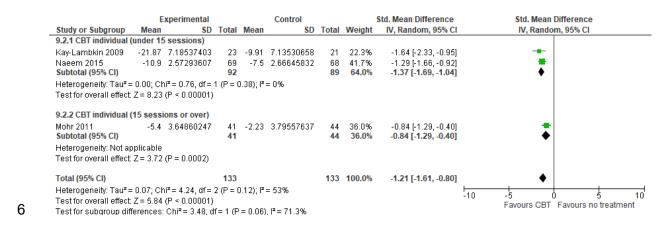
	Experimental		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Usaf 1990	12	31	6	29	100.0%	1.87 [0.81, 4.33]	+
Total (95% CI)		31		29	100.0%	1.87 [0.81, 4.33]	-
Total events	12		6				
Heterogeneity: Not as	oplicable						0.01 0.1 1 10 100
Test for overall effect:	Z=1.46 (F	P = 0.14)				0.01 0.1 1 10 100 Favours behavioural group Favours waitlist

More severe: Cognitive and cognitive behavioural therapies individual versus no treatment

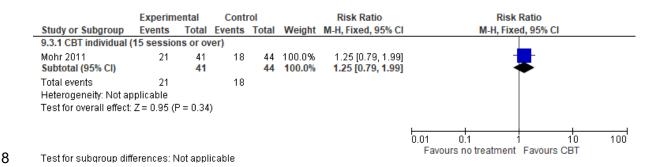
3 Figure 34: Depression symptomatology endpoint



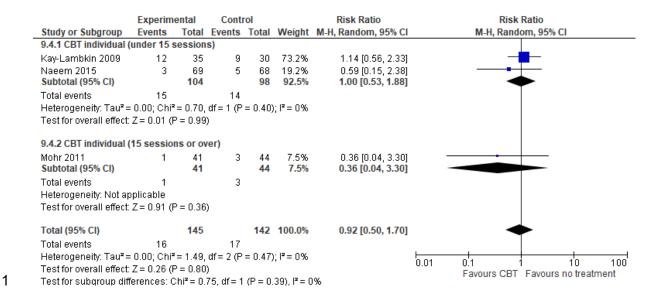
5 Figure 35: Depression symptomatology change score



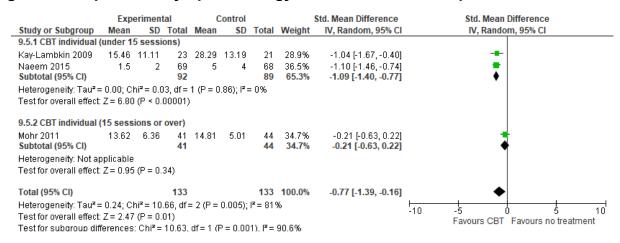
7 Figure 36: Remission (ITT)



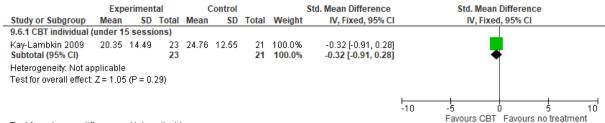
9 Figure 37: Discontinuation (any reason)



2 Figure 38: Depression symptomatology at 3-6 month follow-up

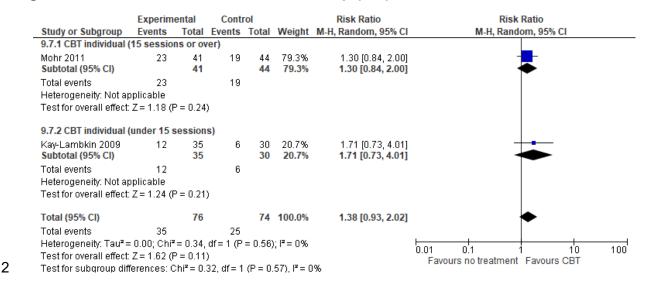


4 Figure 39: Depression symptomatology at 9-month follow-up

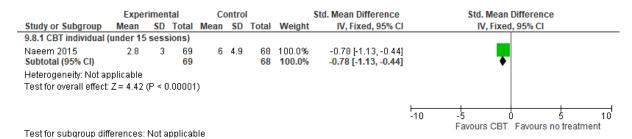


5 Test for subgroup differences: Not applicable

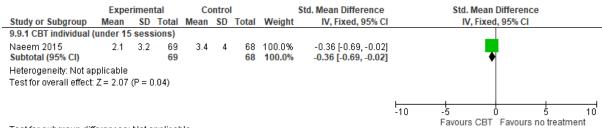
1 Figure 40: Remission at 6-9 month follow-up (ITT)



3 Figure 41: Functional impairment endpoint



5 Figure 42: Functional impairment at 6-month follow-up

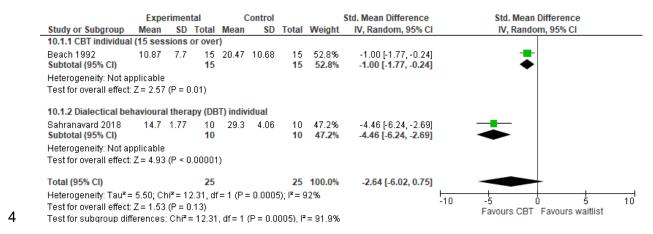


6 Test for subgroup differences: Not applicable

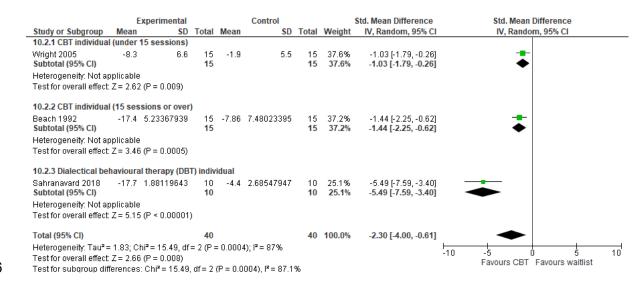
7

1 More severe: Cognitive and cognitive behavioural therapies2 individual versus waitlist

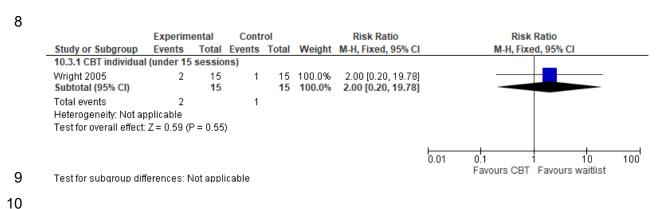
3 Figure 43: Depression symptomatology endpoint



5 Figure 44: Depression symptomatology change score

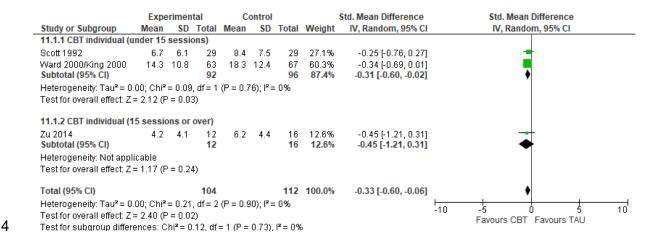


7 Figure 45: Discontinuation (any reason)

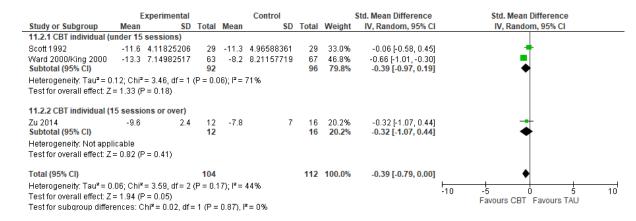


1 More severe: Cognitive and cognitive behavioural therapies2 individual versus TAU

3 Figure 46: Depression symptomatology endpoint

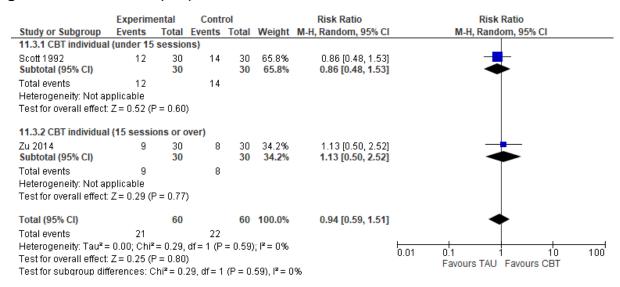


5 Figure 47: Depression symptomatology change score

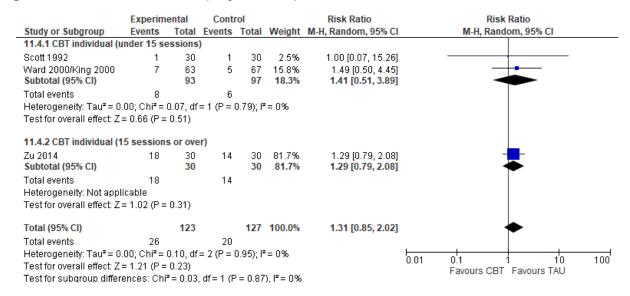


7 Figure 48: Remission (ITT)

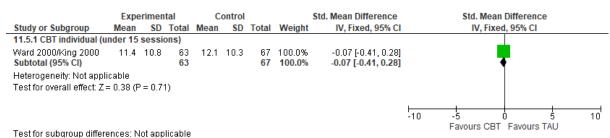
6



1 Figure 49: Discontinuation (any reason)



3 Figure 50: Depression symptomatology at 8-month follow-up



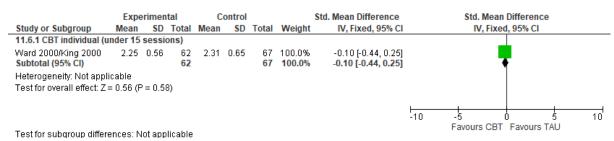
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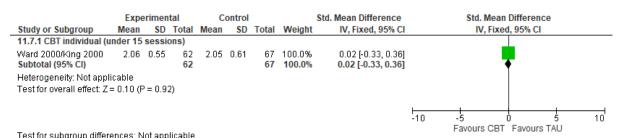
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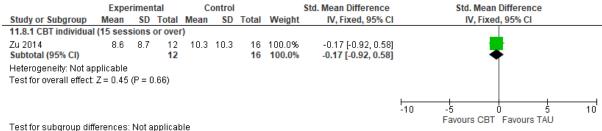
5 Figure 51: Interpersonal problems endpoint



7 Figure 52: Interpersonal problems at 8-month follow-up



1 Figure 53: Functional impairment endpoint



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4 More severe: CBT individual (15 sessions or over) versus IPT

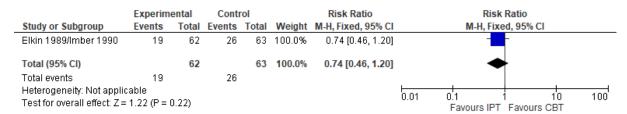
5 Figure 54: **Depression symptomatology endpoint**

	Expe	erimen	tal	C	Control			Std. Mean Difference		Std.	Mean Differ	ence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV,	Random, 959	% CI	
Elkin 1989/Imber 1990	10.7	7.9	59	9.8	7.9	61	55.0%	0.11 [-0.24, 0.47]					
Marshall 2008	6.3	4.81	37	8.4	6.46	35	45.0%	-0.37 [-0.83, 0.10]			-		
Total (95% CI)			96			96	100.0%	-0.10 [-0.57, 0.37]			•		
Heterogeneity: Tau² = 0.0 Test for overall effect: Z =				-10	-5 Favours	0 CBT Favor	5 urs IPT	10					

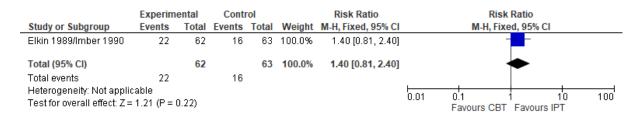
7 Figure 55: Depression symptomatology change score



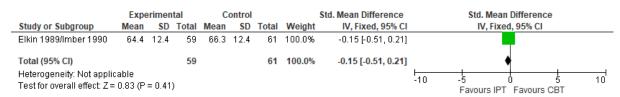
9 Figure 56: Remission (ITT)



1 Figure 57: Discontinuation (any reason)



3 Figure 58: Global functioning endpoint

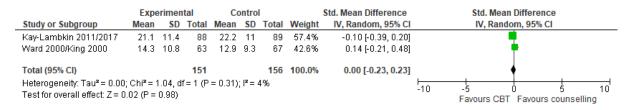


5 Figure 59: Interpersonal problems endpoint

	Expe	rimen	tal	Co				Std. Mean Difference		Std.	Mean Differ	ence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV	, Fixed, 95%	CI	
Elkin 1989/Imber 1990	2.9	0.9	36	2.8	0.9	46	100.0%	0.11 [-0.33, 0.55]					
Total (95% CI) Heterogeneity: Not applic Test for overall effect: Z =		= 0.62	36			46	100.0%	0.11 [-0.33, 0.55]	 -10	-5 Favour	0 s IPT Favo	5 urs CBT	10

8 More severe: CBT individual (under 15 sessions) versus9 counselling

10 Figure 60: Depression symptomatology endpoint



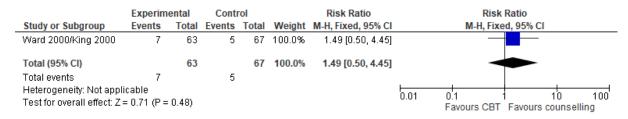
12 Figure 61: Depression symptomatology change score

	E	xperimental			Control			Std. Mean Difference		Std. Mean	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% CI		
Kay-Lambkin 2011/2017	-11.9	7.56835517	88	-8.3	7.4	89	52.9%	-0.48 [-0.78, -0.18]					
Ward 2000/King 2000	-13.3	7.14982517	63	-12.5	6.36238949	67	47.1%	-0.12 [-0.46, 0.23]		•	•		
Total (95% CI)			151			156	100.0%	-0.31 [-0.66, 0.04]		•			
Heterogeneity: Tau² = 0.04; Chi² = 2.41, df = 1 (P = 0.12); l² = 59% Test for overall effect: Z = 1.71 (P = 0.09) Favours CBT Favours counselli												1 5 unsellin	10 g

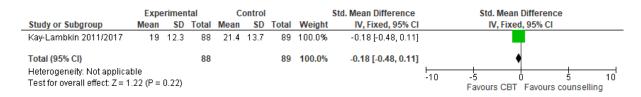
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1 Figure 62: Discontinuation (any reason)



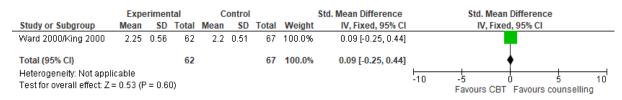
3 Figure 63: Depression symptomatology at 3-month follow-up



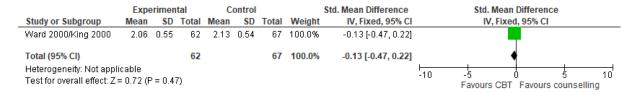
5 Figure 64: Depression symptomatology at 8-9 month follow-up

	Expe	erimen	tal	C	ontrol			Std. Mean Difference		Std.	Mean Diffe	rence		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, I	Random, 9	5% CI		
Kay-Lambkin 2011/2017	19.3	12.3	88	17.9	11.9	89	57.6%	0.12 [-0.18, 0.41]			•			
Ward 2000/King 2000	11.4	10.8	63	11.8	9.6	67	42.4%	-0.04 [-0.38, 0.31]			•			
Total (95% CI)			151			156	100.0%	0.05 [-0.17, 0.27]			•			
	Heterogeneity: Tau ² = 0.00; Chi ² = 0.44, df = 1 (P = 0.50); I ² = 0% Test for overall effect: Z = 0.44 (P = 0.66)											5 ours cou	i Inselling	10

7 Figure 65: Interpersonal problems endpoint



9 Figure 66: Interpersonal problems at 8-month follow-up



10 11

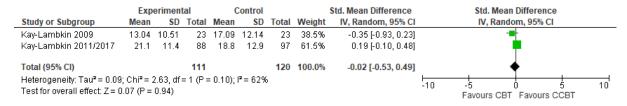
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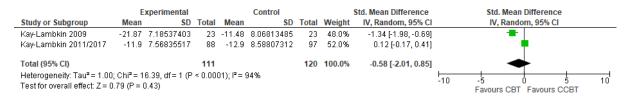
6

1 More severe: CBT individual (under 15 sessions) versus2 computerised-CBT (CCBT)

3 Figure 67: Depression symptomatology endpoint



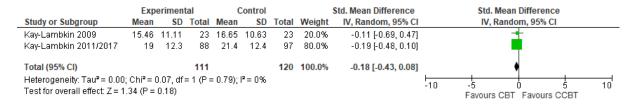
5 Figure 68: Depression symptomatology change score



7 Figure 69: Discontinuation (any reason)



9 Figure 70: Depression symptomatology at 3-month follow-up



11 Figure 71: Depression symptomatology at 9-month follow-up



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1 Figure 72: Remission at 9-month follow-up (ITT)

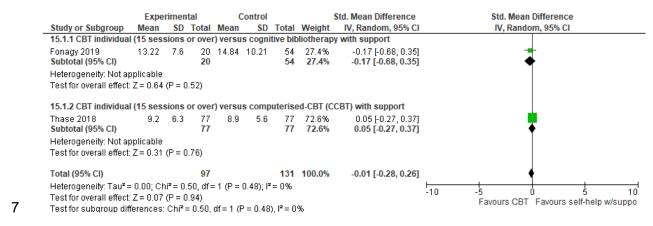


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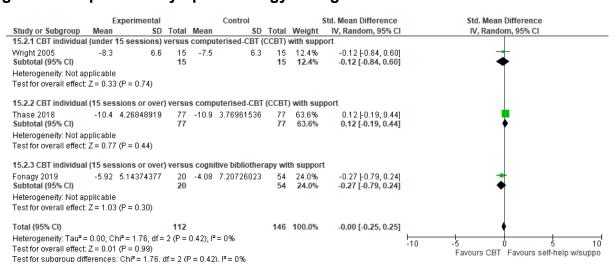
9

4 More severe: Cognitive and cognitive behavioural therapies 5 individual versus self-help with support

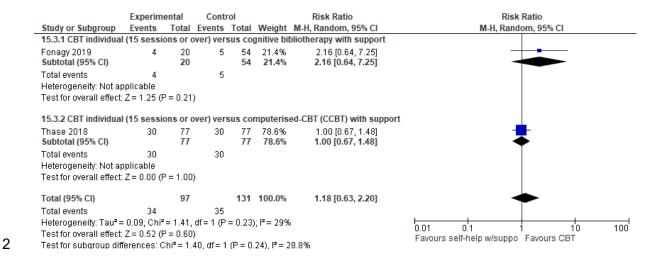
6 Figure 73: Depression symptomatology endpoint



8 Figure 74: Depression symptomatology change score



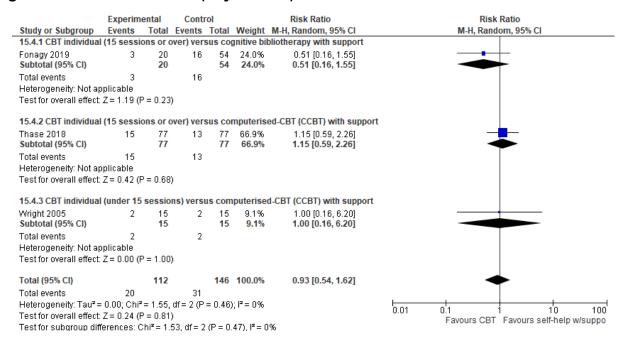
1 Figure 75: Remission (ITT)



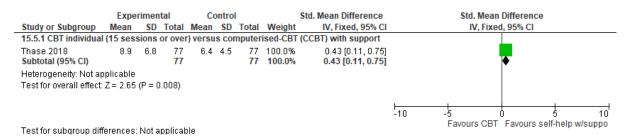
3 Figure 76: Discontinuation (any reason)

4

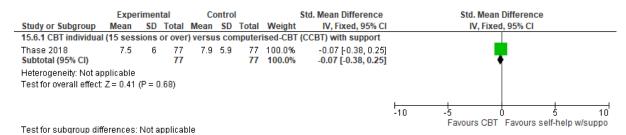
6



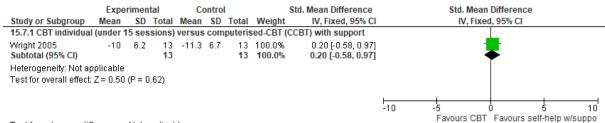
5 Figure 77: Depression symptomatology at 3-month follow-up



1 Figure 78: Depression symptomatology at 6-month follow-up



3 Figure 79: Depression symptomatology change score at 3-month follow-up



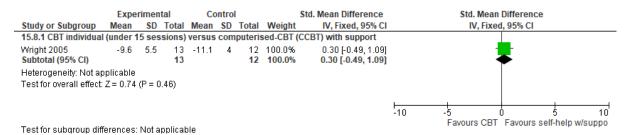
4 Test for subgroup differences: Not applicable

2

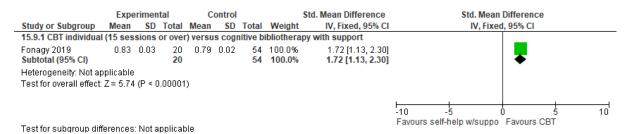
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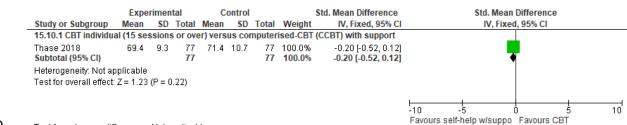
5 Figure 80: Depression symptomatology change score at 6-month follow-up



7 Figure 81: Quality of life endpoint

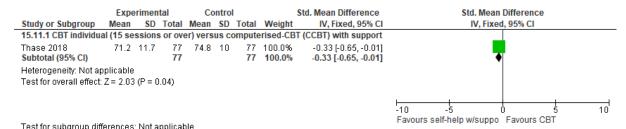


9 Figure 82: Global functioning endpoint



10 Test for subgroup differences: Not applicable

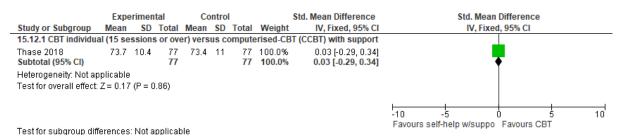
1 Figure 83: Global functioning at 3-month follow-up



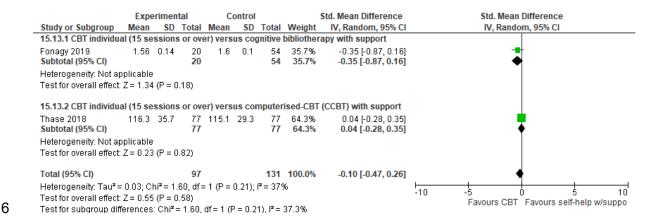
3 Figure 84: Global functioning at 6-month follow-up

2

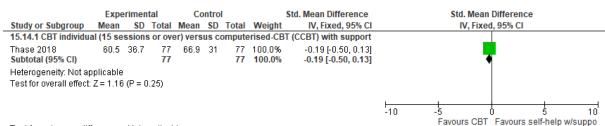
4



5 Figure 85: Interpersonal problems endpoint

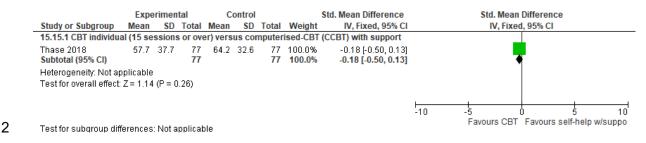


7 Figure 86: Interpersonal problems at 3-month follow-up



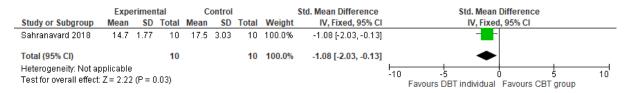
8 Test for subgroup differences: Not applicable

1 Figure 87: Interpersonal problems at 6-month follow-up

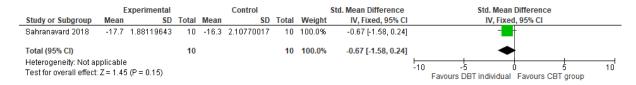


4 More severe: Dialectical behavioural therapy (DBT) individual 5 versus CBT group (under 15 sessions)

6 Figure 88: Depression symptomatology endpoint



8 Figure 89: Depression symptomatology change score

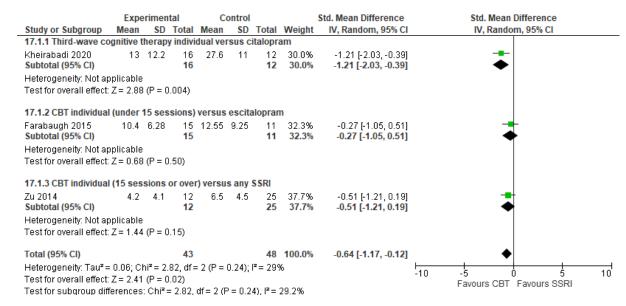


9

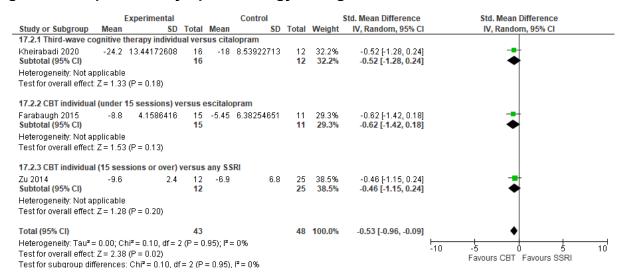
7

1 More severe: Cognitive and cognitive behavioural therapies2 individual versus SSRI

3 Figure 90: Depression symptomatology endpoint

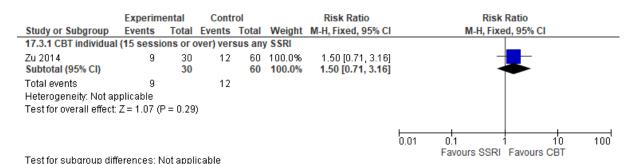


5 Figure 91: Depression symptomatology change score

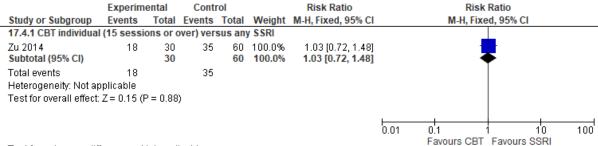


7 Figure 92: Remission (ITT)

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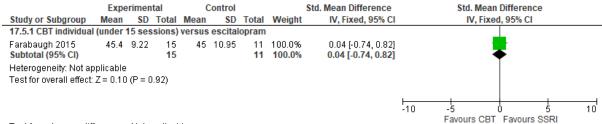


1 Figure 93: Discontinuation (any reason)



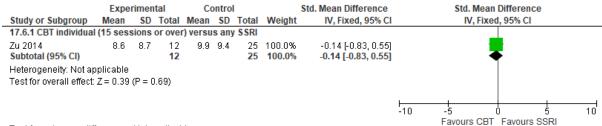
2 Test for subgroup differences: Not applicable

3 Figure 94: Quality of life endpoint



4 Test for subgroup differences: Not applicable

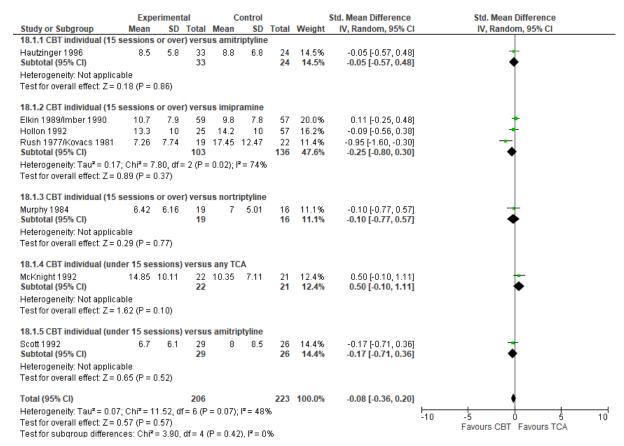
5 Figure 95: Functional impairment endpoint



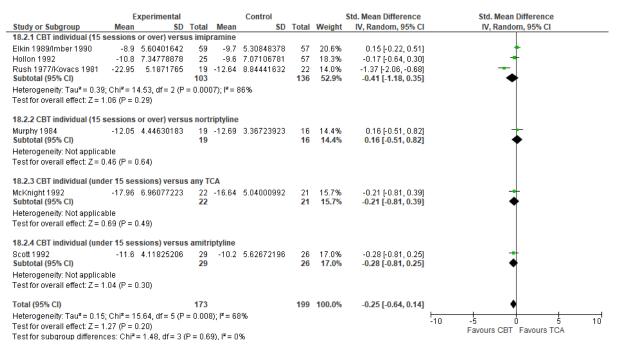
6 Test for subgroup differences: Not applicable

1 More severe: Cognitive and cognitive behavioural therapies2 individual versus TCA

3 Figure 96: Depression symptomatology endpoint



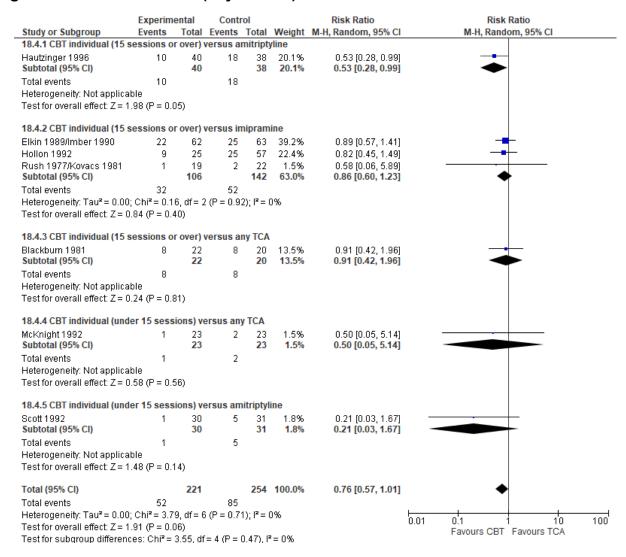
5 Figure 97: Depression symptomatology change score



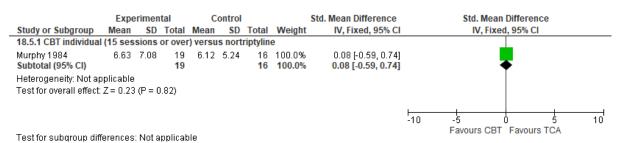
1 Figure 98: Remission (ITT)

	Experim		Contro			Risk Ratio	Risk Ratio
Study or Subgroup	Events				Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
18.3.1 CBT individual (15							
Blackburn 1981 Subtotal (95% CI)	16	22 22	11	20 20	18.7% 18.7 %	1.32 [0.82, 2.12] 1.32 [0.82, 2.12]	*
Total events	16		11				
Heterogeneity: Not applica							
Test for overall effect: Z = 1	1.16 (P = 0.2	25)					
18.3.2 CBT individual (15	sessions o	r over) v	ersus im	ipram	ine		
Elkin 1989/Imber 1990	19	62	21	63	17.4%	0.92 [0.55, 1.53]	-
Hollon 1992	8	25	17	57	12.5%	1.07 [0.53, 2.15]	
Rush 1977/Kovacs 1981	15	19	5	22	10.4%	3.47 [1.55, 7.77]	
Subtotal (95% CI)		106		142	40.3%	1.44 [0.68, 3.06]	*
Total events	42		43				
Heterogeneity: Tau ² = 0.33			(P = 0.02)	!); 2 = 7	74%		
Test for overall effect: Z=1	U.94 (P = U.)	35)					
18.3.3 CBT individual (und	der 15 sess	ions) ve	rsus any	TCA			
McKnight 1992	18	23	19	23	25.4%	0.95 [0.71, 1.26]	+
Subtotal (95% CI)		23		23	25.4%	0.95 [0.71, 1.26]	•
Total events	18		19				
Heterogeneity: Not applica							
Test for overall effect: Z = 1	0.37 (P = 0.7)	1)					
18.3.4 CBT individual (und	der 15 sess	ions) ve	rsus am	itriptyl	ine		
Scott 1992	12	30	15	31	15.7%	0.83 [0.47, 1.46]	
Subtotal (95% CI)		30		31	15.7%	0.83 [0.47, 1.46]	•
Total events	12		15				
Heterogeneity: Not applica		-45					
Test for overall effect: Z = 1	u.oo (F = u.:)1)					
Total (95% CI)		181		216	100.0%	1.14 [0.83, 1.57]	*
Total events	88		88				
Heterogeneity: Tau² = 0.08			5 (P = 0.0)	15); l² =	55%		0.01 0.1 1 10 100
Test for overall effect: Z = 1	,						Favours TCA Favours CBT
Test for subgroup differen	ces: Chi ² =	2.73, df=	= 3 (P = 0)	1.44), l ²	= 0%		

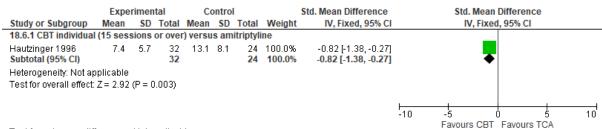
1 Figure 99: Discontinuation (any reason)



3 Figure 100: Depression symptomatology at 1-month follow-up

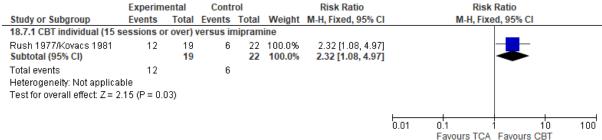


5 Figure 101: Depression symptomatology at 12-month follow-up



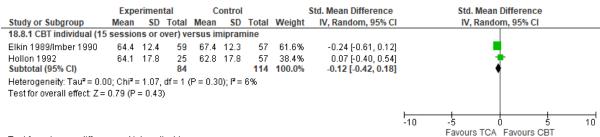
2

1 Figure 102: Remission at 12-month follow-up (ITT)



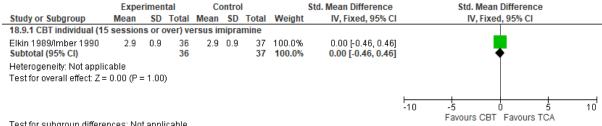
2 Test for subgroup differences: Not applicable

3 Figure 103: Global functioning endpoint



Test for subgroup differences: Not applicable

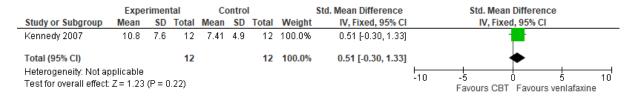
5 Figure 104: Interpersonal problems endpoint



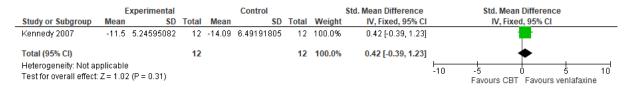
6 Test for subgroup differences: Not applicable

8 More severe: CBT individual (15 sessions or over) versus venlafaxine

10 Figure 105: Depression symptomatology endpoint



12 Figure 106: Depression symptomatology change score



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1 Figure 107: Remission (ITT)



3 Figure 108: Response (ITT)

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5 Figure 109: Discontinuation (any reason)

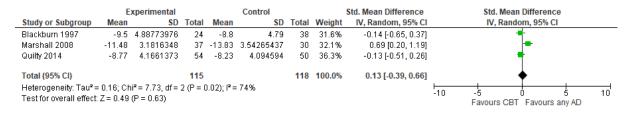


8 More severe: CBT individual (15 sessions or over) versus9 any AD

10 Figure 110: Depression symptomatology endpoint

	Expe	erimen	tal	C	Control			Std. Mean Difference		Std. N	ean Differ	ence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, R	andom, 959	% CI	
Blackburn 1997	10.5	7.2	24	11.58	6.96	38	25.7%	-0.15 [-0.66, 0.36]			+		
Marshall 2008	6.3	4.81	37	4.7	5.32	30	28.7%	0.31 [-0.17, 0.80]			-		
Quilty 2014	8.14	6.28	54	8.19	6.08	50	45.6%	-0.01 [-0.39, 0.38]			•		
Total (95% CI)			115			118	100.0%	0.05 [-0.21, 0.31]			•		
Heterogeneity: Tau² = Test for overall effect:					-10	-5 Favours (0 CBT Favor	5 urs any AD	10				

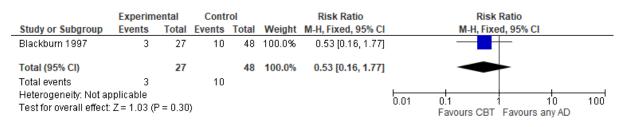
12 Figure 111: Depression symptomatology change score



1 Figure 112: Remission (ITT)



3 Figure 113: Discontinuation (any reason)



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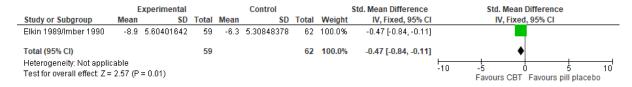
6 More severe: CBT individual (15 sessions or over) versus pill placebo

8 Figure 114: Depression symptomatology endpoint

	Expe	Experimental Control				Std. Mean Difference		Std.	Mean Differe	ence			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV	, Fixed, 95%	CI	
Elkin 1989/Imber 1990	10.7	7.9	59	13.2	7.8	62	100.0%	-0.32 [-0.68, 0.04]					
Total (95% CI)			59			62	100.0%	-0.32 [-0.68, 0.04]			•		
Heterogeneity: Not applic Test for overall effect: Z =)						-10	-5 Favours	0 CBT Favo	5 urs pill plac	10 cebo		

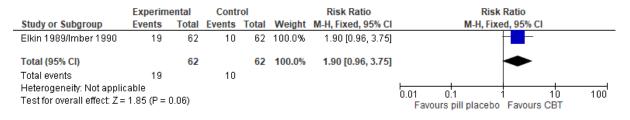
9

10 Figure 115: Depression symptomatology change score

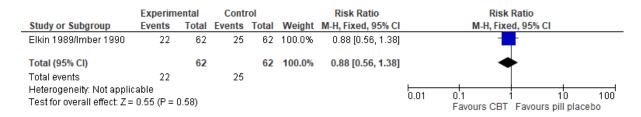


11

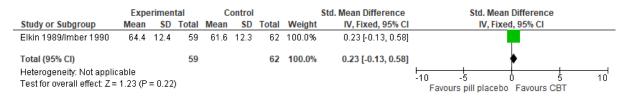
12 Figure 116: Remission (ITT)



1 Figure 117: Discontinuation (any reason)



3 Figure 118: Global functioning endpoint



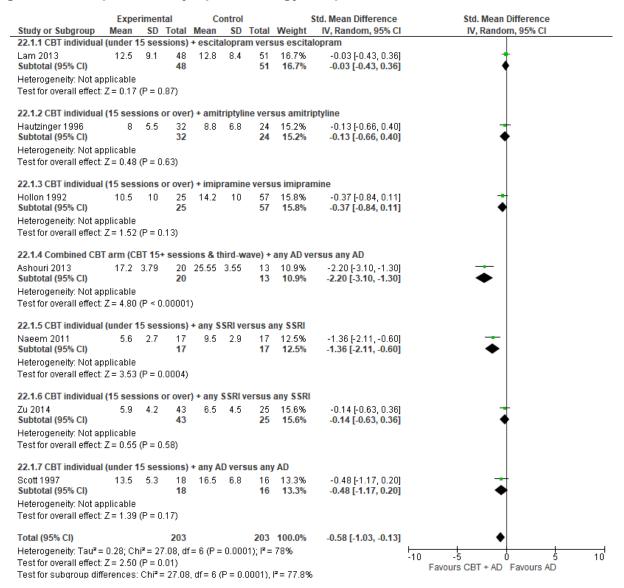
5 Figure 119: Interpersonal problems endpoint

	Expe	rimen	tal	Control				Std. Mean Difference		Std. Me	an Differ	ence		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, F	xed, 95%	CI		
Elkin 1989/Imber 1990	2.9	0.9	36	3.1	0.9	34	100.0%	-0.22 [-0.69, 0.25]						
Total (95% CI)			36			34	100.0%	-0.22 [-0.69, 0.25]			•			
Heterogeneity: Not applic Test for overall effect: Z =		= 0.36)						-10	-5 Favours C	0 BT Favo	urs pill	j place	10 bo

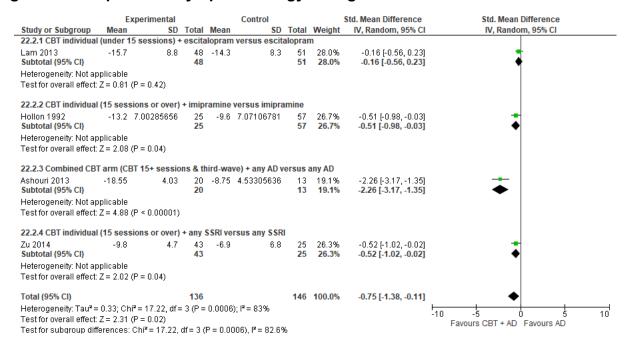
2

More severe: Cognitive and cognitive behavioural therapies individual + AD versus AD

3 Figure 120: Depression symptomatology endpoint

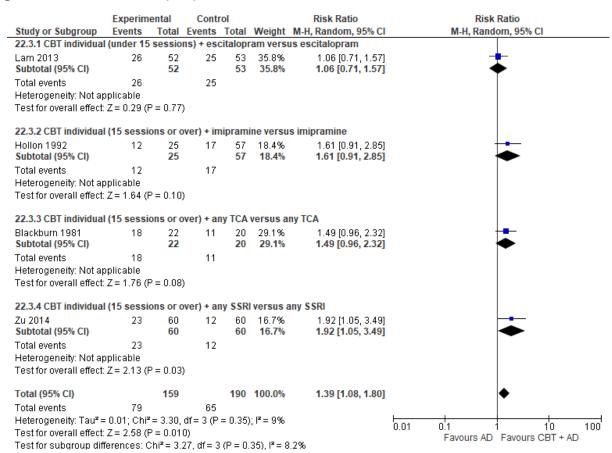


1 Figure 121: Depression symptomatology change score

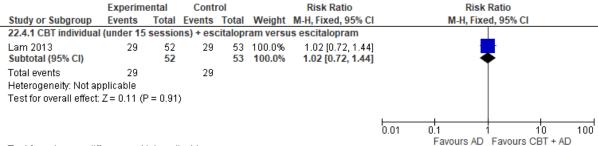


3 Figure 122: Remission (ITT)

2



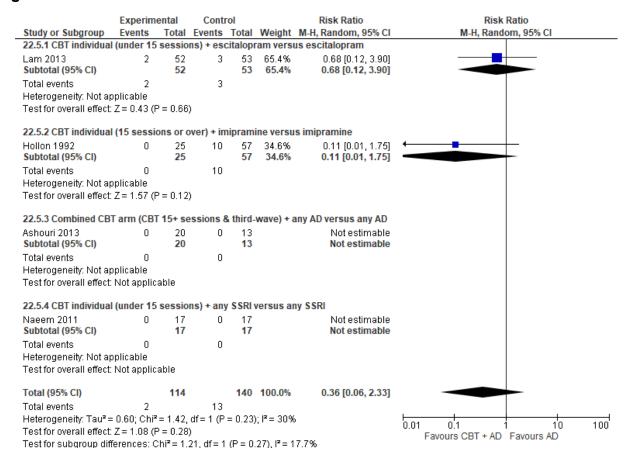
1 Figure 123: Response (ITT)



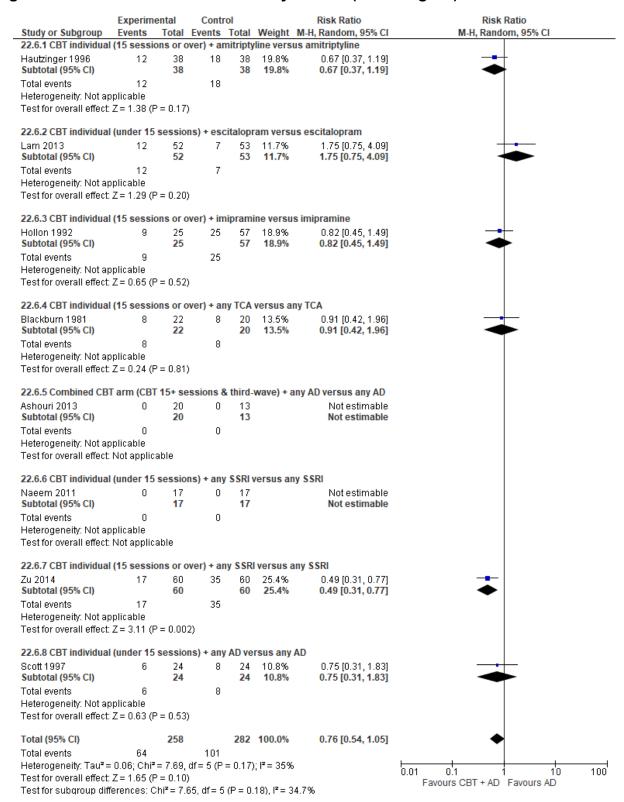
2 Test for subgroup differences: Not applicable

4

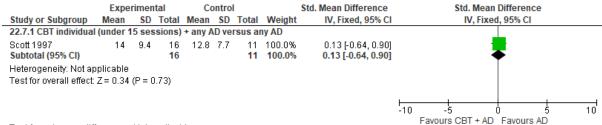
3 Figure 124: Discontinuation due to SE



1 Figure 125: Discontinuation due to any reason (including SE)

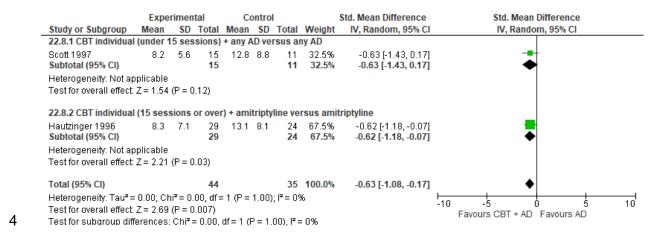


1 Figure 126: Depression symptomatology at 3-month follow-up

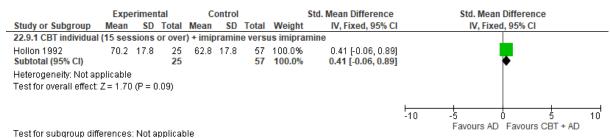


2 Test for subgroup differences: Not applicable

3 Figure 127: Depression symptomatology at 6-12 month follow-up

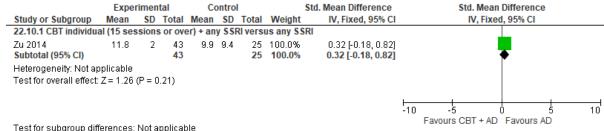


5 Figure 128: Global functioning endpoint



6 Test for subgroup differences: Not applicable

7 Figure 129: Functional impairment endpoint

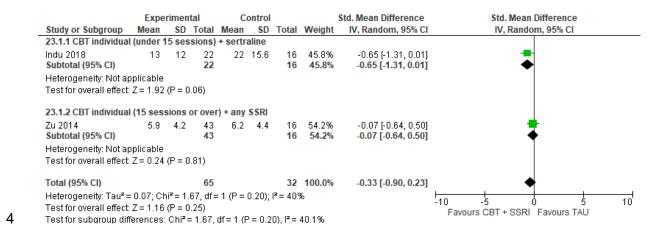


.....

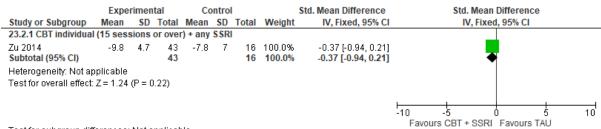
9

More severe: Cognitive and cognitive behavioural therapies individual + SSRI versus TAU

3 Figure 130: Depression symptomatology endpoint

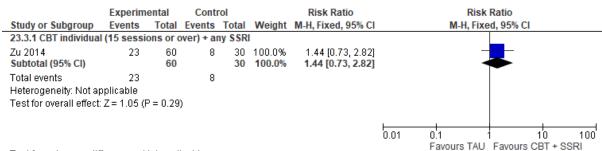


5 Figure 131: Depression symptomatology change score



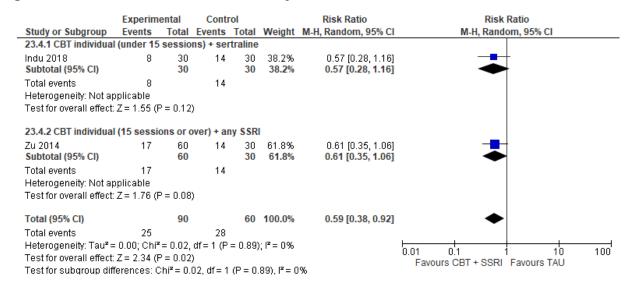
6 Test for subgroup differences: Not applicable

7 Figure 132: Remission (ITT)

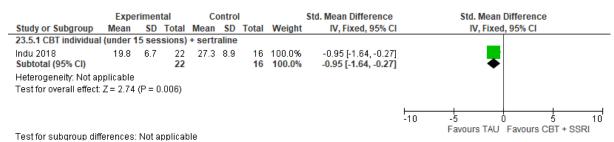


8 Test for subgroup differences: Not applicable

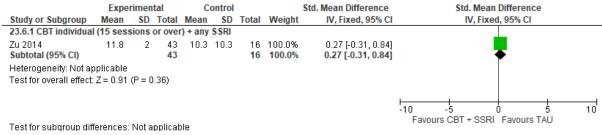
1 Figure 133: Discontinuation due to any reason



3 Figure 134: Quality of life endpoint



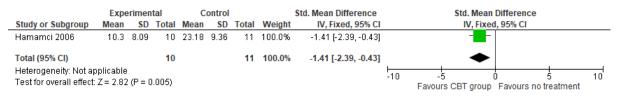
5 Figure 135: Functional impairment endpoint



6

8 More severe: CBT group (under 15 sessions) versus no treatment

10 Figure 136: Depression symptomatology endpoint



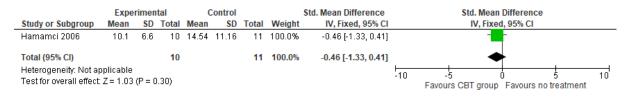
2

4

1 Figure 137: Depression symptomatology change score



3 Figure 138: Depression symptomatology at 6-month follow-up

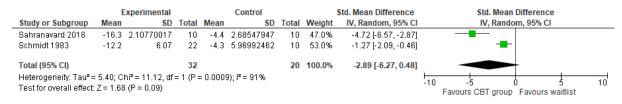


6 More severe: CBT group (under 15 sessions) versus waitlist

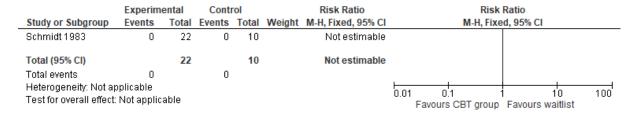
7 Figure 139: Depression symptomatology endpoint

	Expe	erimen	ıtal	C	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Sahranavard 2018	17.5	3.03	10	29.3	4.06	10	46.3%	-3.15 [-4.55, -1.76]	-
Schmidt 1983	12.75	8.76	22	21.7	9	10	53.7%	-0.99 [-1.78, -0.20]	-
Total (95% CI)			32			20	100.0%	-1.99 [-4.11, 0.13]	-
Heterogeneity: Tau² = Test for overall effect:				: 1 (P =	0.008)	; I² = 86		-10 -5 0 5 10 Favours CBT group Favours waitlist	

9 Figure 140: Depression symptomatology change score



11 Figure 141: Discontinuation due to any reason



2

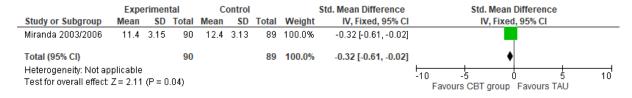
4 5

8

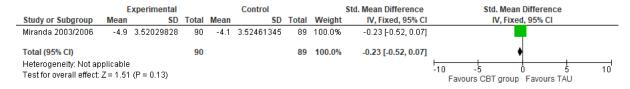
10

1 More severe: CBT group (under 15 sessions) versus TAU

2 Figure 142: Depression symptomatology endpoint



4 Figure 143: Depression symptomatology change score



6 Figure 144: Discontinuation due to any reason

3

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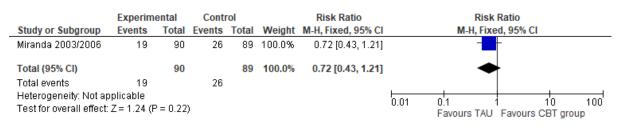
7

9 10

14

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Miranda 2003/2006	22	90	18	89	100.0%	1.21 [0.70, 2.09]	—
Total (95% CI)		90		89	100.0%	1.21 [0.70, 2.09]	*
Total events	22		18				
Heterogeneity: Not ap	plicable						0.01 0.1 1 10 100
Test for overall effect:	Z = 0.68 (F	P = 0.50)				Favours CBT group Favours TAU

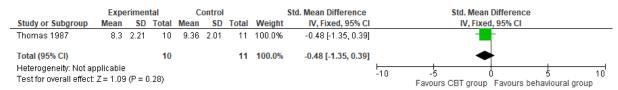
8 Figure 145: Remission at 9-month follow-up (ITT)



11 More severe: CBT group (under 15 sessions) versus

12 behavioural activation (BA) group

13 Figure 146: Depression symptomatology endpoint



1 Figure 147: Discontinuation du to any reason

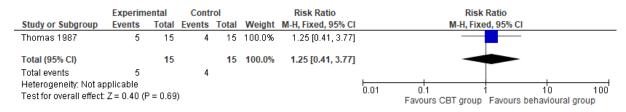
2

4 5

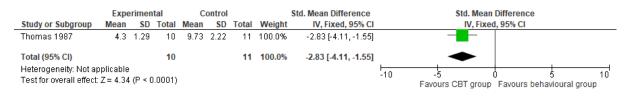
9

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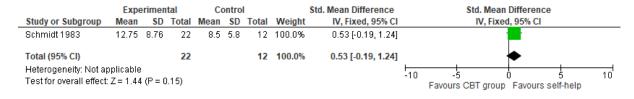


3 Figure 148: Depression symptomatology at 1-month follow-up

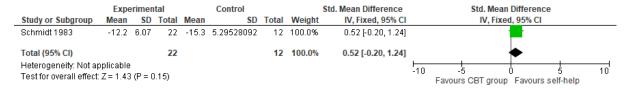


6 More severe: CBT group (under 15 sessions) versus7 cognitive bibliotherapy

8 Figure 149: Depression symptomatology endpoint



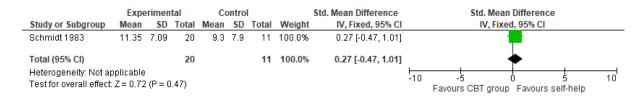
10 Figure 150: Depression symptomatology change score



12 Figure 151: Discontinuation due to any reason



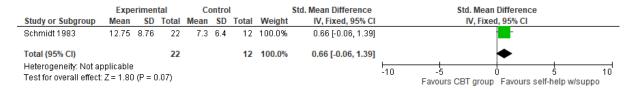
1 Figure 152: Depression symptomatology at 2-month follow-up



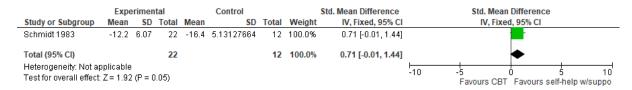
4 More severe: CBT group (under 15 sessions) versus

5 cognitive bibliotherapy with support

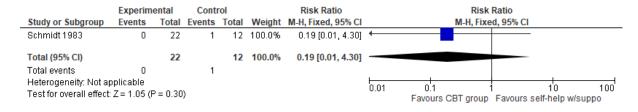
6 Figure 153: Depression symptomatology endpoint



8 Figure 154: Depression symptomatology change score



10 Figure 155: Discontinuation due to any reason



12 Figure 156: Depression symptomatology at 2-month follow-up

	Expe	rimen	tal	Co	ontro	I		Std. Mean Difference		Std. Mean Dit	fference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 9	95% CI		
Schmidt 1983	11.35	7.09	20	8.4	7.8	11	100.0%	0.39 [-0.35, 1.13]		-	ŀ		
Total (95% CI)			20			11	100.0%	0.39 [-0.35, 1.13]		•	▶ .		
Heterogeneity: Not ap Test for overall effect:			.30)						-10	-5 0 Favours CBT group F	5 avours self-h	elp w/suppo	10

13

9

11

1 More severe: CBT group (under 15 sessions) versus

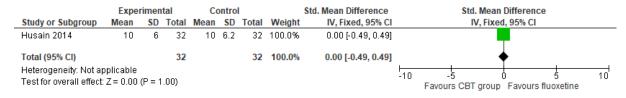
2 fluoxetine

4

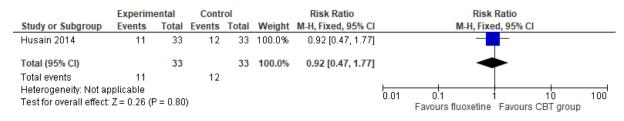
6

8

3 Figure 157: Depression symptomatology endpoint



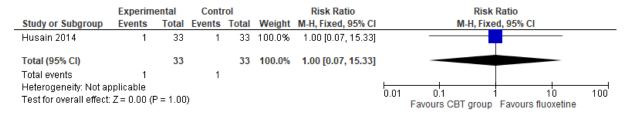
5 Figure 158: Remission (ITT)



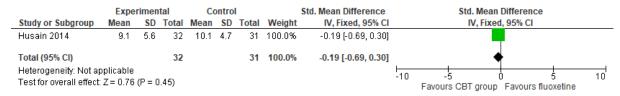
7 Figure 159: Response (ITT)

	Experime	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Husain 2014	18	33	19	33	100.0%	0.95 [0.62, 1.45]	+
Total (95% CI)		33		33	100.0%	0.95 [0.62, 1.45]	*
Total events	18		19				
Heterogeneity: Not ap	oplicable						0.01 0.1 1 10 100
Test for overall effect:	Z= 0.25 (F	P = 0.80)				Favours fluoxetine Favours CBT group

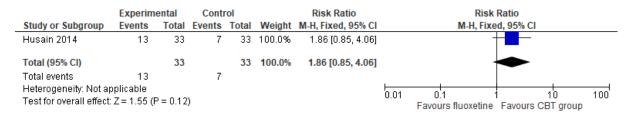
9 Figure 160: Discontinuation due to any reason



11 Figure 161: Depression symptomatology at 3-month follow-up



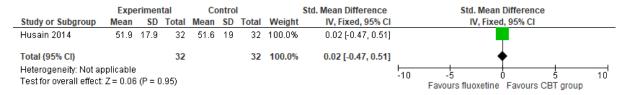
1 Figure 162: Remission at 3-month follow-up (ITT)



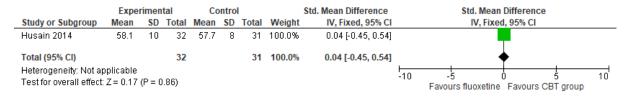
3 Figure 163: Response at 3-month follow-up (ITT)



5 Figure 164: Quality of life endpoint

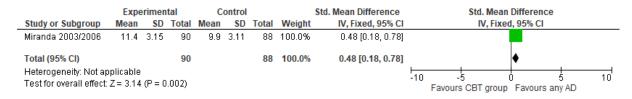


7 Figure 165: Quality of life at 3-month follow-up



10 More severe: CBT group (under 15 sessions) versus any AD

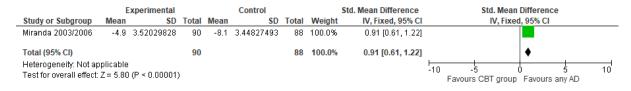
11 Figure 166: Depression symptomatology endpoint



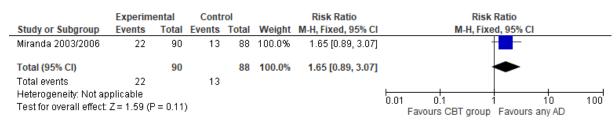
2

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1 Figure 167: Depression symptomatology change score



3 Figure 168: Discontinuation due to any reason



5 Figure 169: Remission at 9-month follow-up (ITT)



8 More severe: CBT group (under 15 sessions) + any AD9 versus any AD

10 Figure 170: Depression symptomatology endpoint

	Experimental			Control				Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Randoi			
Solati 2016	32.73	2.95	20	37.09	2.26	20	45.6%	-1.63 [-2.35, -0.90]	-			
Tong 2020	11.12	3.58	43	13.07	2.54	45	54.4%	-0.63 [-1.05, -0.20]	-			
Total (95% CI)			63			65	100.0%	-1.08 [-2.06, -0.10]	•			
Heterogeneity: Tau² = Test for overall effect:				-10 -5 C Favours CBT group + AD	5 Favours AD	10						

12 Figure 171: Depression symptomatology change score

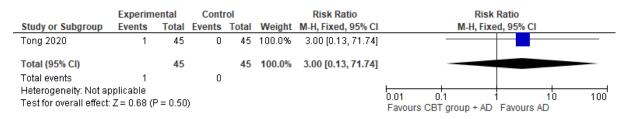
	E	xperimental			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD Total Mean			SD	Total	Weight IV, Random, 95% CI		IV, Random, 95% CI
Solati 2016	-8.72	2.53449206	20	-5.56	3.50025713	20	29.7%	-1.01 [-1.68, -0.35]	-#-
Tong 2020	-19.04	3.38221821	43	-16.66	3.60979224	45	70.3%	-0.67 [-1.10, -0.24]	<u> </u>
Total (95% CI)			63			65	100.0%	-0.77 [-1.14, -0.41]	◆
Heterogeneity: Tau² = Test for overall effect			-10 -5 0 5 10 Favours CBT group+any AD Favours any AD						

11

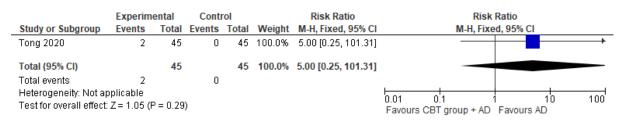
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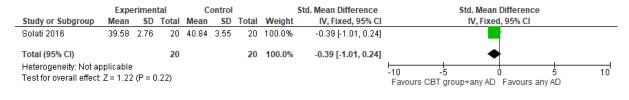
1 Figure 172: Discontinuation due to SE



3 Figure 173: Discontinuation due to any reason including SE



5 Figure 174: Depression symptomatology at 6-month follow-up



8 More severe: Problem solving individual versus waitlist

9 Figure 175: Depression symptomatology endpoint

	Experimental			Control				Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fix	red, 95% CI		
Kramer 2014	29.2	10.66	131	35.21	9.68	132	100.0%	-0.59 [-0.84, -0.34]				
Total (95% CI)			131			132	100.0%	-0.59 [-0.84, -0.34]		•		
Heterogeneity: Not applicable Test for overall effect: Z = 4.67 (P < 0.00001)									-10 -5 Favours problem solvir	0 Ig Favours wait	t 5 list	10

11 Figure 176: Depression symptomatology change score



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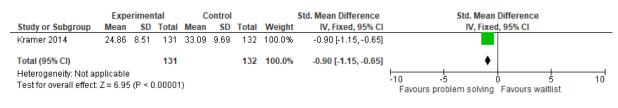
2

4

1 Figure 177: Discontinuation due to any reason



3 Figure 178: Depression symptomatology at 2-month follow-up

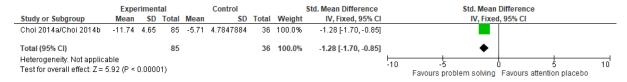


6 More severe: Problem solving individual versus attention7 placebo

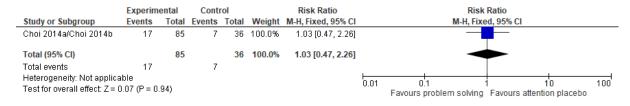
8 Figure 179: Depression symptomatology endpoint

	Expe	rimen	tal	Control				Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, F	ixed, 95% CI		
Choi 2014a/Choi 2014b	13.88	6.3	85	18.93	7.02	36	100.0%	-0.77 [-1.17, -0.37]					
Total (95% CI)			85			36	100.0%	-0.77 [-1.17, -0.37]			•		
Heterogeneity: Not applica Test for overall effect: Z = 3	0.000	2)						-10	-5 Favours problem solv	0 ing Favours a	ttention place	10 ebo	

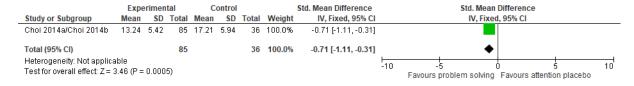
10 Figure 180: Depression symptomatology change score



12 Figure 181: Discontinuation due to any reason



14 Figure 182: Depression symptomatology at 3-month follow-up



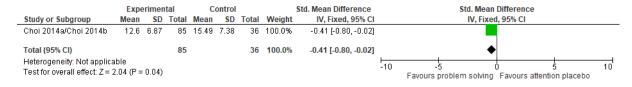
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1 Figure 183: Depression symptomatology at 6-month follow-up



3 Figure 184: Functional impairment endpoint

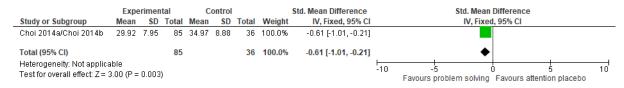
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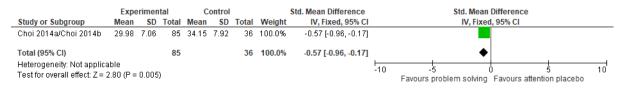
8 9

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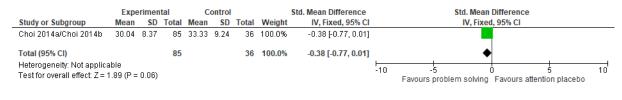
14



5 Figure 185: Functional impairment at 3-month follow-up

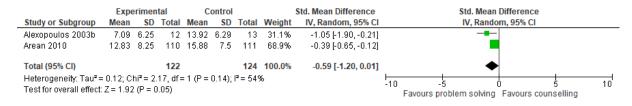


7 Figure 186: Functional impairment at 6-month follow-up

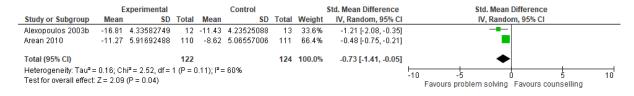


10 More severe: Problem solving individual versus counselling

11 Figure 187: Depression symptomatology at endpoint



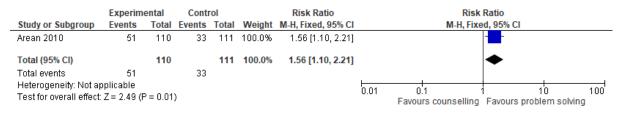
13 Figure 188: Depression symptomatology change score



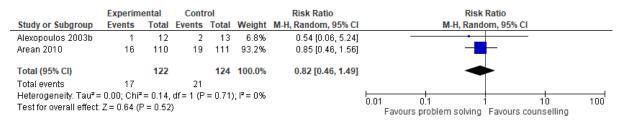
1 Figure 189: Remission (ITT)



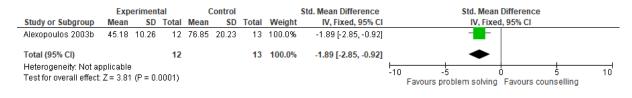
3 Figure 190: Response (ITT)



5 Figure 191: Discontinuation due to any reason



7 Figure 192: Functional impairment at endpoint

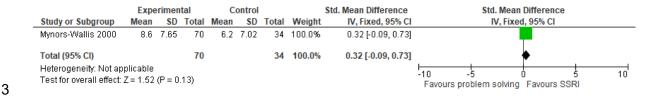


8 9

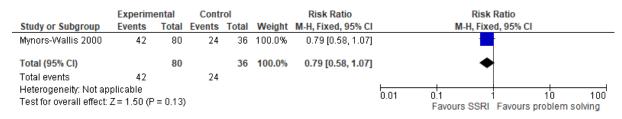
6

1 More severe: Problem solving individual versus any SSRI

2 Figure 193: Depression symptomatology endpoint



4 Figure 194: Remission (ITT)



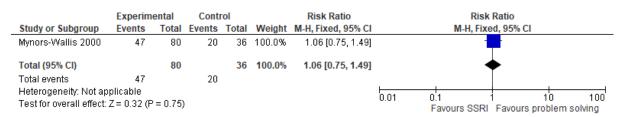
6 Figure 195: Discontinuation due to any reason

	Experim	Conti	rol		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Mynors-Wallis 2000	23	80	6	36	100.0%	1.73 [0.77, 3.87]	+
Total (95% CI)		80		36	100.0%	1.73 [0.77, 3.87]	•
Total events	23		6				
Heterogeneity: Not ap Test for overall effect:	•	= 0.19)					0.01 0.1 1 10 100 Favours problem solving Favours SSRI

8 Figure 196: Depression symptomatology at 9-month follow-up

	Experimental Control						Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Mynors-Wallis 2000	5.85	6.78	53	7.2	5.49	30	100.0%	-0.21 [-0.66, 0.24]	•
Total (95% CI)			53			30	100.0%	-0.21 [-0.66, 0.24]	*
Heterogeneity: Not ap Test for overall effect:			.36)						-10 -5 0 5 10 Favours problem solving Favours SSRI

10 Figure 197: Remission at 9-month follow-up (ITT)



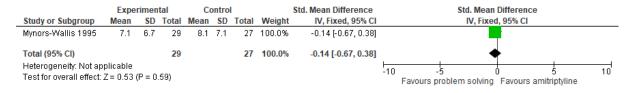
11 12

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1 More severe: Problem solving individual versus amitriptyline

2 Figure 198: Depression symptomatology endpoint



4 Figure 199: Depression symptomatology change score



6 Figure 200: Remission (ITT)

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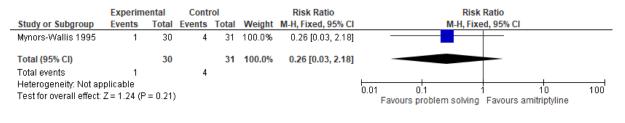
7

9 10

13

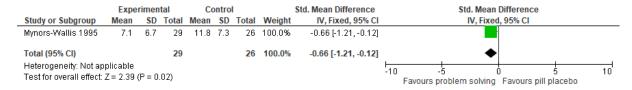
	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Mynors-Wallis 1995	18	30	16	31	100.0%	1.16 [0.74, 1.82]	-
Total (95% CI)		30		31	100.0%	1.16 [0.74, 1.82]	◆
Total events	18		16				
Heterogeneity: Not ap Test for overall effect:	•	9 = 0.51)	ı				0.01 0.1 10 100 Favours amitriptyline Favours problem solving

8 Figure 201: Discontinuation due to any reason

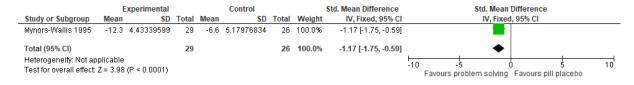


11 More severe: Problem solving individual versus pill placebo

12 Figure 202: Depression symptomatology endpoint



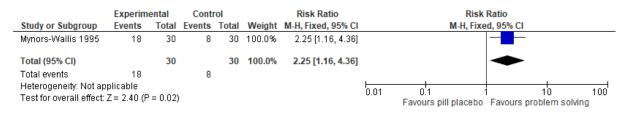
1 Figure 203: Depression symptomatology change score



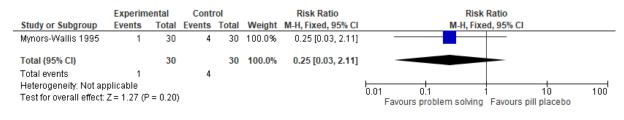
3 Figure 204: Remission (ITT)

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5 Figure 205: Discontinuation due to any reason



8 More severe: Problem solving individual + any SSRI versus9 any SSRI

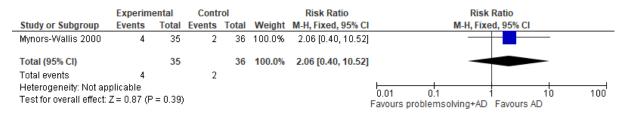
10 Figure 206: Depression symptomatology endpoint

	Experimental Control							Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed,	95% CI		
Mynors-Wallis 2000	7.5	6.41	31	6.2	7.02	34	100.0%	0.19 [-0.30, 0.68]					
Total (95% CI)			31			34	100.0%	0.19 [-0.30, 0.68]		•	•		
Heterogeneity: Not ap Test for overall effect: :	•		.44)						-10 -5 avours problems	0 solving+AD	Favours AD		10

12 Figure 207: Remission (ITT)

	Experimental Control					Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	ed, 95% CI		
Mynors-Wallis 2000	21	35	24	36	100.0%	0.90 [0.63, 1.28]		-	-		
Total (95% CI)		35		36	100.0%	0.90 [0.63, 1.28]		•	•		
Total events	21		24								
Heterogeneity: Not applicable Test for overall effect: Z = 0.58 (P = 0.56)							0.01	0.1 Favours AD	1 Favours pro	10 oblems	100 olving+AD

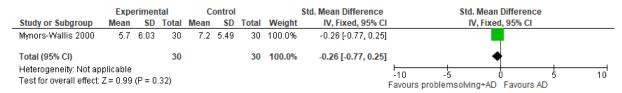
1 Figure 208: Discontinuation due to SE



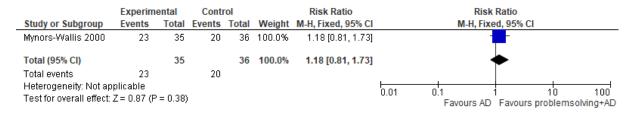
3 Figure 209: Discontinuation due any reason including SE



5 Figure 210: Depression symptomatology at 9-month follow-up

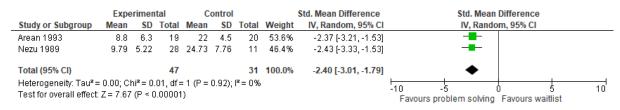


7 Figure 211: Remission at 9-month follow-up (ITT)



10 More severe: Problem solving group versus waitlist

11 Figure 212: Depression symptomatology endpoint



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1 Figure 213: Depression symptomatology change score

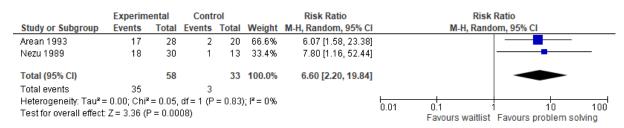


3 Figure 214: Remission (ITT)

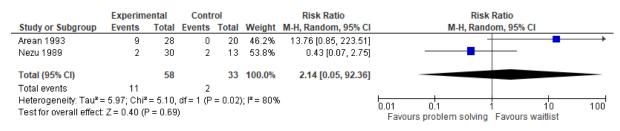
6 7

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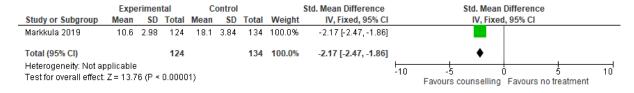


5 Figure 215: Discontinuation due to any reason



8 More severe: Counselling versus no treatment

9 Figure 216: Depression symptomatology endpoint



11 Figure 217: Depression symptomatology change score

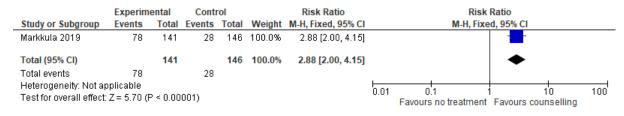
	E	xperimental			Control			Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed	I, 95% CI		
Markkula 2019	-14.4	6.95035251	124	-3.9	6.25856214	134	100.0%	-1.59 [-1.87, -1.31]					
Total (95% CI)			124			134	100.0%	-1.59 [-1.87, -1.31]		•			
Heterogeneity: Not ap Test for overall effect:	•		1)						-10	-5 Favours counselling	Favours no	5 treatment	10

1 Figure 218: Response (ITT)

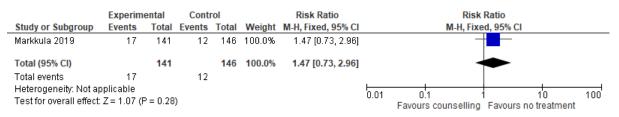
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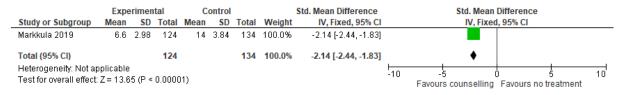
8



3 Figure 219: Discontinuation due to any reason



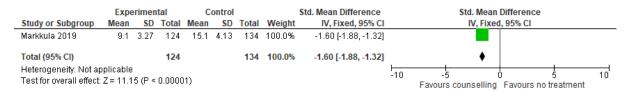
5 Figure 220: Depression symptomatology at 5-month follow-up



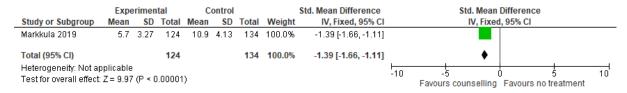
7 Figure 221: Response at 5-month follow-up (ITT)



9 Figure 222: Functional impairment endpoint



11 Figure 223: Functional impairment at 5-month follow-up

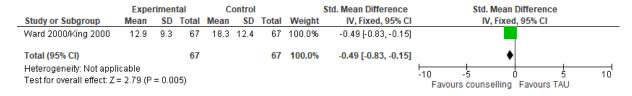


12

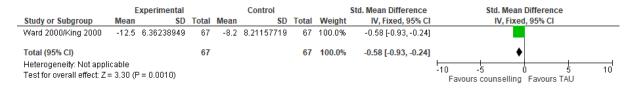
10

1 More severe: Counselling versus TAU

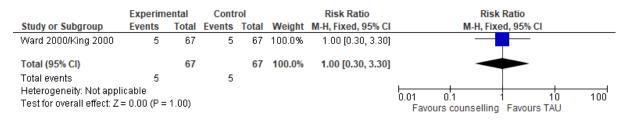
2 Figure 224: Depression symptomatology endpoint



4 Figure 225: Depression symptomatology change score



6 Figure 226: Discontinuation due to any reason



8 Figure 227: Depression symptomatology at 8-month follow-up

	Experimental			C	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Ward 2000/King 2000	11.8	9.6	67	12.1	10.3	67	100.0%	-0.03 [-0.37, 0.31]	<u> </u>
Total (95% CI)			67			67	100.0%	-0.03 [-0.37, 0.31]	•
Heterogeneity: Not appli Test for overall effect: Z		= 0.86	3)						-10 -5 0 5 10 Favours counselling Favours TAU

10 Figure 228: Interpersonal problems endpoint

	Experimental			C	ontrol			Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed	I, 95% CI		
Ward 2000/King 2000	2.2	0.51	67	2.31	0.65	67	100.0%	-0.19 [-0.53, 0.15]					
Total (95% CI)			67			67	100.0%	-0.19 [-0.53, 0.15]	L	. •			
Heterogeneity: Not appli Test for overall effect: Z =		o = 0.2	8)						-10 - Favours	5 counselling	Favours TA	5 JU	10

12 Figure 229: Interpersonal problems at 8-month follow-up

	Experimental			Control				Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed	, 95% CI		
Ward 2000/King 2000	2.13	0.54	67	2.05	0.61	67	100.0%	0.14 [-0.20, 0.48]					
Total (95% CI)			67			67	100.0%	0.14 [-0.20, 0.48]		•	•		
Heterogeneity: Not appli Test for overall effect: Z		9 = 0.4	2)						-10 - Favours	t 1 5 Counselling	Favours TA	U	10

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1 More severe: Counselling versus computerised-CBT (CCBT)

2 Figure 230: Depression symptomatology endpoint

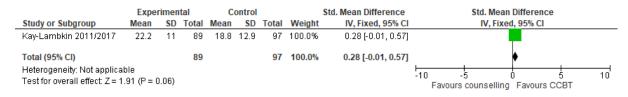
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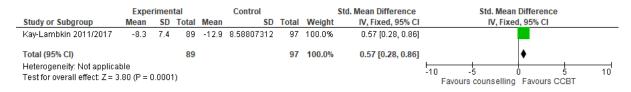
9

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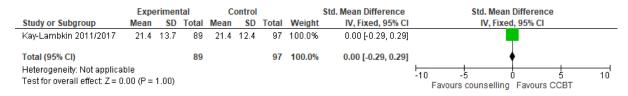
13



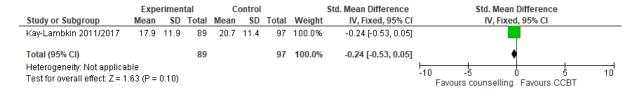
4 Figure 231: Depression symptomatology change score



6 Figure 232: Depression symptomatology at 3-month follow-up

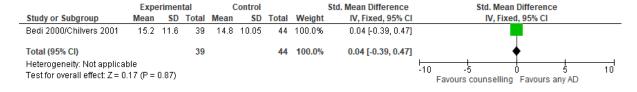


8 Figure 233: Depression symptomatology at 9-month follow-up



11 More severe: Counselling versus any AD

12 Figure 234: Depression symptomatology endpoint

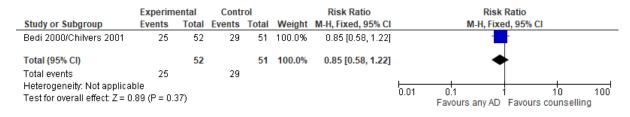


1 Figure 235: Remission (ITT)

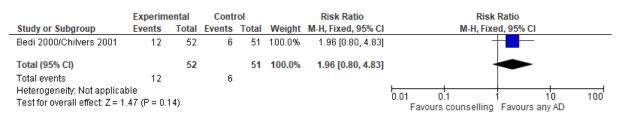
2

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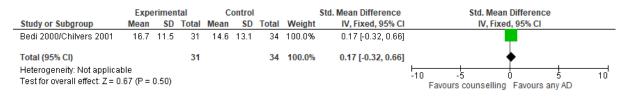
8 9



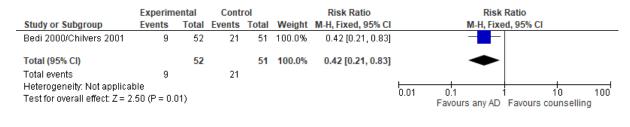
3 Figure 236: Discontinuation due to any reason



5 Figure 237: Depression symptomatology at 10-month follow-up



7 Figure 238: Remission at 10 months follow-up (ITT)

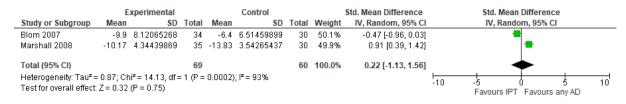


10 More severe: IPT versus any AD

11 Figure 239: Depression symptomatology endpoint



1 Figure 240: Depression symptomatology change score



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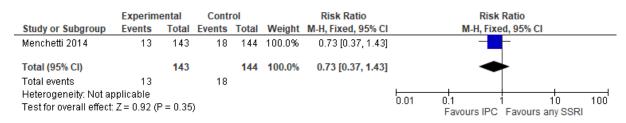
4 More severe: Interpersonal counselling individual versus any5 SSRI

6 Figure 241: Remission (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Menchetti 2014	84	143	65	144	100.0%	1.30 [1.04, 1.63]	
Total (95% CI)		143		144	100.0%	1.30 [1.04, 1.63]	◆
Total events	84		65				
Heterogeneity: Not ap Test for overall effect:		P = 0.02)				0.01 0.1 1 10 100
	,		•				Favours any SSRI Favours IPC

7

8 Figure 242: Discontinuation due to any reason



9 10

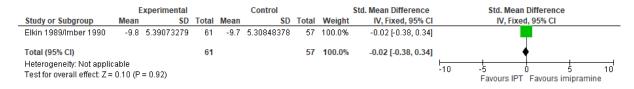
11 More severe: IPT versus imipramine

12 Figure 243: Depression symptomatology endpoint

	Experimental			Co	ontro	I	Std. Mean Difference			Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV	Fixed, 9	95% CI		
Elkin 1989/Imber 1990	9.8	7.9	61	9.8	7.8	57	100.0%	0.00 [-0.36, 0.36]						
Total (95% CI)			61			57	100.0%	0.00 [-0.36, 0.36]			•			
Heterogeneity: Not applic Test for overall effect: Z=		= 1.00)						-10	-5 Favour	s IPT F	avours im	i iprami	10 ne

13

14 Figure 244: Depression symptomatology change score

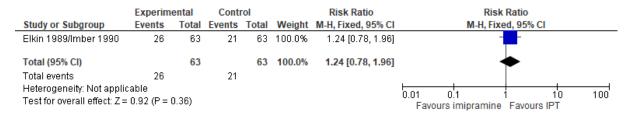


1 Figure 245: Remission (ITT)

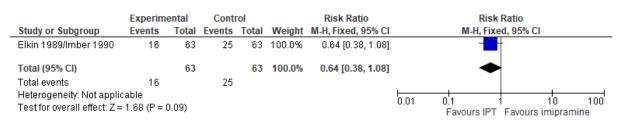
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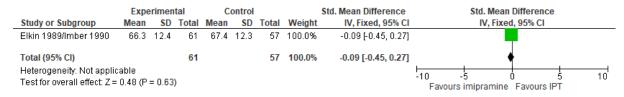
8 9



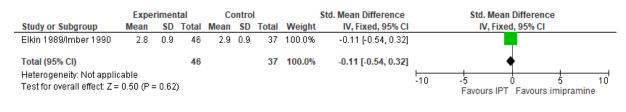
3 Figure 246: Discontinuation due to any reason



5 Figure 247: Global functioning endpoint

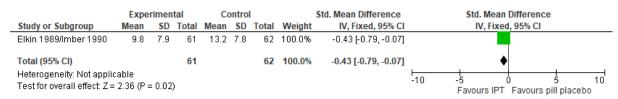


7 Figure 248: Interpersonal problems endpoint



10 More severe: IPT versus pill placebo

11 Figure 249: Depression symptomatology endpoint



1 Figure 250: Depression symptomatology change score



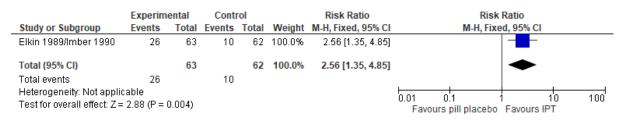
3 Figure 251: Remission (ITT)

2

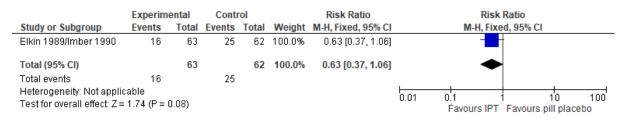
4

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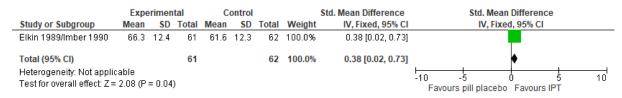
8



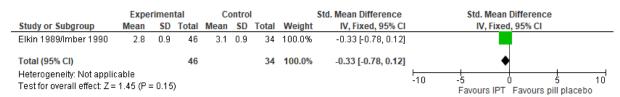
5 Figure 252: Discontinuation due to any reason



7 Figure 253: Global functioning endpoint

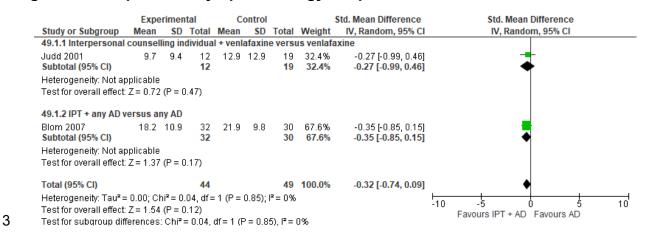


9 Figure 254: Interpersonal problems endpoint

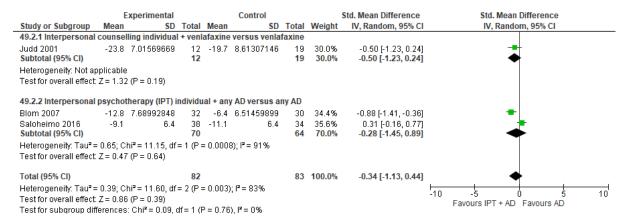


1 More severe: IPT + AD versus AD

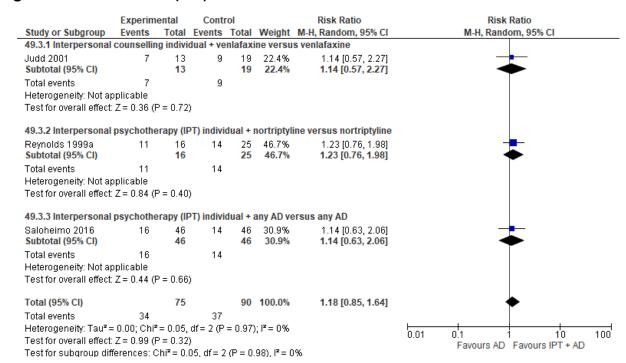
2 Figure 255: Depression symptomatology endpoint



4 Figure 256: Depression symptomatology change score

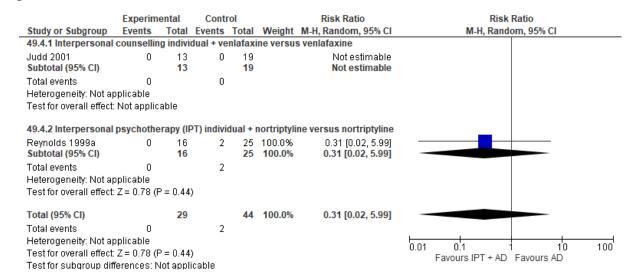


1 Figure 257: Remission (ITT)

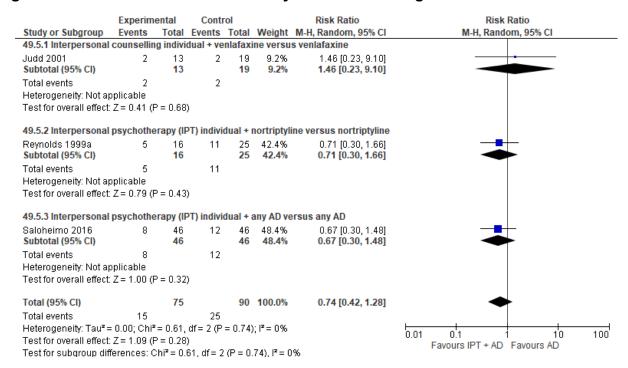


3 Figure 258: Discontinuation due to SE

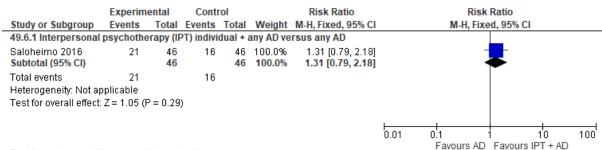
2



1 Figure 259: Discontinuation due to any reason including SE



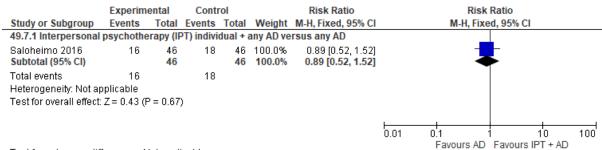
3 Figure 260: Remission at 3-month follow-up (ITT)



4 Test for subgroup differences: Not applicable

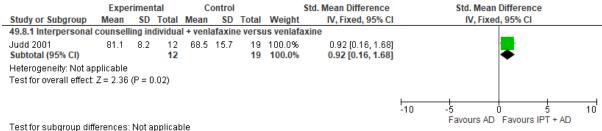
2

5 Figure 261: Remission at 9-month follow-up (ITT)<Insert graphic title here>



6 Test for subgroup differences: Not applicable

1 Figure 262: Global functioning endpoint



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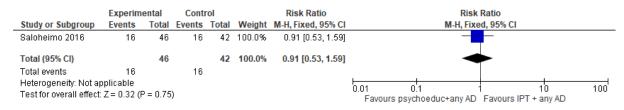
7

4 More severe: IPT + any AD versus psychoeducation group + any AD 5

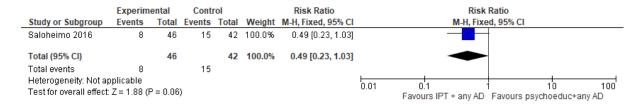
6 Figure 263: Depression symptomatology change score

	Expe	rimen				ı		Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fi	xed, 95% C	CI	
Saloheimo 2016	-9.1	6.4	38	-8.3	6.3	27	100.0%	-0.12 [-0.62, 0.37]					
Total (95% CI)			38			27	100.0%	-0.12 [-0.62, 0.37]			•		
Heterogeneity: Not ap Test for overall effect:		(P = 0).62)						-10	-5 Favours IPT + any	0 AD Favou	5 rs psychoeduc+a	10 any AD

8 Figure 264: Remission (ITT)

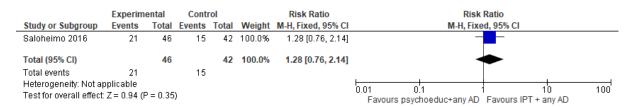


10 Figure 265: Discontinuation due to any reason

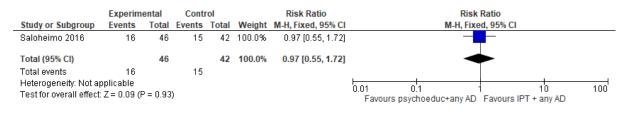


11

12 Figure 266: Remission at 3-month follow-up (ITT)



1 Figure 267: Remission at 9-month follow-up (ITT)

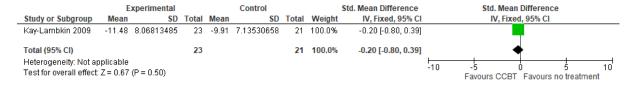


4 More severe: Computerised-CBT (CCBT) versus no treatment

5 Figure 268: Depression symptomatology endpoint

	Exp	eriment	tal	(Control			Std. Mean Difference					
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI			
Farrer 2011/Farrer 2012	23.04	13.1	45	35.1	13.9	27	59.2%	-0.89 [-1.39, -0.39]			-		
Kay-Lambkin 2009	17.09	12.14	23	22.95	10.46	21	40.8%	-0.51 [-1.11, 0.10]			-		
Total (95% CI)			68			48	100.0%	-0.73 [-1.12, -0.35]			•		
Heterogeneity: Tau² = 0.00 Test for overall effect: Z = 3	,	= 0.34);	I ² = 0%				-10	-5 Favours C	0 CBT Favou	5 irs no treatr	10 nent		

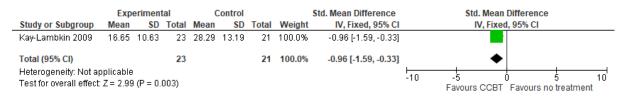
7 Figure 269: Depression symptomatology change score



9 Figure 270: Discontinuation due to any reason



11 Figure 271: Depression symptomatology at 3-month follow-up

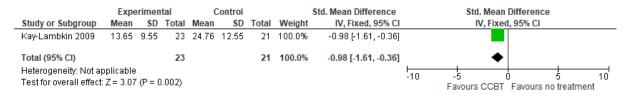


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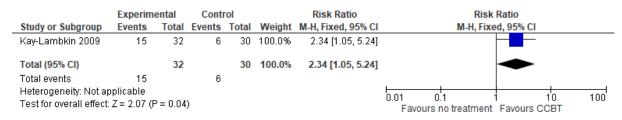
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1 Figure 272: Depression symptomatology at 9-month follow-up



3 Figure 273: Remission at 9-month follow-up (ITT)



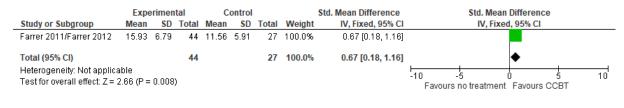
5 Figure 274: Quality of life endpoint

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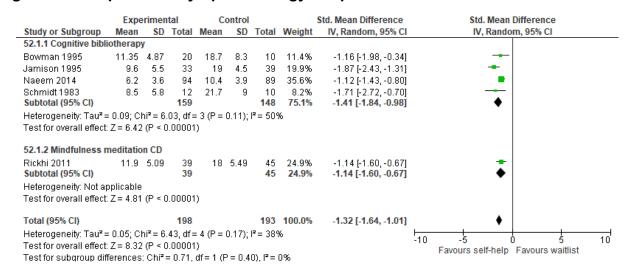
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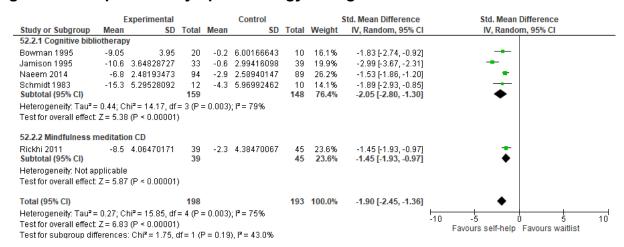


8 More severe: Self-help versus waitlist

9 Figure 275: Depression symptomatology endpoint

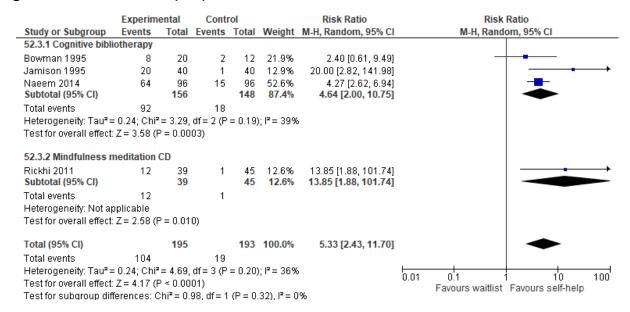


1 Figure 276: Depression symptomatology change score

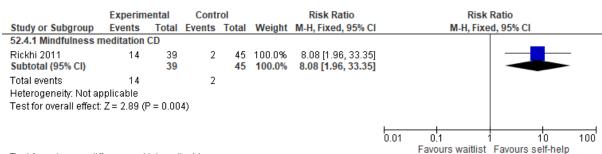


3 Figure 277: Remission (ITT)

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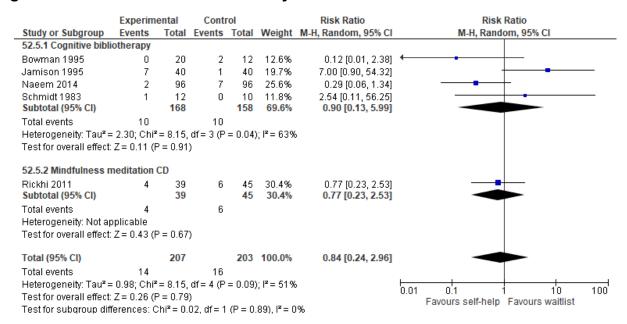


5 Figure 278: Response (ITT)

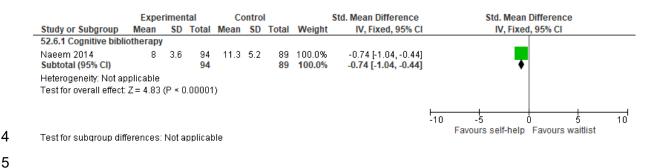


6 Test for subgroup differences: Not applicable

1 Figure 279: Discontinuation due to any reason

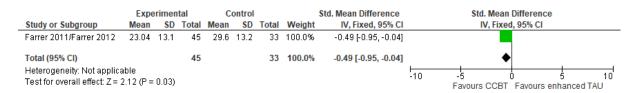


3 Figure 280: Functional impairment endpoint

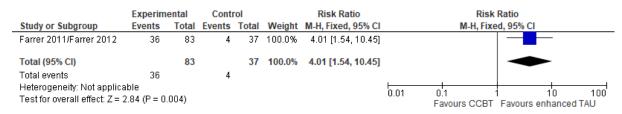


6 More severe: Computerised-CBT (CCBT) versus enhanced7 TAU

8 Figure 281: Depression symptomatology endpoint

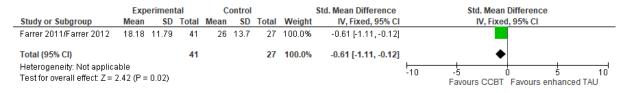


10 Figure 282: Discontinuation due to any reason



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1 Figure 283: Depression symptomatology at 6-month follow-up



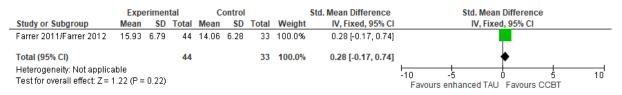
3 Figure 284: Quality of life endpoint

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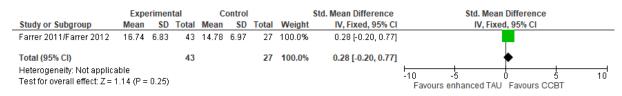
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5 Figure 285: Quality of life at 6-month follow-up

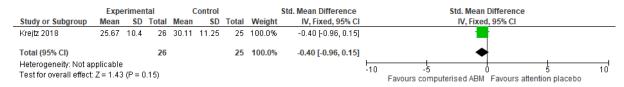


7 Figure 286: Quality of life at 12-month follow-up

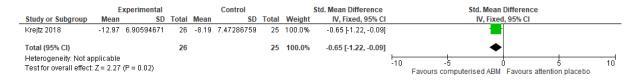
	Experimental				ontrol			Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI				
Farrer 2011/Farrer 2012	17.08	5.92	35	15.77	7.67	22	100.0%	0.19 [-0.34, 0.73]	•				
Total (95% CI)			35			22	100.0%	0.19 [-0.34, 0.73]	•				
Heterogeneity: Not applica									-10 -5 0 5 10				
Test for overall effect: $Z = 0$	0.71 (P =	0.48)							Favours enhanced TAU Favours CCBT				

More severe: Computerised attentional bias modificationversus attention placebo

12 Figure 287: Depression symptomatology endpoint



14 Figure 288: Depression symptomatology change score

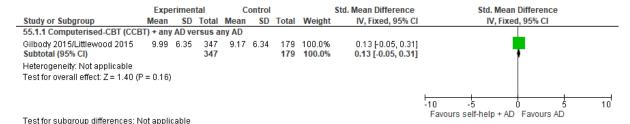


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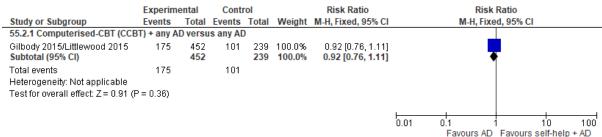
1 More severe: Self-help + AD versus AD

2 Figure 289: Depression symptomatology endpoint



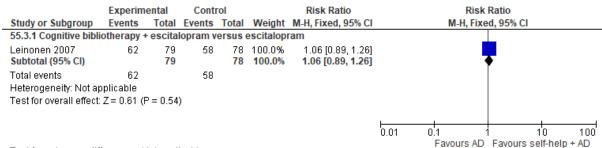
4 Figure 290: Remission (ITT)

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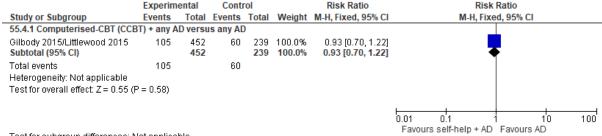
5 Test for subgroup differences: Not applicable

6 Figure 291: Response (ITT)



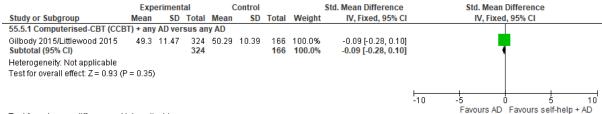
7 Test for subgroup differences: Not applicable

8 Figure 292: Discontinuation due to any reason



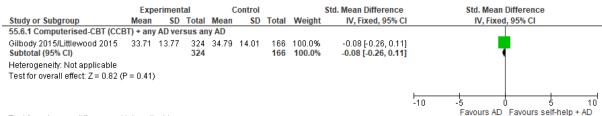
9 Test for subgroup differences: Not applicable

1 Figure 293: Quality of life physical health component endpoint



2 Test for subgroup differences: Not applicable

3 Figure 294: Quality of life mental health component endpoint

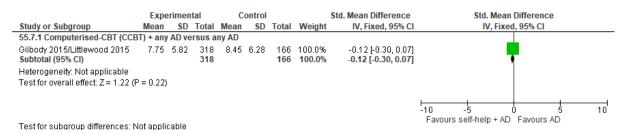


4 Test for subgroup differences: Not applicable

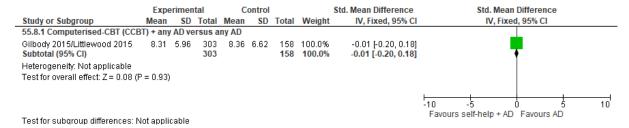
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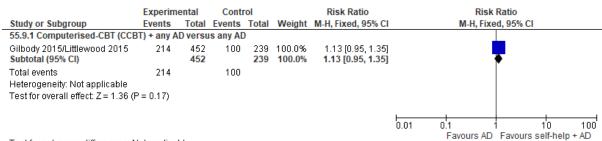
5 Figure 295: Depression symptomatology at 8-month follow-up



7 Figure 296: Depression symptomatology at 20-month follow-up

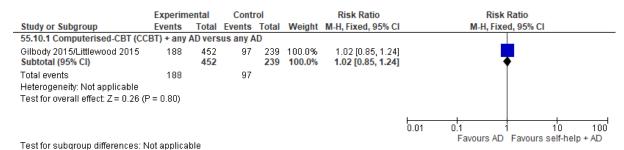


9 Figure 297: Remission at 8-month follow-up (ITT)

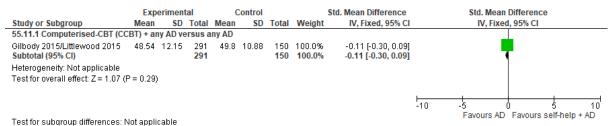


10 Test for subgroup differences: Not applicable

1 Figure 298: Remission at 20-month follow-up (ITT)



3 Figure 299: Quality of life physical health component at 8-month follow-up



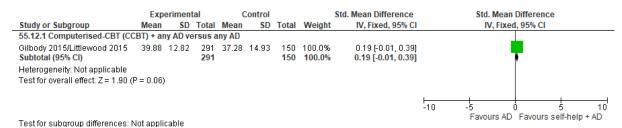
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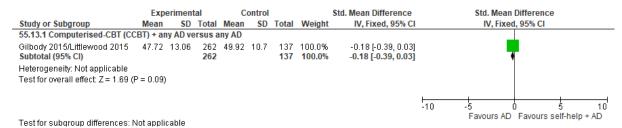
6

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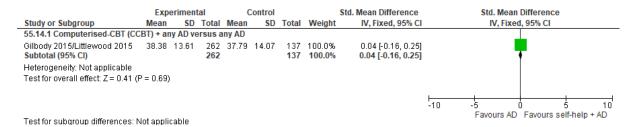
5 Figure 300: Quality of life mental health component at 8-month follow-up



7 Figure 301: Quality of life physical health component at 20-month follow-up

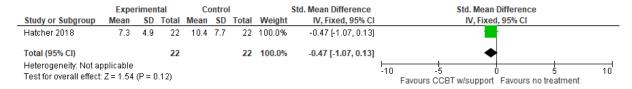


9 Figure 302: Quality of life mental health component at 20-month follow-up

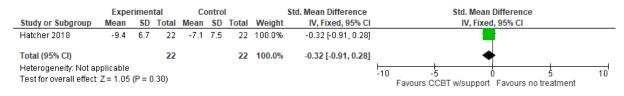


1 More severe: Computerised-CBT (CCBT) with support versus2 no treatment

3 Figure 303: Depression symptomatology endpoint



5 Figure 304: Depression symptomatology change score



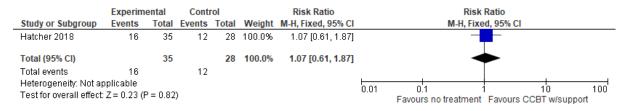
7 Figure 305: Remission (ITT)

6

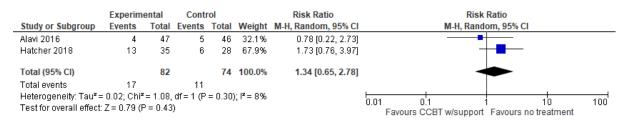
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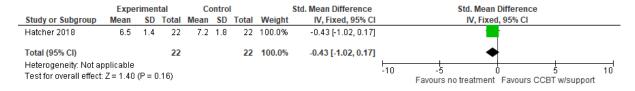
12 13



9 Figure 306: Discontinuation due to any reason

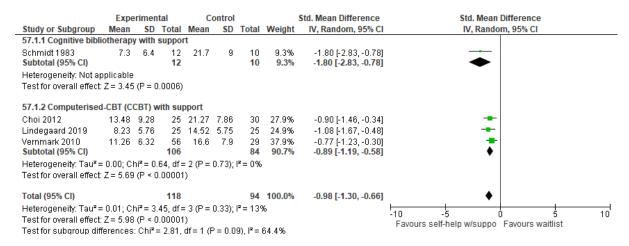


11 Figure 307: Quality of life endpoint

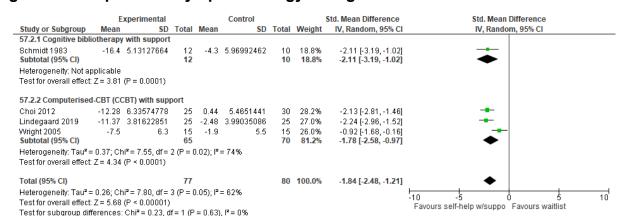


1 More severe: Self-help with support versus waitlist

2 Figure 308: Depression symptomatology endpoint



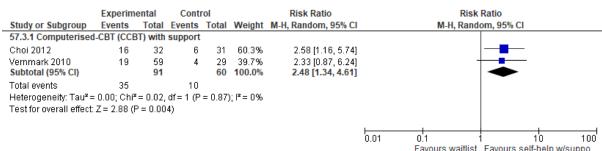
4 Figure 309: Depression symptomatology change score



6 Figure 310: Remission (ITT)

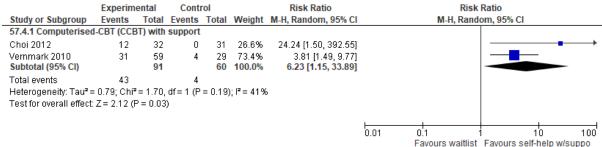
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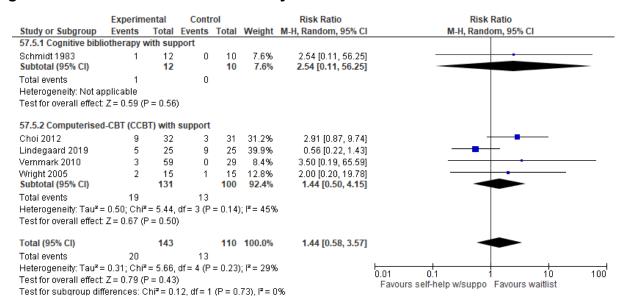
7 Test for subgroup differences: Not applicable

1 Figure 311: Response (ITT)



2 Test for subgroup differences: Not applicable

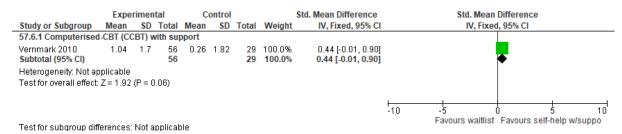
3 Figure 312: Discontinuation due to any reason



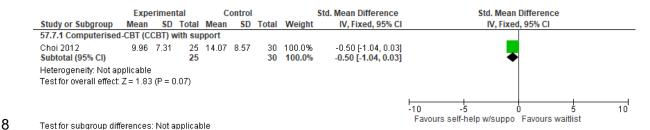
5 Figure 313: Quality of life endpoint

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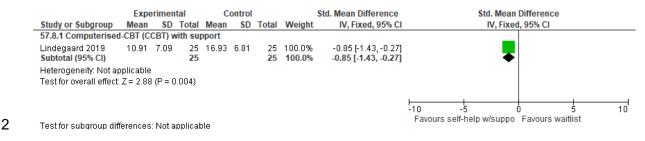
7 Figure 314: Functional impairment endpoint



1 Figure 315: Sleeping difficulties endpoint

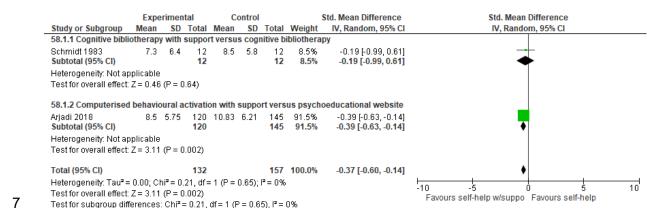
3

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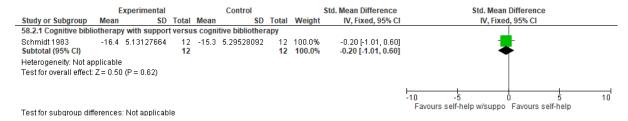


4 More severe: Self-help with support versus self-help (without 5 support)

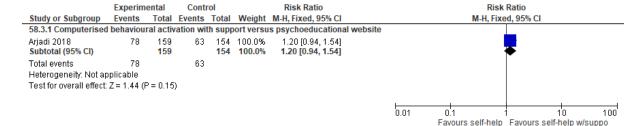
6 Figure 316: Depression symptomatology endpoint



8 Figure 317: Depression symptomatology change score

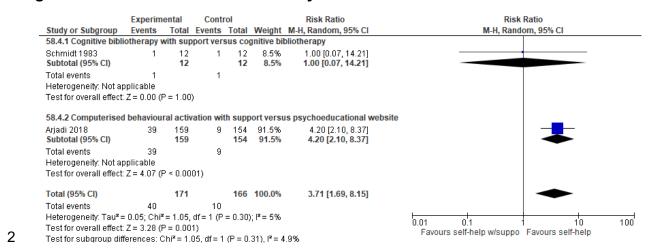


10 Figure 318: Remission (ITT)

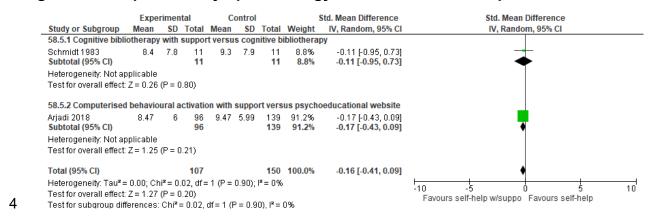


11 Test for subgroup differences: Not applicable

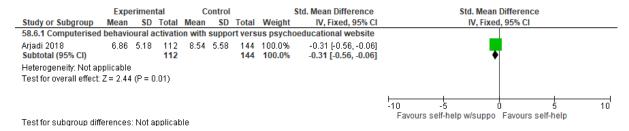
1 Figure 319: Discontinuation due to any reason



3 Figure 320: Depression symptomatology at 2-3 month follow-up

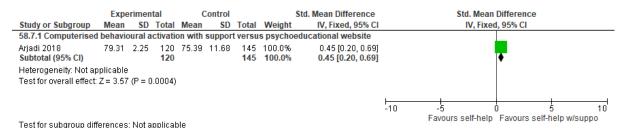


5 Figure 321: Depression symptomatology at 6-month follow-up

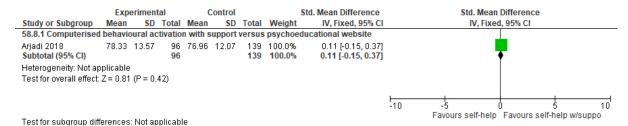


7 Figure 322: Quality of life endpoint

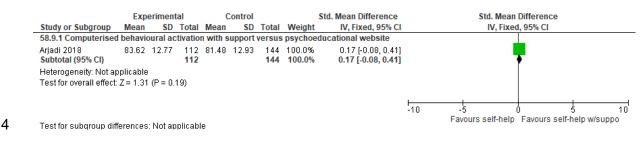
6



1 Figure 323: Quality of life at 3-month follow-up



3 Figure 324: Quality of life at 6-month follow-up

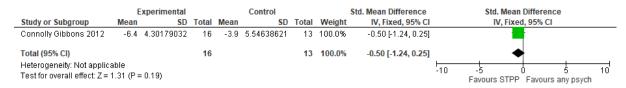


6 More severe: Short-term psychodynamic psychotherapies7 individual versus any psychotherapy

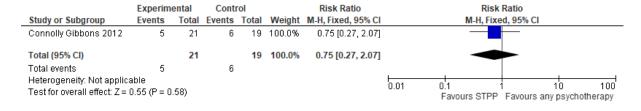
8 Figure 325: Depression symptomatology endpoint

	Expe	rimen	ental Control					Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI			
Connolly Gibbons 2012	16.6	6.5	16	15.8	7.62	13	100.0%	0.11 [-0.62, 0.84]		+	-		
Total (95% CI)			16			13	100.0%	0.11 [-0.62, 0.84]		•	•		
Heterogeneity: Not applica Test for overall effect: Z = 0		0.77)							-10	-5 Favours STPP	0 Favours any	1 5 psycho	10 therapy

10 Figure 326: Depression symptomatology change score



12 Figure 327: Discontinuation due to any reason



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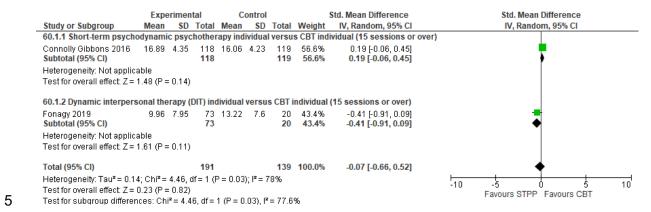
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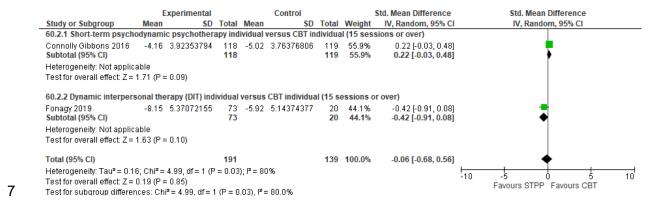
1 More severe: Short-term psychodynamic psychotherapy

- 2 individual versus cognitive and cognitive behavioural
- 3 therapies individual

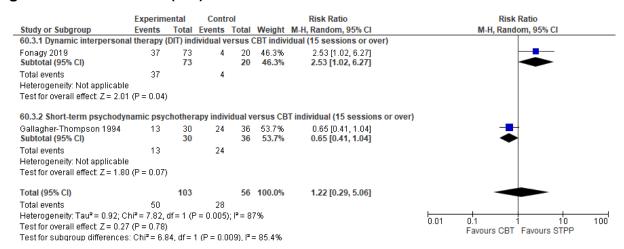
4 Figure 328: Depression symptomatology endpoint



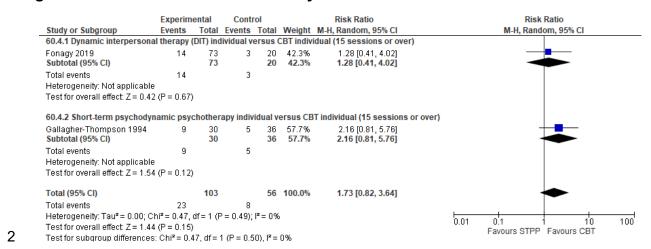
6 Figure 329: Depression symptomatology change score



8 Figure 330: Remission (ITT)



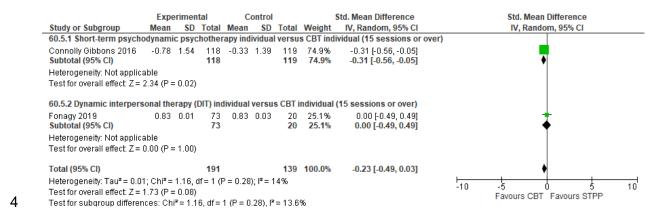
1 Figure 331: Discontinuation due to any reason



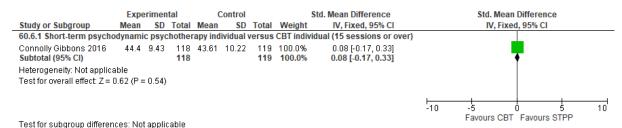
3 Figure 332: Quality of life endpoint

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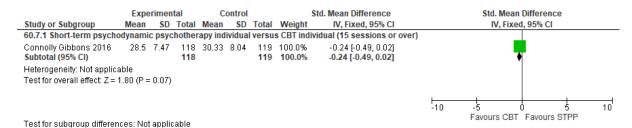
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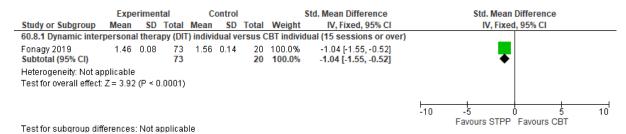
5 Figure 333: Quality of life physical health component endpoint



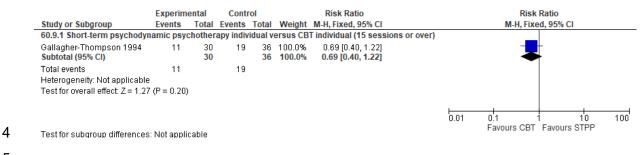
7 Figure 334: Quality of life mental health component endpoint



1 Figure 335: Interpersonal problems endpoint



3 Figure 336: Remission at 3-month follow-up (ITT)



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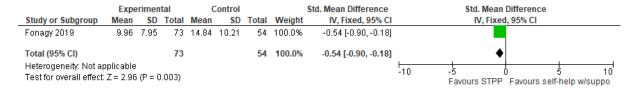
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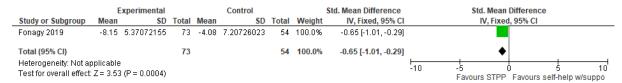
2

6 More severe: Dynamic interpersonal therapy (DIT) individual versus cognitive bibliotherapy with support

8 Figure 337: Depression symptomatology endpoint



10 Figure 338: Depression symptomatology change score



12 Figure 339: Remission (ITT)



1 Figure 340: Discontinuation due to any reason

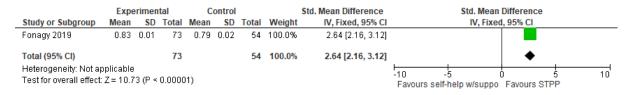


3 Figure 341: Quality of life endpoint

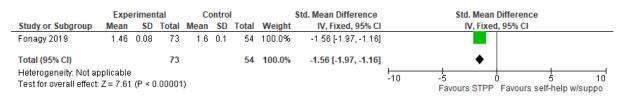
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5 Figure 342: Interpersonal problems endpoint



8 More severe: Short-term psychodynamic psychotherapies individual versus fluoxetine

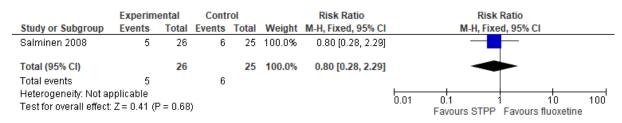
10 Figure 343: Depression symptomatology change score

	Experimental				ontro	l		Std. Mean Difference		Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI				
Salminen 2008	-11	6.44	26	-11.2	4.6	25	100.0%	0.04 [-0.51, 0.58]						
Total (95% CI)			26			25	100.0%	0.04 [-0.51, 0.58]			•			
Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90)									-10	-5 Favours S	0 TPP Favoι	5 Irs fluoxeti	10 ine	

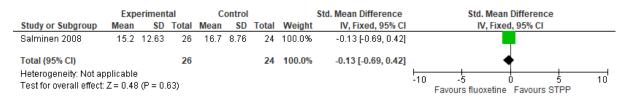
12 Figure 344: Remission (ITT)

	Experimental		Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Salminen 2008	12	26	12	25	100.0%	0.96 [0.54, 1.72]	—
Total (95% CI)		26		25	100.0%	0.96 [0.54, 1.72]	•
Total events	12		12				
Heterogeneity: Not ap	plicable						0.01 0.1 1 10 100
Test for overall effect:	Z = 0.13 (F	P = 0.89)				Favours fluoxetine Favours STPP

1 Figure 345: Discontinuation due to any reason



3 Figure 346: Global functioning change score



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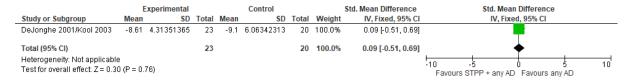
6 More severe: Short-term psychodynamic psychotherapy 7 individual + any AD versus any AD

8 Figure 347: Depression symptomatology endpoint

	Experimental Control						Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	I IV, Fixed, 95% CI
DeJonghe 2001/Kool 2003	11.09	6.52	23	12.1	9.01	20	100.0%	-0.13 [-0.73, 0.47]	1
Total (95% CI)			23			20	100.0%	-0.13 [-0.73, 0.47]	1 ♦
Heterogeneity: Not applicable Test for overall effect: Z = 0.42		68)							-10 -5 0 5 10 Favours STPP + any AD Favours any AD

9

10 Figure 348: Depression symptomatology change score



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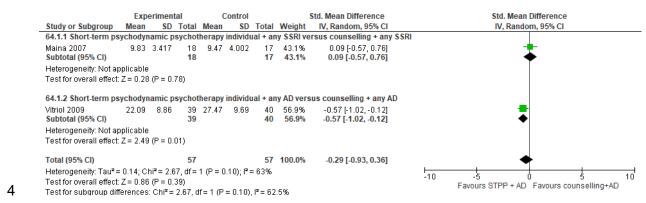
12 Figure 349: Quality of life endpoint

	Experimental			al Control				Std. Mean Difference		Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV,	Fixed, 95% C	1		
DeJonghe 2001/Kool 2003	26.83	6.1	23	23.25	9.37	20	100.0%	0.45 [-0.16, 1.06]						
Total (95% CI)			23			20	100.0%	0.45 [-0.16, 1.06]			•			
Heterogeneity: Not applicable Test for overall effect: Z = 1.40		5)							-10	-5 Favours an	0 NV AD Favour	5 rs STPP	10 + anv AD	

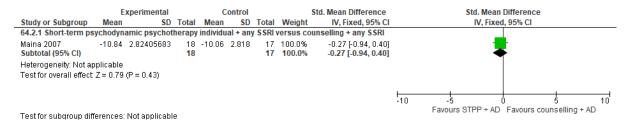
13

More severe: Short-term psychodynamic psychotherapy individual + AD versus counselling + AD

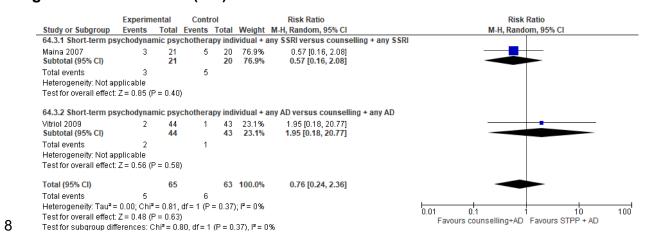
3 Figure 350: Depression symptomatology endpoint



5 Figure 351: Depression symptomatology change score

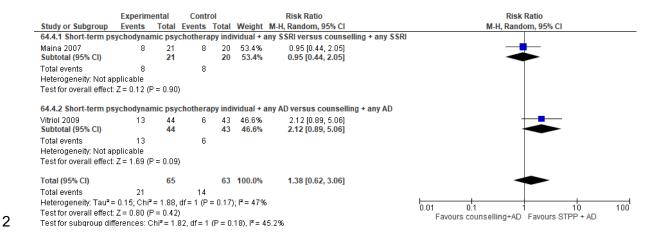


7 Figure 352: Remission (ITT)

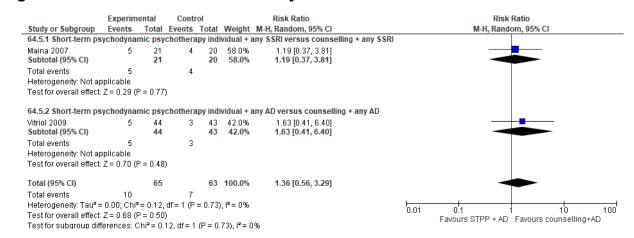


1 Figure 353: Response (ITT)

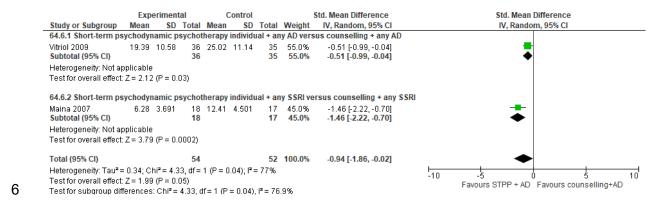
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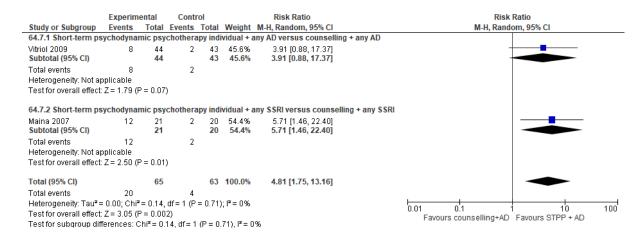
3 Figure 354: Discontinuation due to any reason



5 Figure 355: Depression symptomatology at 3-6 month follow-up



1 Figure 356: Remission at 3-6 month follow-up (ITT)

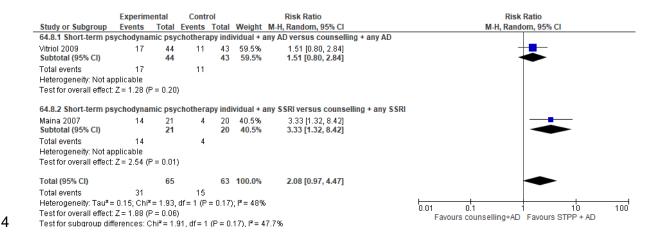


3 Figure 357: Response at 3-6 month follow-up (ITT)

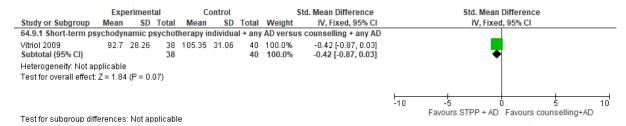
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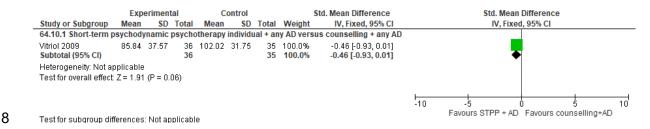
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5 Figure 358: Functional impairment endpoint



7 Figure 359: Functional impairment at 3-month follow-up

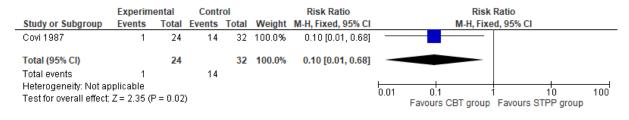


1 More severe: Short-term psychodynamic psychotherapy

2 group versus cognitive and cognitive behavioural therapies

3 group

4 Figure 360: Remission (ITT)



6

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7 More severe: Long-term psychodynamic psychotherapy

8 individual versus fluoxetine

9 Figure 361: Depression symptomatology endpoint

	Expe	rimen	tal	C	ontrol			Std. Mean Difference		Std. Mean	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% CI		
Bastos 2015	5.28	3.59	73	14.16	2.54	67	100.0%	-2.82 [-3.29, -2.35]					
Total (95% CI)			73			67	100.0%	-2.82 [-3.29, -2.35]		•			
Heterogeneity: Not ap Test for overall effect:	•		0.0000	01)					-10	-5 Favours LTPP	0 5 Favours fluc	5 10 oxetine	ď

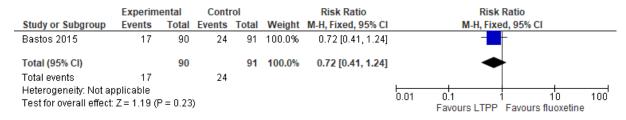


11 Figure 362: Remission (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Bastos 2015	67	90	20	91	100.0%	3.39 [2.26, 5.08]	-
Total (95% CI)		90		91	100.0%	3.39 [2.26, 5.08]	•
Total events	67		20				
Heterogeneity: Not as	oplicable						0.01 0.1 1 10 100
Test for overall effect:	Z = 5.90 (8)	⊃ < 0.00	001)				Favours fluoxetine Favours LTPP



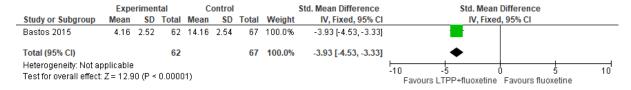
13 Figure 363: Discontinuation due to any reason



1 More severe: Long-term psychodynamic psychotherapy

2 individual + fluoxetine versus fluoxetine

3 Figure 364: Depression symptomatology endpoint



5 Figure 365: Remission (ITT)

6

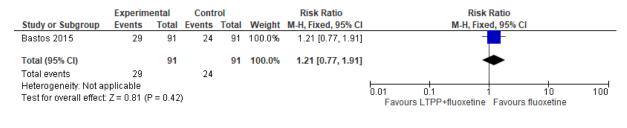
8 9

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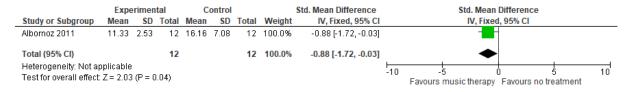


7 Figure 366: Discontinuation due to any reason

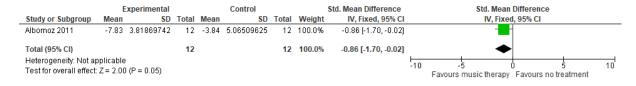


10 More severe: Music therapy group versus no treatment

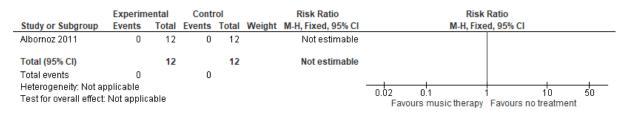
11 Figure 367: Depression symptomatology at endpoint



13 Figure 368: Depression symptomatology change score



1 Figure 369: Discontinuation due to any reason

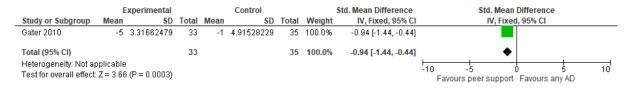


4 More severe: Peer support group versus any AD

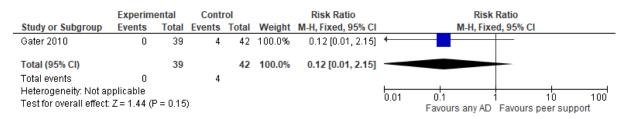
5 Figure 370: Depression symptomatology endpoint

	Exper	imen	tal	Co	ntro	I		Std. Mean Difference		Std. Mean	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed	l, 95% CI		
Gater 2010	14.3	4	33	16.9	7	35	100.0%	-0.45 [-0.93, 0.03]					
Total (95% CI)			33			35	100.0%	-0.45 [-0.93, 0.03]		•			
Heterogeneity: Not ap Test for overall effect		(P = 0).07)						-10 Favours	t 5 peer support) Favours any	AD	10

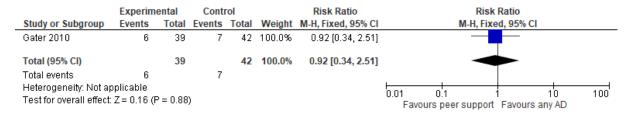
7 Figure 371: Depression symptomatology change score



9 Figure 372: Remission (ITT)



11 Figure 373: Discontinuation due to any reason

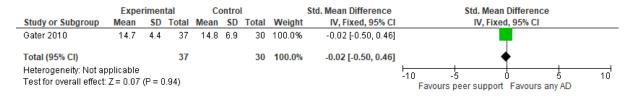


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1 Figure 374: Depression symptomatology at 6-month follow-up



3 Figure 375: Remission at 6-month follow-up (ITT)



5 More severe: Peer support group + any AD versus any AD

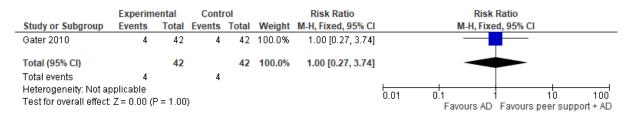
6 Figure 376: Depression symptomatology endpoint

	Expe	rimen	tal	Co	ntro	I		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gater 2010	14.5	5.4	36	16.9	7	35	100.0%	-0.38 [-0.85, 0.09]	
Total (95% CI)			36			35	100.0%	-0.38 [-0.85, 0.09]	. •
Heterogeneity: Not ap Test for overall effect:		(P = 0	1.11)						-10 -5 0 5 10 Favours peer support + AD Favours AD

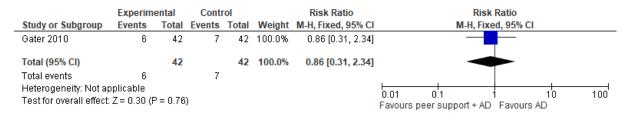
8 Figure 377: Depression symptomatology change score

	Е	xperimental			Control			Std. Mean Difference		Std. Mear	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% CI		
Gater 2010	-5.7	3.89358447	36	-1	4.91528229	35	100.0%	-1.05 [-1.55, -0.55]					
Total (95% CI)			36			35	100.0%	-1.05 [-1.55, -0.55]		•			
Heterogeneity: Not ap Test for overall effect:									-10 Favours	-5 peer support+AD	0 Favours any	AD	10

10 Figure 378: Remission (ITT)



12 Figure 379: Discontinuation due to any reason



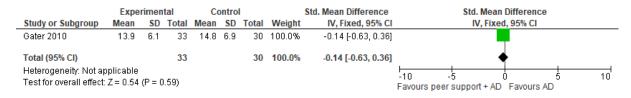
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1 Figure 380: Depression symptomatology at 6-month follow-up



3 Figure 381: Remission at 6-month follow-up (ITT)

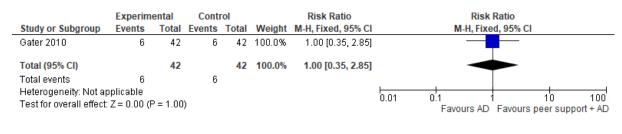
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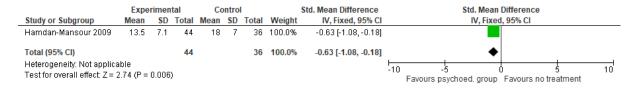
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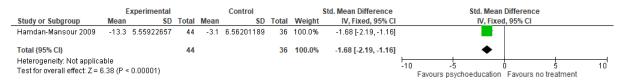


6 More severe: Psychoeducation group versus no treatment

7 Figure 382: Depression symptomatology endpoint



9 Figure 383: Depression symptomatology change score



11 Figure 384: Discontinuation due to any reason



¹ More severe: Psychoeducation group + any AD versus any

2 **AD**

4

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3 Figure 385: Depression symptomatology change score

	Expe	rimen	tal	Co	ontro	I		Std. Mean Difference	Std. Mean D	ifference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed,	95% CI	
Saloheimo 2016	-8.3	6.3	27	-11.1	6.4	34	100.0%	0.43 [-0.08, 0.95]			
Total (95% CI)			27			34	100.0%	0.43 [-0.08, 0.95]		▶ .	
Heterogeneity: Not ap Test for overall effect:		(P = 0	1.10)						-10 -5 0 Favours psychoeduc+any AD	5 Favours any AD	10

5 Figure 386: Remission (ITT)

	Experim	ental	Contr	rol		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI		
Saloheimo 2016	16	42	14	46	100.0%	1.25 [0.70, 2.24]		_		
Total (95% CI)		42		46	100.0%	1.25 [0.70, 2.24]		•		
Total events	16		14							
Heterogeneity: Not ap Test for overall effect:	•	P = 0.45)				0.01 0.1 Fa	vours any AD Favours	10 psychoeduo	100 c+any AD

7 Figure 387: Discontinuation due to any reason

	Experim	ental	Conti	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Saloheimo 2016	15	42	12	46	100.0%	1.37 [0.73, 2.58]	-
Total (95% CI)		42		46	100.0%	1.37 [0.73, 2.58]	•
Total events	15		12				
Heterogeneity: Not ap Test for overall effect:	•	P = 0.33)				0.01 0.1 10 100 Favours psychoeduc+any AD Favours any AD

9 Figure 388: Remission at 3-month follow-up (ITT)

	Experim	ental	Contr	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Saloheimo 2016	15	42	16	46	100.0%	1.03 [0.58, 1.81]	-
Total (95% CI)		42		46	100.0%	1.03 [0.58, 1.81]	*
Total events	15		16				
Heterogeneity: Not ap Test for overall effect:	•	° = 0.93)				0.01 0.1 10 100 Favours any AD Favours psychoeduc+any AD

11 Figure 389: Remission at 9-month follow-up (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Saloheimo 2016	15	42	18	46	100.0%	0.91 [0.53, 1.57]	-
Total (95% CI)		42		46	100.0%	0.91 [0.53, 1.57]	•
Total events	15		18				
Heterogeneity: Not ap Test for overall effect:	•	P = 0.74)				0.01 0.1 10 100 Favours any AD Favours psychoeduc+any AD

1 More severe: Mindfulness-based cognitive therapy (MBCT)

2 group versus no treatment

4

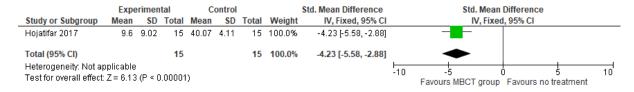
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14 15

3 Figure 390: Depression symptomatology endpoint



5 Figure 391: Depression symptomatology change score

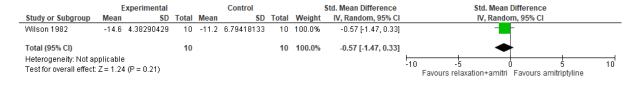


7 More severe: Progressive muscle relaxation + amitriptyline 8 versus amitriptyline

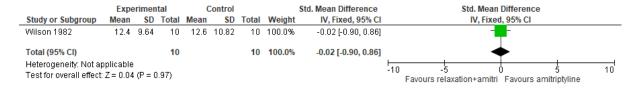
9 Figure 392: Depression symptomatology endpoint

	Expe	erimen	tal	C	ontrol			Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
Wilson 1982	8.5	6.35	10	14.6	9.73	10	100.0%	-0.71 [-1.62, 0.20]	-	
Total (95% CI)			10			10	100.0%	-0.71 [-1.62, 0.20]	•	
Heterogeneity: Not ap Test for overall effect:).13)						-10 -5 0 5 Favours relaxation+amitri Favours amitript	10 tyline

11 Figure 393: Depression symptomatology change score

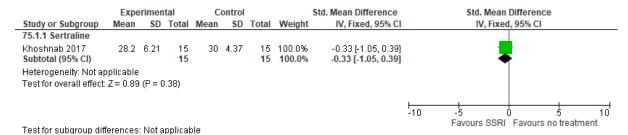


13 Figure 394: Depression symptomatology at 6-month follow-up



1 More severe: SSRIs versus no treatment

2 Figure 395: Depression symptomatology endpoint



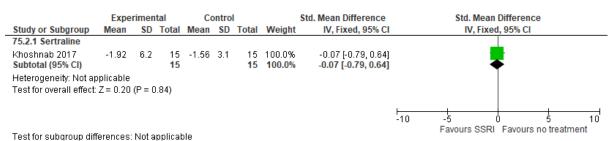
4 Figure 396: Depression symptomatology change score

3

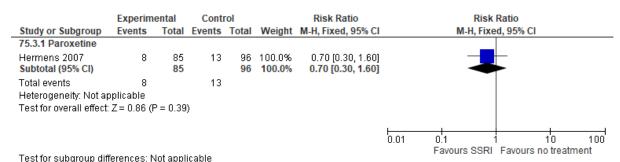
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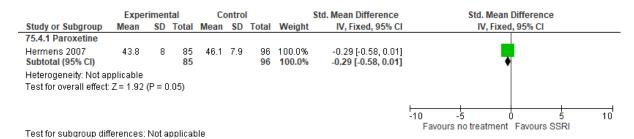
9



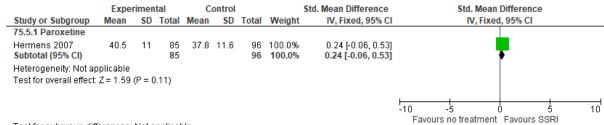
6 Figure 397: Discontinuation due to any reason



8 Figure 398: Quality of life physical health component endpoint



1 Figure 399: Quality of life mental health component endpoint



2 Test for subgroup differences: Not applicable

1 More severe: SSRIs versus placebo

3

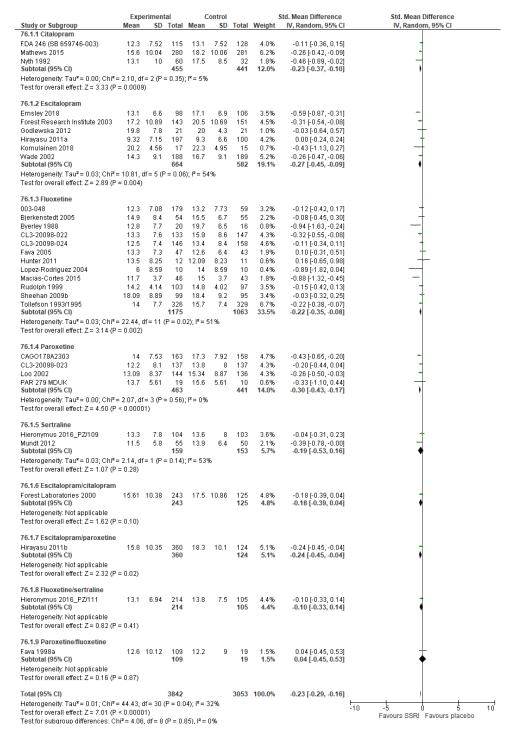
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2 Figure 400: Depression symptomatology endpoint



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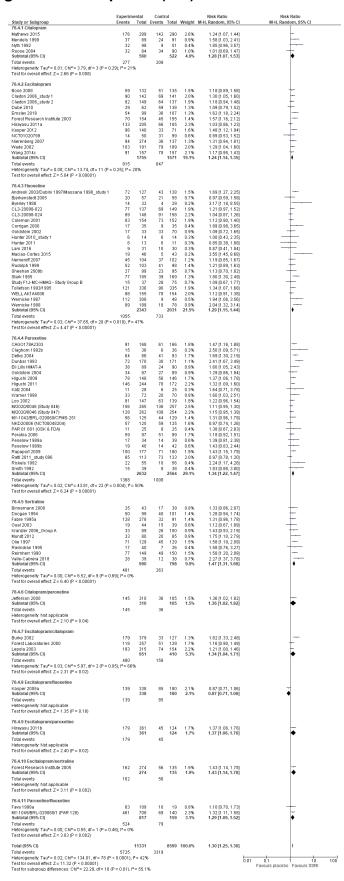
2 Figure 401: Depression symptomatology change score

tudy or Subgroup 6.2.1 Citalopram	Mean	erimental SD	Total	Mean	Control SD	Total	Weight	td. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
athews 2015	-15.9	10.04	280	-13.6	10.06	281	2.1%	-0.23 [-0.39, -0.06]	-
ontgomery 1992 rth 1992		8.81 17106781	60	-10.56 -6.7	7.76 5.97578447	64 32	1.4% 0.9%	-0.21 [-0.51, 0.09] -0.95 [-1.40, -0.49]	-1
udy 89306 (FDA) ibtotal (95% CI)	-16.94	13.24	185 654	-15.95	13.22	88 465	1.6% 6.1%	-0.07 [-0.33, 0.18] -0.31 [-0.57, -0.05]	•
eterogeneity: Tau# = 0.05; Chi# = 11.07, df = 3 (P = i est for overall effect: Z = 2.31 (P = 0.02)	0.01); = 73%	5							
6.2.2 Escitalopram									
ose 2008 layton 2006_study 1	-12.1 -14.2	10.22 8.07	129 133	-10.6 -12.1	10.42 7.98	134 130	1.7% 1.7%	-0.14 [-0.39, 0.10] -0.26 [-0.50, -0.02]	<u> </u>
layton 2006_study 2	-12.9	8.07	133	-11.9	7.86	126	1.7%	-0.13 [-0.37, 0.12]	4
ube 2010 msley 2018	-15 -13.6 4.7	8.82 0319041	54 98	-13 -9.5	8.84 4.82804308	122	1.3%	-0.23 [-0.55, 0.10] -0.86 [-1.14, -0.57]	-7
orest Laboratories 2010	-11.55	9.85	637	-8.5	8.8 10.57	215	2.2%	-0.32 [-0.47, -0.16]	-
orest Research Institute 2003 iodlewska 2012		10.62 6139516	143 21	-10 -3.3	3.11688947	151 21	1.8% 0.6%	-0.31 [-0.54, -0.08] -0.25 [-0.86, 0.35]	7
asper 2012 omulainen 2018	-19 -1.9 3.0	10.61 15569959	139 17	-13.4 -2.2	9.27 3.29146624	71 15	1.5% 0.5%	-0.55 [-0.84, -0.26] 0.09 [-0.60, 0.79]	1
ICT01020799	-11.7	10.99	49	-11.45	10.18	94	1.2%	-0.02 [-0.37, 0.32]	+
lierenberg 2007 Vade 2002	-7.22 -14.9 6.5	6.62 6658206	274 188	-5.97 -12	6.79 6.78196137	137 189	1.9% 1.9%	-0.19 [-0.39, 0.02] -0.43 [-0.64, -0.23]	
ubtotal (95% CI) leterogeneity: Tau² = 0.02; Chi² = 27.64, df = 12 (P =	0.006); 2 = 5	7%	2015			1511	19.4%	-0.30 [-0.41, -0.19]	'
est for overall effect Z = 5.24 (P < 0.00001)									
6.2.3 Fluoxetine	122		127	0.6	4.47	120	1.60	1.02 (1.20 . 0.77)	_
ndreoli 2002/Dubini 1997/Massana 1998_study 1 jerkenstedt 2005	-13.3 -8.9	4.6 8	127 54	-8.6 -9.7	4.47 7	128 55	1.6% 1.1%	-1.03 [-1.29, -0.77] 0.11 [-0.27, 0.48]	+
ava 2005 DA 244 (EMD 68 843-009)	-6.3 5.3 -9.1	8098504 7.4	47 89	-7.3 -9.3	4.6400431 7.8	43 95	1.0%	0.20 [-0.22, 0.61] 0.03 [-0.26, 0.32]	‡
DA 245 (EMD 68 843-010)	-11.1	7.67 8727915	92 12	-10.2	7.96	99	1.5%	-0.11 [-0.40, 0.17]	
lunter 2011 am 2016	-8.8	9.9	31	-8.64 -6.5	5.99548163 9.6	11 30	0.8%	-0.17 [-0.99, 0.65] -0.23 [-0.74, 0.27]	+
lacias-Cortes 2015 heehan 2009b	-11.42 6.4	15051015 16107963		-5.7 -11.02	2.46880538 6.86603233	43 95	0.9% 1.5%	-1.29 [-1.75, -0.83] -0.06 [-0.34, 0.22]	-1
ramek 1995 tark 1985	-8.6 -11	6.3 10.1	72 185	-6.4 -8.2	6.7	70 169	1.3%	-0.34 [-0.67, -0.01] -0.29 [-0.50, -0.08]	7
tudy 62b (FDA)	-8.82	8.71	297	-5.69	8.65	48	1.4%	-0.36 [-0.66, -0.05]	1
tudy F1J-MC-HMAQ - Study Group B ollefson 1993/1995	-7.63 -8.1	7.6	37 326	-7.1 -6.4	6.96 7.1	72 329	1.1% 2.2%	-0.08 [-0.47, 0.32] -0.23 [-0.38, -0.08]	7
VELL AK1A4006 Vernicke 1987	-13.9 -8.83	10.87 8.67	146 297	-12.2 -5.7	9.73 8.6	148 48	1.8%	-0.16 [-0.39, 0.06] -0.36 [-0.67, -0.05]	1
Vernicke 1907 Vernicke 1988 Jubtotal (95% CI)	-10.6	8.3	183 2140	-7	8.6	77 1560	1.6%	-0.43 [-0.70, -0.16] -0.28 [-0.44, -0.13]	7
leterogeneity: Tau ² = 0.08; Chi ² = 71.86, df = 16 (P <	0.00001); 2 =	78%	2 (40			1500	22.070	-0.20 [-0.44, -0.13]	*
est for overall effect Z = 3.60 (P = 0.0003)									
6.2.4 Paroxetine 9060 07 001	-13.08	10.2191	12	-10.91	9.386048	11	0.4%	-0.21 [-1.03, 0.61]	
aune 2018	-15.96	8.58	52	-8	8.38	48	1.0%	-0.93 [-1.34, -0.52]	-
laghorn 1992a laghorn 1992b	-10.72 -11.44	9.39 8.32	32 32	-4.59 -5.49	9.35 8.31	27 27	0.7% 0.7%	-0.65 [-1.17, -0.12] -0.71 [-1.23, -0.18]	=
letke 2004 II LIIIy HMAT-A	-11.7 -7.4	4.61 6.44	85 87	-8.8 -4.78	4.82 6.42	93 89	1.4%	-0.61 [-0.91, -0.31] -0.41 [-0.70, -0.11]	-
abre 1992	-9.13	8.14	38	-3.06	8.1	36	0.8%	-0.74 [-1.21, -0.27]	-
iolden 2002_448 iolden 2002_449	-11.89 -12.69	8.19 8.2	206 218	-9.9 -10.2	8.04 8.18	101 110	1.7%	-0.24 [-0.48, -0.00] -0.30 [-0.53, -0.07]	7
liguchi 2009 Iliguchi 2011	-9.4 -12.7	6.9 7.47	148 241	-8.3 -10.4	5.8 8.11	145 171	1.8%	-0.17 [-0.40, 0.06] -0.30 [-0.49, -0.10]	1
eller 2006_Study 062	-17.25	8.05	161	-14	8.87	154	1.8%	-0.38 [-0.61, -0.16]	_
oo 2002 N2020/0046 (Study 046)	-12.5	3938298 8.45	243	-12.06 -11.5	6.85867334 8.45	136 247	1.7% 2.1%	-0.33 [-0.56, -0.09] -0.12 [-0.30, 0.06]	J
l/2020/0046 (Study 047) liller 1989a	-11.8 -6	7.64 5.9	242 19	-10.1 -6.2	7.27 7.2	239 22	2.0%	-0.23 [-0.41, -0.05] 0.03 [-0.58, 0.64]	1
IY-1042/BRL-029060/CPMS-251 IKD20006 (NCT00048204)	-10.23 -11.1	7.67 7.9	120 117	-8.25 -10.9	7.56 7.8	123	1.7%	-0.26 [-0.51, -0.01] -0.03 [-0.28, 0.23]	1
AR 01 001 (GSK & FDA)	-13.36	7.93	22	-11.33	7.93	21	0.6%	-0.25 [-0.85, 0.35]	+
apaport 2009 EN XR 367 (FDA)	-12.11 -11.26	8.02 10.55	173 80	-8.85 -13.1	8 10.63	178 81	1.4%	-0.41 [-0.62, -0.19] 0.17 [-0.14, 0.48]	7
ubtotal (95% CI) leterogeneity: Tau ^a = 0.02; Chi ^a = 42.78, df = 20 (P =	0.002); I*= 5	3%	2472			2177	29.0%	-0.31 [-0.40, -0.21]	'
est for overall effect Z = 6.55 (P < 0.00001)	//.								
6.2.5 Sertraline	-13.42	701	20	-10.18	7.57	24	0.8%	-0.42 [-0.93, 0.09]	
lumenthal 2007/Hoffman 2011	-6.1	7.61 6.7	49	-6.1	7.57 7.3	31 49	1.1%	0.00 [-0.40, 0.40]	7
abre 1995a Ileronymus 2016_PZ/109	-9.89 -8.7 5.7	8.57	261 104	-7.6 -7.9	7.5 5.89576119	86 103	1.7%	-0.27 [-0.52, -0.03] -0.14 [-0.41, 0.14]	1
ranzler 2006_Group A	-10.8 -13.4	6.5	89	-9.6	7.8	100	1.5%	-0.17 [-0.45, 0.12] -0.44 [-0.82, -0.05]	
lundt 2012 leimherr 1990	-11.66	5.7 8.24	55 142	-10.7 -8.16	6.6 7.85	141	1.1%	-0.43 [-0.67, -0.20]	-
ER 315 (FDA) ubtotal (95% CI)	-8.9	4.52	76 806	-7.8	8	73 633	1.3% 10.7%	-0.17 [-0.49, 0.15] -0.26 [-0.37, -0.15]	7
leterogeneity: Tau r = 0.00; Ch r = 6.44, df = 7 (P = 0. est for overall effect: Z = 4.72 (P < 0.00001)	49); I*= 0%								
6.2.6 Citalopram/paroxetine									
efferson 2000	-14.7	10.56	296	-12.1	11.05	101	1.8%	-0.24 [-0.47, -0.02]	-
ubtotal (95% CI) leterogeneity: Not applicable			296			101	1.8%	-0.24 [-0.47, -0.02]	•
est for overall effect Z = 2.10 (P = 0.04)									
6.2.7 Escitalopram/citalopram	100	0.05	200			440	1.00	0.971.050.01**	
urke 2002 orest Laboratories 2000	-12.9 -12.95	9.25 9.89	366 243	-9.4 -11.2	9.82 10.35	119 125	1.9%	-0.37 [-0.58, -0.16] -0.17 [-0.39, 0.04]]
ubtotal (95% CI) leterogeneity: Tau# = 0.01; Chi# = 1.68, df = 1 (P = 0.	20); F= 40%		609			244	3.7%	-0.28 [-0.47, -0.08]	•
est for overall effect Z = 2.78 (P = 0.005)	,,								
6.2.8 Escitalopram/sertraline	10.00	40.0-	200	40.	40.01	400	4.00	0.071.050.07**	
orest Research Institute 2005 ubtotal (95% CI)	-16.26	10.37	266 266	-12.4	10.34	132 132	1.9% 1.9%	-0.37 [-0.58, -0.16] -0.37 [-0.58, -0.16]	ě
leterogeneity: Not applicable est for overall effect: Z = 3.47 (P = 0.0005)									
6.2.9 Fluoxetine/sertraline lieronymus 2016_PZ/111	-11.15	5.52	214	-10.4	6.02826675	105	1.7%	-0.13 [-0.37, 0.10]	1
ubtotal (95% CI) leterogeneity: Not applicable			214			105	1.7%	-0.13 [-0.37, 0.10]	1
est for overall effect Z = 1.10 (P = 0.27)									
6.2.10 Paroxetine/fluoxetine									
ava 1998a IY-1045/BRL-029060/1 (PAR 128)	-10.95 -12.39	9.41 8.77	109 694	-11.6 -9	8.9 8.63	19 136	0.8%	0.07 [-0.42, 0.56] -0.39 [-0.57, -0.20]	
ubtotal (95% CI)		0.11	803	-0	0.03	155	2.8%	-0.22 [-0.65, 0.22]	•
leterogeneity: Tau ^a = 0.07; Chi ^a = 2.95, df= 1 (P = 0. est for overall effect: Z = 0.98 (P = 0.33)	oa), 1°= 66%								
			10275			7083	100.0%	-0.29 [-0.34, -0.24]	
otal (95% CI)									

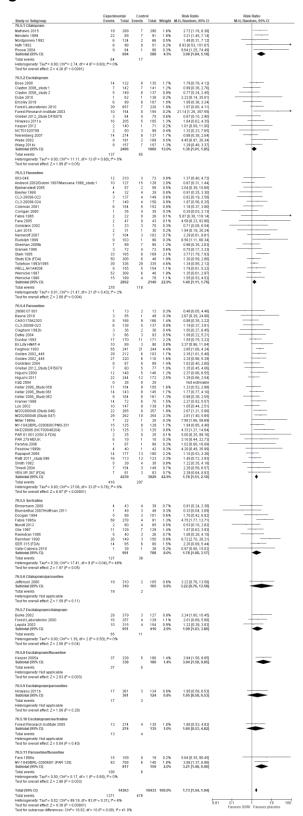
1 Figure 402: Remission (ITT)

tudy or Subgroup	Experim Events		Contr Events		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.3.1 Citalopram coose 2004	27	84	30	90	2.1%	0.96 [0.63, 1.48]	
ubtotal (95% CI)		84	-	90	2.1%	0.96 [0.63, 1.48]	*
otal events	27		30				
eterogeneity: Not applicable est for overall effect: Z = 0.17 (P = 0.87)							
5.3.2 Escitalopram							
ose 2008	44	132	39	135	2.7%	1.15 [0.81, 1.65]	+
ayton 2006_study 1 ayton 2006_study 2	65 56	142 149	40 48	141 137	3.1% 3.2%	1.61 [1.17, 2.22] 1.07 [0.79, 1.46]	
ayion 2000_stady 2 ibe 2010	23	62	38	138	2.1%	1.35 [0.88, 2.06]	
rest Research Institute 2003	42	154	27	155	2.1%	1.57 [1.02, 2.40]	 -
asper 2012 CT01020799	57 10	140 50	14 12	71 99	1.6% 0.8%	2.06 [1.24, 3.44] 1.65 [0.77, 3.55]	
erenberg 2007	69	274	27	137	2.4%	1.28 [0.86, 1.90]	
ang 2014c	62	157 1260	54	157 1170	3.4% 21.4%	1.15 [0.86, 1.53]	<u> </u>
ibtotal (95% CI) ital events	428	1200	299	1170	21.470	1.33 [1.16, 1.51]	*
eterogeneity: Tau² = 0.00; Chi² = 8.68, df = 8 (P = 0.		•					
est for overall effect: Z = 4.18 (P < 0.0001)							
5.3.3 Fluoxetine ndreoli 2002/Dubini 1997/Massana 1998_study 1	57	127	34	128	2.8%	1 60 11 10 2 201	
erkenstedt 2005	15	57	4	58	0.5%	1.69 [1.19, 2.39] 3.82 [1.35, 10.80]	
L3-20098-022	25	137	24	149	1.6%	1.13 [0.68, 1.89]	+
L3-20098-024 oleman 2001	30 58	148 154	38 46	158 152	2.1% 3.1%	0.84 [0.55, 1.29] 1.24 [0.91, 1.71]	
ava 2005	14	47	9	43	0.9%	1.42 [0.69, 2.95]	+
oldstein 2002	10	33	22	70	1.2%	0.96 [0.52, 1.80]	_+
lunter 2011 am 2016	3 6	13 31	3 9	11 30	0.3% 0.6%	0.85 [0.21, 3.38] 0.65 [0.26, 1.59]	
acias-Cortes 2015	7	46	2	43	0.2%	3.27 [0.72, 14.89]	+
lemeroff 2007	28 23	104	22	102 98	1.7%	1.25 [0.77, 2.03] 1.29 [0.73, 2.26]	
udolph 1999 heehan 2009b	23 15	103 99	17 14	98 95	1.4%	1.03 [0.53, 2.26]	
tudy F1J-MC-HMAQ - Study Group B	11	37	21	75	1.2%	1.06 [0.57, 1.96]	+
ollefson 1993/1995 /ELL AK1A4006	71 55	336 155	44 51	335 154	2.8% 3.2%	1.61 [1.14, 2.27] 1.07 [0.79, 1.46]	
ubtotal (95% CI)		1627		1701	24.7%	1.24 [1.07, 1.43]	♦
otal events	428	220	360				
eterogeneity: Tau² = 0.02; Chi² = 19.18, df = 15 (P = est for overall effect: Z = 2.83 (P = 0.005)	0.21); i= :	22%					
6.3.4 Paroxetine AGO178A2303	37	168	22	166	1.8%	1.66 [1.03, 2.69]	<u> </u>
L3-20098-023	36	138	27	137	2.0%	1.32 [0.85, 2.05]	+-
etke 2004	38	86	28	93	2.4%	1.47 [0.99, 2.17]	<u></u>
li Lilly HMAT-A eighner 1993	31 59	89 241	18 31	90 244	1.7% 2.3%	1.74 [1.05, 2.88] 1.93 [1.30, 2.87]	=
olden 2002_448	94	212	38	103	3.4%	1.20 [0.90, 1.61]	+
olden 2002_449	105	220	37	110	3.3%	1.42 [1.05, 1.91]	<u> </u>
oldstein 2004 liguchi 2009	31 49	87 148	26 32	89 146	2.1% 2.5%	1.22 [0.79, 1.87] 1.51 [1.03, 2.21]	<u> </u>
liguchi 2011	86	244	40	172	3.1%	1.52 [1.10, 2.09]	_
ramer 1998 oo 2002	24 37	72 147	12 21	70 139	1.2%	1.94 [1.06, 3.58] 1.67 [1.03, 2.70]	
KD20006 (NCT00048204)	32	125	29	125	2.0%	1.10 [0.71, 1.71]	+
erahia 2006	42	97	33	99	2.7%	1.30 [0.91, 1.86]	
apaport 2009 atti 2011 study 096	71 58	177 113	50 48	180 123	3.3% 3.5%	1.44 [1.07, 1.94] 1.32 [0.99, 1.75]	<u> </u>
ubtotal (95% CI)		2364		2086	39.0%	1.42 [1.30, 1.56]	◆
otal events leterogeneity: Tau² = 0.00: Chi² = 8.73. df = 15 (P = (830	ov.	492				
est for overall effect: Z = 7.43 (P < 0.00001)	J.08), I = U	70					
6.3.5 Sertraline							
innemann 2008	18	43	8	39	0.9%	2.04 [1.00, 4.16]	
lumenthal 2007/Hoffman 2011	23	49	15	49	1.6%	1.53 [0.92, 2.57]	 -
alle-Cabrera 2018 ubtotal (95% CI)	20	39 131	6	38 126	0.8% 3.3%	3.25 [1.47, 7.20] 1.99 [1.31, 3.03]	→
otal events	61		29			. ,,	
eterogeneity: Tau ^z = 0.03; Chi ^z = 2.48, df = 2 (P = 0. est for overall effect: Z = 3.22 (P = 0.001)	29); I² = 19	%					
6.3.6 Citalopram/paroxetine	70	24.0	40	405	2.00	1 44 10 00 0 00	
efferson 2000 ubtotal (95% CI)	79	310 310	19	105 105	2.0% 2.0%	1.41 [0.90, 2.21] 1.41 [0.90, 2.21]	₩
otal events	79		19			,,	
eterogeneity: Not applicable est for overall effect: Z = 1.49 (P = 0.14)							
6.3.7 Escitalopram/fluoxetine						0	
asper 2005a ubtotal (95% CI)	117	338 338	76	180 180	4.3% 4.3%	0.82 [0.65, 1.03] 0.82 [0.65, 1.03]	•
otal events	117		76				1
leterogeneity: Not applicable est for overall effect: Z = 1.73 (P = 0.08)							
6.3.8 Escitalopram/sertraline		_			_		
orest Research Institute 2005 ubtotal (95% CI)	122	274 274	36	135 135	3.2% 3.2%	1.67 [1.23, 2.28] 1.67 [1.23, 2.28]	_
otal events	122	2.7	36	.55	U.E. 19	[20, 2.20]	•
leterogeneity: Not applicable							
est for overall effect: Z = 3.25 (P = 0.001)							
otal (95% CI)		6388		5593	100.0%	1.34 [1.24, 1.44]	•
otal events leterogeneity: Tau² = 0.02; Chi² = 68.53, df = 47 (P =	2092	2104	1341				
							0.01 0.1 1 10

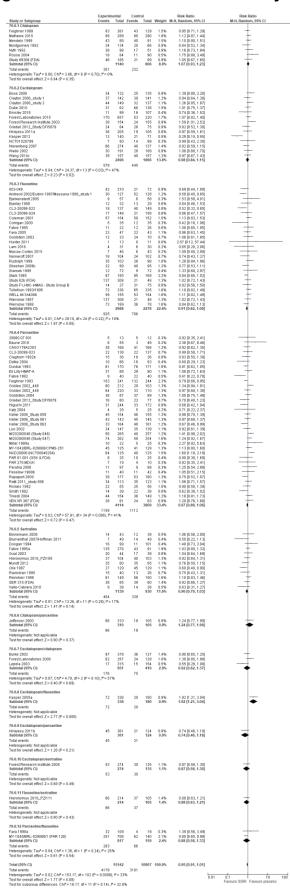
1 Figure 403: Response (ITT)



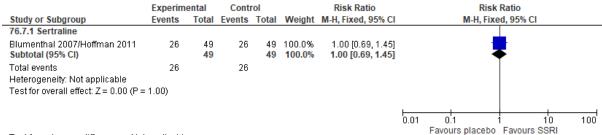
1 Figure 404: Discontinuation due to SE



1 Figure 405: Discontinuation due to any reason including SE



1 Figure 406: Remission at 12-month follow-up (ITT)



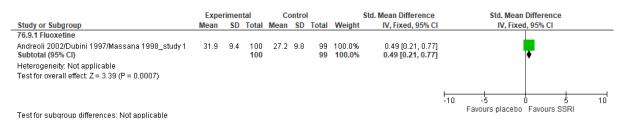
2 Test for subgroup differences: Not applicable

3 Figure 407: Quality of life change score

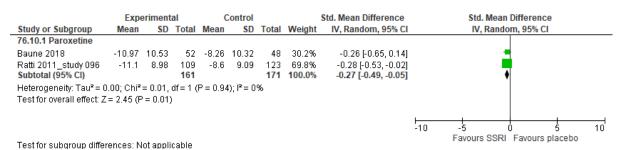
	Exp	eriment	tal	C	Control			Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI	
76.8.1 Paroxetine											
Rapaport 2009 Subtotal (95% CI)	11.49	17.22	145 145	5.34	17.15	150 150	100.0% 100.0 %	0.36 [0.13, 0.59] 0.36 [0.13, 0.59]		.	
Heterogeneity: Not ap Test for overall effect:			002)								
									-10	-5 0 5 Favours placebo Favours SSRI	10

4 Test for subgroup differences: Not applicable

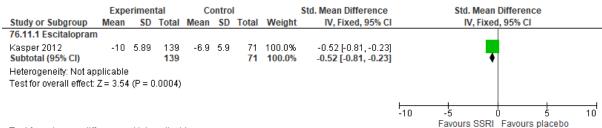
5 Figure 408: Global functioning endpoint



7 Figure 409: Functional impairment change score



9 Figure 410: Sleeping difficulties change score endpoint



10 Test for subgroup differences: Not applicable

11

6

- 1 More severe: SSRIs versus TCAs
- 2 Figure 411: Depression symptomatology endpoint

Study or Subgroup	Mean	erimenta SD		Mean	ontrol SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
7.1.1 Fluoxetine versus a								,,,	
emyttenaere 1998	9.9	6.3	35	7.2	4.5	31	2.7%	0.48 [-0.01, 0.97]	-
e Ronchi 1998	14.22	8.31	32	13.94	9.4	33	2.7%	0.03 [-0.46, 0.52]	+
awcett 1989	12.8	6.5	19	14.6	7.9	19	1.9%	-0.24 [-0.88, 0.39]	+
udd 1993	9.6	6.2	23	11.6	6	23	2.1%	-0.32 [-0.90, 0.26]	-
aakmann 1988	8.96	7.52	36	6.59	7.52	43	3.0%	0.31 [-0.13, 0.76]	 -
aakmann 1991.	9.47	7.56	62	9.65	7.86	62	3.8%	-0.02 [-0.38, 0.33]	+
farchesi 1998	8.9	6.6	67	8.1	6.9	75	4.1%	0.12 [-0.21, 0.45]	+
Intiveros Sanchez 1998	7.8	6.21	21	5.8	5.45	21	2.0%	0.34 [-0.27, 0.95]	+
eters 1990	10	6	41	11	9	40	3.1%	-0.13 [-0.57, 0.31]	+
Suleman 1997	7.2	2.5	15	7	2.6	15	1.6%	0.08 [-0.64, 0.79]	+
ersiani 1999	9.9	8.4	77	8.1	7	79	4.2%	0.23 [-0.08, 0.55]	+
Subtotal (95% CI)			428			441	31.2%	0.10 [-0.03, 0.24]	•
leterogeneity: Tau² = 0.00 est for overall effect: Z = 1			10 (P	= 0.51)	; I² = 0%	•			
7.1.2 Fluoxetine versus o									
loguera 1991	6.21	4.57	60	6.66	4.93	60	3.8%	-0.09 [-0.45, 0.26]	†
Ropert 1989	9.4	7	54	11.8	8	46	3.4%	-0.32 [-0.71, 0.08]	7
ubtotal (95% CI)			114			106	7.2%	-0.20 [-0.46, 0.07]	7
eterogeneity: Tau² = 0.00 est for overall effect: Z = 1			: 1 (P =	= 0.41);	l* = 0%				
7.1.3 Fluoxetine versus i	miprami	ne							
yerley 1988	12.8	7.7	20	13.7	8.5	24	2.1%	-0.11 [-0.70, 0.49]	+
ohn 1984b	14.72	8.81		14.54	8.85	31	2.7%	0.02 [-0.46, 0.50]	+
errano-Blanco 2006	9.5	8.2	49	8.8	8.2	45	3.3%	0.08 [-0.32, 0.49]	†
ollefson 1994	11.6	7.6	62	12.2	7.9	60	3.8%	-0.08 [-0.43, 0.28]	1
Subtotal (95% CI)			166		_	160	12.0%	-0.01 [-0.23, 0.20]	•
Heterogeneity: Tau² = 0.00 Test for overall effect: Z = 0			: 3 (P =	= 0.93);	l² = 0%				
7.1.4 Fluoxetine versus n									
lashemi 2012	16.16	4.02	48	19.71	4.21	49	3.2%	-0.86 [-1.27, -0.44]	
ubtotal (95% CI)			48			49	3.2%	-0.86 [-1.27, -0.44]	•
leterogeneity: Not applica		0.00041							
est for overall effect: Z = 4	.02 (P < I	0.0001)							
7.1.5 Paroxetine versus	amitripty	/line							
hristiansen 1996	8.1	5.9	56	6.9	6.2	57	3.7%	0.20 [-0.17, 0.57]	+
eushle 2003	12.7	8.2	40	10.5	7.1	40	3.0%	0.28 [-0.16, 0.72]	+
reed 1999	13.7	10.24	149	16.58	10.89	157	5.3%	-0.27 [-0.50, -0.05]	+
foller 1993	11.5	8.3	72	9.3	6.3	68	4.0%	0.30 [-0.04, 0.63]	+
AR 29060/281	16.1	8.59	76	12.4	8.59	79	4.2%	0.43 [0.11, 0.75]	-
PAR MDUK 032	12	8.07	29	12.2	8.07	30	2.5%	-0.02 [-0.53, 0.49]	+
BER-CHN-1	5.53	6.94	113	6.47	7.24	118	4.9%	-0.13 [-0.39, 0.13]	†
Staner 1995	17.8	11.3	21	10.7	7.9	19	1.8%	0.71 [0.07, 1.35]	
Subtotal (95% CI)		205 46	556 = 7 (P	- 0.001	2): 2 = 7	568 0%	29.6%	0.14 [-0.08, 0.37]	Ī
Heterogeneity: Tau² = 0.07				- 0.002	71				
Heterogeneity: Tau² = 0.07 Test for overall effect: Z = 1	.24 (P =	0.22)	. (- 0.002	-,,,				
Heterogeneity: Tau² = 0.07 Test for overall effect: Z = 1 T.1.6 Paroxetine versus	.24 (P = imipram	0.22) ine							
Heterogeneity: Tau ^z = 0.07 Test for overall effect: Z = 1 T 7.1.6 Paroxetine versus urminen 1992	.24 (P = imipram 8.76	0.22) ine 5.63	21	11.21	9.45	29	2.2%	-0.30 [-0.86, 0.27]	-
Heterogeneity: Tau ^z = 0.07 Test for overall effect: Z = 1 T 7.1.6 Paroxetine versus Taminen 1992 Chiu 1996	.24 (P = imipram	0.22) ine	21 15			29 15	1.5%	-0.47 [-1.20, 0.26]	
Heterogeneity: Tau ^z = 0.07 Test for overall effect: Z = 1 T 7.1.6 Paroxetine versus urminen 1992	.24 (P = imipram 8.76 7.4	0.22) ine 5.63 9.6	21 15 36	11.21 11.7	9.45 8.1	29			-
leterogeneity: Tau² = 0.07 Test for overall effect: Z = 1 T.1.6 Paroxetine versus arminen 1992 Chiu 1996 subtotal (95% CI) leterogeneity: Tau² = 0.00 Test for overall effect: Z = 1	.24 (P = 1 imipram 8.76 7.4 ; Chi² = 0 .60 (P = 1	0.22) ine 5.63 9.6 1.14, df= 0.11)	21 15 36	11.21 11.7	9.45 8.1	29 15	1.5%	-0.47 [-1.20, 0.26]	-
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus syminen 1992 Shiu 1996 Subtotal (95% CI) Heterogeneity: Tau* = 0.00 Fest for overall effect: Z = 1 F.1.7 Paroxetine versus	.24 (P = imipram 8.76 7.4 ; Chi² = 0 .60 (P =	0.22) ine 5.63 9.6 1.14, df= 0.11)	21 15 36 :1 (P=	11.21 11.7 = 0.71);	9.45 8.1 I ² = 0%	29 15 44	1.5% 3.7%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08]	•
leterogeneity: Tau² = 0.07 Fest for overall effect: Z = 1 Formal 1992 Formal 1996 Subtotal (95% CI) Heterogeneity: Tau² = 0.00 Fest for overall effect: Z = 1 Formal 1996 Form	.24 (P = 1 imipram 8.76 7.4 ; Chi² = 0 .60 (P = 1	0.22) ine 5.63 9.6 1.14, df= 0.11)	21 15 36 :1 (P =	11.21 11.7	9.45 8.1	29 15 44	1.5% 3.7% 3.1%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41]	-
leterogeneity: Tau² = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus rminen 1992 Chiu 1996 Subtotal (95% CI) Heterogeneity: Tau² = 0.00 Fest for overall effect: Z = 1 F.1.7 Paroxetine versus HSK_29060/103 Subtotal (95% CI)	.24 (P = imipram 8.76 7.4 ; Chi² = 0 .60 (P = infepram 13.5	0.22) ine 5.63 9.6 1.14, df= 0.11)	21 15 36 :1 (P=	11.21 11.7 = 0.71);	9.45 8.1 I ² = 0%	29 15 44	1.5% 3.7%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus rminen 1992 Fibiu 1996 Subtotal (95% CI) Heterogeneity: Tau* = 0.00 Fest for overall effect: Z = 1 F.1.7 Paroxetine versus FSK_29060/103 Subtotal (95% CI) Heterogeneity: Not applica	.24 (P = imipram 8.76 7.4 (Chi² = 0 .60 (P = lofepram 13.5	0.22) ine 5.63 9.6 1.14, df = 0.11) nine 11.4	21 15 36 :1 (P =	11.21 11.7 = 0.71);	9.45 8.1 I ² = 0%	29 15 44	1.5% 3.7% 3.1%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41]	
leterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus forminen 1992 Chiu 1996 Subtotal (95% CI) Heterogeneity: Tau* = 0.00 Fest for overall effect: Z = 1 F.1.7 Paroxetine versus SSK_29060/103 Subtotal (95% CI) Heterogeneity: Not applica Fest for overall effect: Z = 0	24 (P = imipram 8.76 7.4 ; Chi² = 0.60 (P = iofepram 13.5 ble .13 (P = iofe pram 13.5 chie .13 (P = iof	0.22) ine 5.63 9.6 1.14, df = 0.11) nine 11.4	21 15 36 :1 (P =	11.21 11.7 = 0.71);	9.45 8.1 I ² = 0%	29 15 44	1.5% 3.7% 3.1%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41]	
leterogeneity: Tau* = 0.07 lest for overall effect: Z = 1 left for overall effect: Z = 0 left	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = iofepram 13.5 ble 13 (P = iofepram 1.13 (P =	0.22) ine 5.63 9.6 1.14, df = 0.11) nine 11.4 0.90)	21 15 36 :1 (P = 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 I ² = 0% 8.4	29 15 44 36 36	1.5% 3.7% 3.1% 3.1%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 For Tau = 1992 Foliu 1996 Subtotal (95% CI) Heterogeneity: Tau* = 0.00 Fest for overall effect: Z = 1 For Tau = 10.00 Fest for overall effect: Z = 1 For Tau = 10.00 Fest for overall effect: Z = 1 For Tau = 10.00 Fest for overall effect: Z = 0 For Tau = 10.00 F	24 (P = imipram 8.76 7.4 ; Chi² = 0.60 (P = iofepram 13.5 ble .13 (P = iofe pram 13.5 chie .13 (P = iof	0.22) ine 5.63 9.6 1.14, df = 0.11) nine 11.4	21 15 36 :1 (P = 45 45	11.21 11.7 = 0.71);	9.45 8.1 I ² = 0%	29 15 44 36 36	1.5% 3.7% 3.1% 3.1% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73]	
leterogeneity: Tau* = 0.07 lest for overall effect: Z = 1 left. Z = 0.00 lest for overall effect: Z = 1 left. Z = 0.00 lest for overall effect: Z = 1 left. Z = 0.00 leterogeneity: Tau* = 0.00 lest for overall effect: Z = 0 leterogeneity: Not applica lest for overall effect: Z = 0 leterogeneity: Not applica lest for overall effect: Z = 0 leterogeneity: Not applica leterogeneity: Not applica leterogeneity: Not applica leterogeneity: Not applica	.24 (P = 1 imipram 8.76 7.4 (Chi² = 0 .60 (P = 1 13.5 ble .13 (P = 1 nortripty 9.6 ble .13 (P = 1 ble .13 (P = 1 nortripty 9.6 ble .	0.22) ine 5.63 9.6 i.14, df= 0.11) ine 11.4 0.90) tine 4.6	21 15 36 :1 (P = 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 I ² = 0% 8.4	29 15 44 36 36	1.5% 3.7% 3.1% 3.1%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41]	
leterogeneity: Tau² = 0.07 rest for overall effect: Z = 1 7.1.6 Paroxetine versus rminen 1992 chiu 1996 subtotal (95% CI) rest for overall effect: Z = 1 7.1.7 Paroxetine versus rest (29060/103) subtotal (95% CI) rest for overall effect: Z = 0 7.1.8 Paroxetine versus rest for overall effect: Z = 0 7.1.8 Paroxetine versus rest for overall effect: Z = 0 7.1.8 Paroxetine versus rest for overall effect: Z = 0 7.1.8 Paroxetine versus rest for overall effect: Z = 0 7.1.8 Paroxetine versus rest for overall effect: Z = 0	.24 (P = 1 imipram 8.76 7.4 (Chi² = 0 .60 (P = 1 13.5 ble .13 (P = 1 nortripty 9.6 ble .13 (P = 1 ble .13 (P = 1 nortripty 9.6 ble .	0.22) ine 5.63 9.6 i.14, df= 0.11) ine 11.4 0.90) tine 4.6	21 15 36 :1 (P = 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 I ² = 0% 8.4	29 15 44 36 36	1.5% 3.7% 3.1% 3.1% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73]	•
leterogeneity: Tau² = 0.07 lest for overall effect: Z = 1 leterogeneity: Tau² = 0.07 leterogeneity: Tau² = 0.00 leterogeneity: Not applica	24 (P = imipram 8.76 7.4 (Chi² = 0.60 (P = 13.5 13.5 13.6 14.6 15.6	0.22) ine 5.63 9.6 1.14, df= 0.11) nine 11.4 0.90) line 4.6	21 15 36 :1 (P = 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 I ² = 0% 8.4	29 15 44 36 36	1.5% 3.7% 3.1% 3.1% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus Firminen 1992 Finiu 1996 Fin	24 (P = imipram 8.76 7.4 (Chi² = 0.60 (P = 13.5 13.5 13.6 14.6 15.6	0.22) ine 5.63 9.6 1.14, df= 0.11) nine 11.4 0.90) line 4.6	21 15 36 11 (P= 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 I ² = 0% 8.4	29 15 44 36 36 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus Firminen 1992 Finiu 1996 Fin	24 (P = 1 imipram 8.76 7.4 (Chi ² = 0.60 (P = 1 13.5 ble 13 (P = 1 nortripty 9.6 ble 1.75 (P = 1 mitripty)	0.22) ine 5.63 9.6 1.14, df= 0.11) nine 11.4 0.90) line 4.6 0.45) ine	21 15 36 36 11 (P=	11.21 11.7 = 0.71); 13.8	9.45 8.1 1 ² = 0% 8.4	29 15 44 36 36 36	1.5% 3.7% 3.1% 3.1% 2.4% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73]	
leterogeneity: Tau² = 0.07 lest for overall effect: Z = 1 leterogeneity: Tau² = 0.07 leterogeneity: Tau² = 0.00 leterogeneity: Not applica	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = iofepram 13.5 ble 13 (P = iortripty 9.6 ble 7.75 (P = iortripty 16 ble ble ble ble iortripty 16 ble	0.22) ine 5.63 9.6 1.14, df = 0.11) ine 11.4 0.90) time 4.6 0.45)	21 15 36 11 (P= 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 1 ² = 0% 8.4	29 15 44 36 36 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus Framinen 1992 Framinen 1996 Framinen 1996 Framinen 1997 Framinen 1998 Fram	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = iofepram 13.5 ble 13 (P = iortripty 9.6 ble 7.75 (P = iortripty 16 ble ble ble ble iortripty 16 ble	0.22) ine 5.63 9.6 1.14, df = 0.11) ine 11.4 0.90) time 4.6 0.45)	21 15 36 11 (P= 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 1 ² = 0% 8.4	29 15 44 36 36 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 F.1.6 Paroxetine versus rminen 1992 chiu 1996 Subtotal (95% CI) Heterogeneity: Tau* = 0.00 Fest for overall effect: Z = 1 F.1.7 Paroxetine versus SK_29060/103 Subtotal (95% CI) Heterogeneity: Not applica Fest for overall effect: Z = 0 F.1.8 Paroxetine versus Fullsant 1999 Subtotal (95% CI) Heterogeneity: Not applica Fest for overall effect: Z = 0 F.1.9 Sertraline versus Fest for overall effect: Z = 0 F.1.9 Sertraline versus Fest for overall effect: Z = 0 F.1.9 Sertraline versus Fest for overall effect: Z = 0 F.1.9 Sertraline versus Fest for overall effect: Z = 0 F.1.9 Sertraline versus Fest for overall effect: Z = 0 Fest for overall effect: Z = 0 Fest for overall effect: Z = 0	24 (P = imipram 8.76 7.4 (Chi² = 0.60 (P = iofepram 13.5 de iofepram 9.6 de iofepram 9.6 de iofepram 15.5 (P = iofepram 15.5 de iofepram 15.5 (P = iofepram 15.5 de iofepram 15.5 (P = iofepram 15.5 de iofepram 1	0.22) ine 5.63 9.6 1.14, df = 0.11) inine 11.4 0.90) tline 4.6 0.45) ine 6.5	21 15 36 11 (P= 45 45	11.21 11.7 = 0.71); 13.8	9.45 8.1 1 ² = 0% 8.4	29 15 44 36 36 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.4%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 For Tau = 1992 For Tau = 1992 For Tau = 1995 For Tau	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = 13.5 ble 13.5 (P = 14.75 (P = 14	ine 5.63 9.6 1.14, df = 0.11) inine 11.4 4.6 = 4.6 0.45) ine 6.5 11.00) ine ine	21 15 36 36 1 (P = 45 45 29 29 31 31	11.21 11.7 0.71); 13.8 8.8	9.45 8.1 P=0% 8.4 3	29 15 44 36 36 27 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.6%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 For. 1.6 Paroxetine versus Friminen 1992 Friminen 1996 F	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = iofepram 13.5 ble 13 (P = iofepram 15.5 (P = iofepram 15.5 (P = iofepram 16.00 (P = iofepram 14.23 iofepram 14.23	0.22) ine 5.63 9.6 1.14, df = 0.11) 11.4 0.90) ine 4.6 6.5 1.00) ine 3.51	21 15 36 36 1 (P = 45 45 29 29	11.21 11.7 0.71); 13.8 8.8	9.45 8.1 F=0% 8.4 3	29 15 44 36 36 27 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.4% 2.6% 2.6%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.03 [-0.32, 0.73] -0.20 [-0.32, 0.73] -0.00 [-0.50, 0.50] -0.00 [-0.50, 0.50]	
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Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 For Tau = 0.07 Fest for overall effect: Z = 1 For Tau = 0.00 Fest for overall effect: Z = 0.00 Fest for overall effect: Z = 0.00 Fest for overall effect: Z = 0 For Tau = 0.00 Fest for overall effect: Z = 0 For Tau = 0.00 Fest for overall effect: Z = 0 For Tau = 0.00 For Tau = 0	24 (P = imipram 8.76 7.4 (Chi² = 0.60 (P = 13.5 ble 13.7 (P = 16.75 (P = 16.7	0.22) ine 5.63 9.6 1.14, df = 0.11) inine 11.4 0.90) ine 6.5 1.00) ine 3.51 1.235	21 15 36 36 1 (P= 45 45 29 29 31 31 30 27 57	11.21 11.7 0.71); 13.8 8.8 16	9.45 8.1 P=0% 8.4 3 6.1 4.74 11.8	29 15 44 36 36 27 27 27	1.5% 3.7% 3.1% 3.1% 2.4% 2.4% 2.6% 2.6%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.03 [-0.32, 0.73] -0.20 [-0.32, 0.73] -0.00 [-0.50, 0.50] -0.00 [-0.50, 0.50]	
leterogeneity: Tau² = 0.07 lest for overall effect: Z = 1 leterogeneity: Tau² = 0.07 leterogeneity: Tau² = 0.00 leterogeneity: Tou = 0.00 leterogeneity: Not applica leterogeneity: Not	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = imipram 13.5 ble 13 (P = imitriptyl 16 ble 100 (P = imipram 14.23 14.44 (Chi ² = 0.60 (Chi ² =	0.22) ine 5.63 9.6 1.14, df= 0.11) ine 11.4 4.6 0.45) ine 6.5 1.00) ine 3.51 12.35	21 15 36 36 1 (P= 45 45 29 29 31 31 30 27 57	11.21 11.7 0.71); 13.8 8.8 16	9.45 8.1 P=0% 8.4 3 6.1 4.74 11.8	29 15 44 36 36 37 27 27 30 30 30	1.5% 3.7% 3.1% 3.1% 2.4% 2.4% 2.6% 2.6%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73] 0.00 [-0.50, 0.50] 0.00 [-0.50, 0.50]	
leterogeneity: Tau² = 0.07 est for overall effect. Z = 1 7.1.6 Paroxetine versus irminen 1992 chiu 1996 ubtotal (95% CI) eleterogeneity: Tau² = 0.00 est for overall effect. Z = 1 7.1.7 Paroxetine versus estK_ 29060/103 subtotal (95% CI) eleterogeneity: Not applica est for overall effect. Z = 0 7.1.8 Paroxetine versus fulsant 1999 ubtotal (95% CI) eleterogeneity: Not applica est for overall effect. Z = 0 7.1.9 Sertraline versus alersani 1994 subtotal (95% CI) eleterogeneity: Not applica est for overall effect. Z = 0 7.1.10 Sertraline versus alersani 1994 subtotal (95% CI) eleterogeneity: Not applica est for overall effect. Z = 0 7.1.10 Sertraline versus chargava 2012 orlenza 2001 eleterogeneity: Tau² = 0.00 eleterogeneity: Tau² = 0.00 eleterogeneity: Tau² = 0.00	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = imipram 13.5 ble 13 (P = imitriptyl 16 ble 100 (P = imipram 14.23 14.44 (Chi ² = 0.75 (Chi ² =	0.22) ine 5.63 9.6 1.14, df= 0.11) ine 11.4 4.6 0.45) ine 6.5 1.00) ine 3.51 12.35	21 15 36 36 1 (P= 45 45 29 29 31 31 30 27 57	11.21 11.7 0.71); 13.8 8.8 16	9.45 8.1 P=0% 8.4 3 6.1 4.74 11.8	29 15 44 36 36 37 27 27 30 30 30	1.5% 3.7% 3.1% 3.1% 2.4% 2.4% 2.6% 2.6%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73] 0.00 [-0.50, 0.50] 0.00 [-0.50, 0.50]	
Heterogeneity: Tau* = 0.07 Fest for overall effect: Z = 1 For Tau = 0.07 Fest for overall effect: Z = 1 For Tau = 0.00 Fest for overall effect: Z = 0.00 Fest for overall effect: Z = 0.00 Fest for overall effect: Z = 0 For Tau = 0.00 Fest for overall effect: Z = 0 For Tau = 0.00 Fest for overall effect: Z = 0 For Tau = 0.00 For Tau = 0	24 (P = imipram 8.76 7.4 (Chi ² = 0.60 (P = imipram 13.5 ble 13 (P = imitriptyl 16 ble 100 (P = imipram 14.23 14.44 (Chi ² = 0.75 (Chi ² =	0.22) ine 5.63 9.6 1.14, df = 0.11) nine 11.4 0.90) tine 4.6 0.45) ine 3.51 1.235	21 15 36 36 1 (P= 45 45 29 29 31 31 30 27 57	11.21 11.7 0.71); 13.8 8.8 16	9.45 8.1 P=0% 8.4 3 6.1 4.74 11.8	29 15 44 36 36 36 27 27 27 30 30 30 28 58	1.5% 3.7% 3.1% 3.1% 2.4% 2.4% 2.6% 2.6%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] 0.20 [-0.32, 0.73] 0.00 [-0.50, 0.50] 0.00 [-0.50, 0.50]	
leterogeneity: Tau² = 0.07 est for overall effect. Z = 1 7.1.6 Paroxetine versus rminen 1992 chiut 1996 ubtotal (95% CI) leterogeneity: Tau² = 0.00 est for overall effect. Z = 1 7.1.7 Paroxetine versus iSK_29060/103 ubtotal (95% CI) leterogeneity: Not applica est for overall effect. Z = 0 7.1.8 Paroxetine versus lulsant 1999 ubtotal (95% CI) leterogeneity: Not applica est for overall effect. Z = 0 7.1.9 Sertraline versus a ersani 1994 ubtotal (95% CI) leterogeneity: Not applica est for overall effect. Z = 0 7.1.10 Sertraline versus aresani 1994 ubtotal (95% CI) leterogeneity: Not applica est for overall effect. Z = 0 7.1.10 Sertraline versus chargava 2012 ordenza 2011 ubtotal (95% CI) leterogeneity: Tau² = 0.00 est for overall effect. Z = 0	24 (P = imipram 8.76 7.4 (Chi² = 0.60 (P = ilofepram 13.5 ble .13 (P = ilofepram 13.5 ble .15 (P = ilofepram 16 ble .75 (P = ilofepram 14.23 14.44 (Chi² = 0.73 (P = ilofepram 14.23 (P = ilofe	0.22) ine 5.63 9.6 1.14, df = 0.11) nine 11.4 0.90) line 4.6 6.5 1.00) df = 0.46)	21 15 36 36 36 45 45 45 45 29 29 31 31 31 (P=	11.21 11.7 0.71); 13.8 8.8 16 13.67 12.71 0.98);	9.45 8.1 P = 0% 8.4 3 6.1 4.74 11.8 P = 0%	29 15 44 36 36 36 27 27 27 30 30 28 58	1.5% 3.7% 3.1% 3.1% 2.4% 2.6% 2.6% 2.6% 5.0%	-0.47 [-1.20, 0.26] -0.36 [-0.81, 0.08] -0.03 [-0.47, 0.41] -0.03 [-0.47, 0.41] -0.20 [-0.32, 0.73] -0.20 [-0.32, 0.73] -0.00 [-0.50, 0.50] -0.00 [-0.50, 0.50] -0.13 [-0.37, 0.64] -0.14 [-0.23, 0.50]	+ + -10 -5 0 5

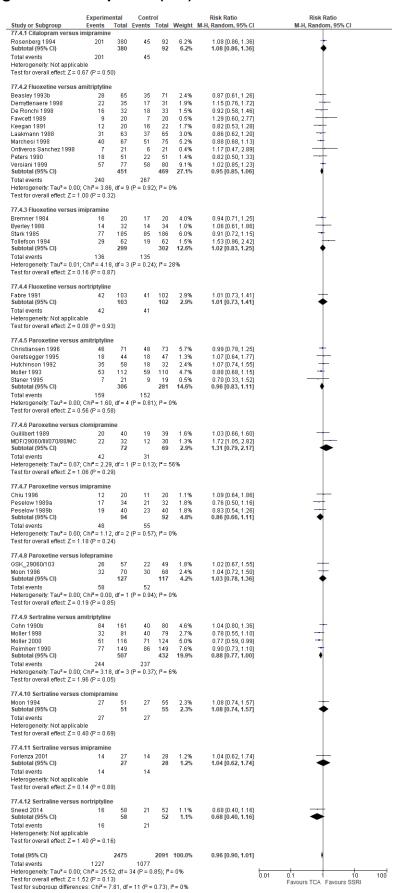
1 Figure 412: Depression symptomatology change score

itudy or Subgroup 7.2.1 Fluoxetine versus an easley 1993b	Mean	erimental SD	Total	Mean	Control SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
rasley 1993h			· Juli	valii	30	. Juli	, . orgint	,	74,11414011,007001
acicy rocop	-12.9	9.9	65	-11.6	10.3	71	3.4%	-0.13 [-0.46, 0.21]	+
emyttenaere 1998		.21366824	35		2.99416098	31	2.5%	0.45 [-0.04, 0.94]	
e Ronchi 1998		.50659605		-12.56	6.3688225	33	2.5%	0.20 [-0.29, 0.68]	
awcett 1989		.69041576	19		5.94011784	19	1.8%	-0.35 [-0.99, 0.29]	Ī
larchesi 1998		.37264222	67		4.59401785	75	3.5%	0.13 [-0.20, 0.46]	J
reskorn 1991 Juleman 1997	-10.1 -10.2 1	7.8 68522996.	29 15	-7.9 -15.0	6.1 2.31516738	31 15	2.4% 1.4%	-0.31 [-0.82, 0.20]	
ersiani 1999	-16.2 1.	7.3	77	-18.1	7.5	79	3.6%	-1.11 [-1.88, -0.33] 0.20 [-0.11, 0.52]	
ubtotal (95% CI)	-10.0	1.5	339	-10.1	7.5	354	20.9%	-0.03 [-0.28, 0.21]	
leterogeneity: Tau² = 0.07;	Chi ² = 16.9°	6. df = 7 (P :		I ² = 59%	6				1
est for overall effect: Z = 0.2			0.02/		•				
7.2.2 Fluoxetine versus cl	omipramin	е							
loguera 1991	-18.09 3.	.36235037	60	-17.94	3.56975489	60	3.3%	-0.04 [-0.40, 0.31]	+
opert 1989	-18.2 4.	.77074418	54	-16.6	5.38516481	46	3.0%	-0.31 [-0.71, 0.08]	
i ubtotal (95% CI) leterogeneity: Tau² = 0.00; i	∩hi² – ∩ aa	df = 1 /P =	114 0.33\:B	= nos		106	6.3%	-0.16 [-0.43, 0.10]	•
est for overall effect: Z = 1.2			0.52), 1	- 070					
7.2.3 Fluoxetine versus im	nipramine								
errano-Blanco 2006	-12.7 6.	.17413962	49	-12.9	6.22253967	45	3.0%	0.03 [-0.37, 0.44]	+
tark 1985	-11	10.1	185	-12	10.1	185	4.3%	0.10 [-0.11, 0.30]	
ollefson 1994	-10	6.7	62	-9.1	8	60	3.3%	-0.12 [-0.48, 0.23]	
ubtotal (95% CI)			296			290	10.6%	0.04 [-0.12, 0.20]	†
leterogeneity: Tau² = 0.00; (est for overall effect: Z = 0.5			0.57); P	°= 0%					
		′							
7.2.4 Fluoxetine versus no khondzadeh 2003	-16.82	11.08	17	-20.3	8.12	20	1.8%	0.36 [-0.30, 1.01]	+
lashemi 2012	-16.96	4.96		-13.14	4.68	49	2.9%	-0.79 [-1.20, -0.37]	
ubtotal (95% CI)			65			69	4.7%	-0.24 [-1.36, 0.87]	
leterogeneity: Tau ² = 0.57; (0.004);	I ² = 88%	Ó				
est for overall effect: Z = 0.4									
7.2.5 Paroxetine versus a								- 0	
9060/299	-14.3	9.35		-14.39	8.39	100	3.8%	0.01 [-0.27, 0.29]	
9060 07 001	-13.08	10.2191		-13.31	11.1051	13	1.4%	0.02 [-0.76, 0.81]	
eushle 2003		.99332963	40	-13.5	7.61072012	40 167	2.7%	0.48 [0.03, 0.92]	
reed 1999 tiuro 2000		.81452126		-15.08 -10.6	7.61073912	157	4.2%	-0.36 [-0.59, -0.14]	
liura 2000 Ioller 1993	-9.2 -187 5	11.5 49272246.	102 72	-10.6 -20.4	11.1 4.49110232	114 68	3.9% 3.4%	0.12 [-0.14, 0.39] 0.34 [0.00, 0.67]	
taner 1995		.93851372	21		5.56866232	19	1.8%	0.34 [0.00, 0.67]	
ubtotal (95% CI)	0.2 7.	55001512	498	10.0	5.55555252	511	21.2%	0.15 [-0.12, 0.42]	
leterogeneity: Tau² = 0.09; •				6); I² = 7	5%				
est for overall effect: Z = 1.0	Jo (F = 0.28	"							
7.2.6 Paroxetine versus c							4 600	0.5014.10.000	
IDF/29060/III/070/88/MC	-20	8.59	24 24	-15	8.22	20 20	1.9% 1.9%	-0.58 [-1.19, 0.02]	
i ubtotal (95% CI) Istorogeneitz Not annlicah	lo		24			20	1.970	-0.58 [-1.19, 0.02]	•
leterogeneity: Not applicab 'est for overall effect: Z = 1.8		i)							
7.2.7 Paroxetine versus in									
7.2.7 Paroxeune versus in hiu 1996	-20.2	9.1	15	-15.3	8.4	15	1.5%	-0.54 [-1.28, 0.19]	_
abre 1992	-9.13	8.14	38	-7.62	8.09	37	2.7%	-0.18 [-0.64, 0.27]	
ubtotal (95% CI)	J. 1 J	0.14	53	1.02	0.08	52	4.2%	-0.28 [-0.67, 0.10]	
leterogeneity: Tau² = 0.00;	Chi² = 0.67	, df = 1 (P =		= 0%		_			1
									1
est for overall effect: Z = 1.4									
est for overall effect: Z = 1.4 7.2.8 Paroxetine versus lo	ofepramine)							
7.2.8 Paroxetine versus l o SK_29060/103	ofepramine -17.8	10.73	45	-17.1	9.6	36	2.8%	-0.07 [-0.51, 0.37]	1
7.2.8 Paroxetine versus lo SK_29060/103 Jubtotal (95% CI)	-17.8		45 45	-17.1	9.6	36 36	2.8% 2.8 %	-0.07 [-0.51, 0.37] - 0.07 [-0.51, 0.37]	
7.2.8 Paroxetine versus lo ISK_29060/103 Iubtotal (95% CI) Ieterogeneity: Not applicab	-17.8 le	10.73		-17.1	9.6				•
7.2.8 Paroxetine versus lo 8K_29060/103 ubtotal (95% CI) leterogeneity: Not applicab est for overall effect: Z = 0.3	-17.8 ile 30 (P = 0.76	10.73		-17.1	9.6				•
7.2.8 Paroxetine versus lo ISK_29060/103 ubtotal (95% CI) leterogeneily: Not applicab est for overall effect: Z = 0.3 7.2.9 Paroxetine versus n	-17.8 ile 30 (P = 0.78 ortriptyline	10.73	45			36	2.8%	-0.07 [-0.51, 0.37]	
7.2.8 Paroxetine versus lo .SK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab set for overall effect Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999	-17.8 ile 30 (P = 0.78 ortriptyline	10.73	45 29		9.6 2.58069758	36 27	2.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35]	-
7.2.8 Paroxetine versus lo ISK_29060/103 ubtotal (95% CI) leterogeneily. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI)	-17.8 de 30 (P = 0.76 ortriptyline -11.3	10.73	45			36	2.8%	-0.07 [-0.51, 0.37]	-
7.2.8 Paroxetine versus lo ISK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect: Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab	-17.8 ile 30 (P = 0.76 ortriptyline -11.3	10.73 3) 3.0528675	45 29			36 27	2.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35]	-
7.2.8 Paroxetine versus lo SRC 29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n luisant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 2.8	-17.8 le 30 (P = 0.76 ortriptyline -11.3 (le 87 (P = 0.00	10.73 3) 3.0528675	45 29			36 27	2.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35]	-
7.2.8 Paroxetine versus lo SEK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect: Z = 0.3 7.2.9 Paroxetine versus n lusant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect: Z = 2.8 7.2.10 Sertraline versus a	-17.8 Ile 30 (P = 0.76 Portriptyline -11.3 () Ile 87 (P = 0.00 Imitriptyline	10.73 3) 3 3.0528675 04)	29 29	-13.6	2.58069758	36 27 27	2.8% 2.2% 2.2%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35]	→
7.2.8 Paroxetine versus lo SIK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 2.8 7.2.10 Sertraline versus a lersani 1994	-17.8 lle 30 (P = 0.76 ortriptyline -11.3 (lle 87 (P = 0.00 unitriptyline -17 4.	10.73 3) 3.0528675 04) e .33128157	29 29 29	-13.6	2.58069758 4.04103947	27 27 27	2.8% 2.2% 2.2%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27]	
7.2.8 Paroxetine versus lo 1.9K _ 29060/103 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n tulsant 1999 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect. Z = 2.8 7.2.10 Sertraline versus a tersani 1994 donn 1990	-17.8 ile 30 (P = 0.76 ortriptyline -11.3 (solide 87 (P = 0.00 omitriptyline -17 413.3	10.73 3) 3.0528675 04) e .33128157 7.76	29 29 29	-13.6 -16 -14.2	2.58069758 4.04103947 7.76	27 27 27	2.8% 2.2% 2.2% 2.4% 3.6%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42]	- •
7.2.8 Paroxetine versus lo SEK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 2.8 7.2.10 Sertraline versus a ersani 1994 John 1990b loller 1998	-17.8 lie 30 (P = 0.76 ortriptyline -11.3	10.73 3) 3.0528675 04) e .33128157 7.76 9.3	29 29 29 31 121 62	-13.6 -16 -14.2 -16.5	2.58069758 4.04103947 7.76 9.4	27 27 27 30 64 59	2.8% 2.2% 2.2% 2.4% 3.6% 3.3%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67]	
7.2.8 Paroxetine versus lo ISK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 2.6 7.2.10 Sertraline versus a ersani 1994 ohn 1990b loller 1990 loller 1990	-17.8 le 30 (P = 0.76 ortriptyline -11.3	10.73 6) 9 3.0528675 04) 9 (33128157 7.76 9.3 7.2	29 29 29 31 121 62 100	-13.6 -16 -14.2 -16.5 -15.3	2.58069758 4.04103947 7.76 9.4 7.1	36 27 27 27 30 64 59 105	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67] 0.21 [-0.07, 0.48]	 + + +
7.2.8 Paroxetine versus lo 1.9K (29060/103 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect: Z = 0.3 7.2.9 Paroxetine versus n tulsant 1999 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect: Z = 2.8 7.2.10 Sertraline versus a tersani 1994 conn 1990b toller 1998 toller 2000 teimherr 1990	-17.8 le 30 (P = 0.76 ortriptyline -11.3 (c) le 87 (P = 0.00 omitriptyline -17 413.3 -13.6 -13.8 -11.66	10.73 3) 9 3.0528675 04) e .33128157 7.76 9.3 7.2 8.24	29 29 29 31 121 62 100 142	-13.6 -16 -14.2 -16.5 -15.3 -12.64	2.58069758 4.04103947 7.76 9.44 7.1 7.97	36 27 27 27 30 64 59 105 144	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.07, 0.48] 0.12 [-0.11, 0.35]	 •
7.2.8 Paroxetine versus lo ISK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 2.6 7.2.10 Sertraline versus a ersani 1994 ohn 1990b loller 1990 loller 1990	-17.8 le 30 (P = 0.76 ortriptyline -11.3	10.73 6) 9 3.0528675 04) 9 (33128157 7.76 9.3 7.2	29 29 29 31 121 62 100	-13.6 -16 -14.2 -16.5 -15.3	2.58069758 4.04103947 7.76 9.4 7.1	36 27 27 27 30 64 59 105	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.64]	 •
7.2.8 Paroxetine versus Io SISK_29060/103 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n tulsant 1999 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect. Z = 2.8 7.2.10 Setrtaline versus a tersani 1994 tohn 1990b toller 1998 toller 2000 tetimherr 1990 ER 316 (FDA) teterogeneity. Tau² = 0.00; teterogeneity. Tau² = 0.00;	-17.8 ile 30 (P = 0.76 ortriptyline -11.3 (Section 1.1) ile 87 (P = 0.00 imitriptyline -17 413.3 -13.6 -13.8 -11.66 -8.9 Chi ² = 4.16,	10.73 3) 9 3.0528675 04) e 8.33128157 7.76 9.3 7.2 8.24 4.52 , df = 5 (P =	29 29 29 31 121 62 100 142 76 532	-13.6 -14.2 -16.5 -15.3 -12.64 -11.6	2.58069758 4.04103947 7.76 9.44 7.1 7.97	36 27 27 27 30 64 59 105 144 70	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.07, 0.48] 0.12 [-0.11, 0.35]	 •
7.2.8 Paroxetine versus lo SIK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect Z = 2.6 7.2.10 Sertraline versus a ersani 1994 ohn 1990b loller 1998 loller 2000 letimherr 1990 l	-17.8 ile 30 (P = 0.76 ortriptyline -11.3 (Section 1.1) ile 87 (P = 0.00 imitriptyline -17 413.3 -13.6 -13.8 -11.66 -8.9 Chi ² = 4.16,	10.73 3) 9 3.0528675 04) e 8.33128157 7.76 9.3 7.2 8.24 4.52 , df = 5 (P =	29 29 29 31 121 62 100 142 76 532	-13.6 -14.2 -16.5 -15.3 -12.64 -11.6	2.58069758 4.04103947 7.76 9.44 7.1 7.97	36 27 27 27 30 64 59 105 144 70	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.64]	 •
7.2.8 Paroxetine versus Io SISK_29060/103 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n tulsant 1999 ubtotal (95% CI) teterogeneity. Not applicab est for overall effect. Z = 2.8 7.2.10 Setrtaline versus a tersani 1994 tohn 1990b toller 1998 toller 2000 tetimherr 1990 ER 316 (FDA) teterogeneity. Tau² = 0.00; teterogeneity. Tau² = 0.00;	-17.8 lle 30 (P = 0.76 ortriptyline -11.3 lle 87 (P = 0.00 mittriptyline -17 4, -13.3 -13.6 -13.8 -11.66 -8.9 ChiF = 4.16, 62 (P = 0.00	10.73 3) 9 3.0528675 04) e 3.3128157 7.76 9.3 7.2 8.24 4.52 , df = 5 (P = 09)	29 29 29 31 121 62 100 142 76 532	-13.6 -14.2 -16.5 -15.3 -12.64 -11.6	2.58069758 4.04103947 7.76 9.44 7.1 7.97	36 27 27 27 30 64 59 105 144 70	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.64]	 •
7.2.8 Paroxetine versus lo SIK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab leterogeneity. Not applicab leterogeneity. Not applicab leterogeneity. Not applicab leterogeneity. Post particular leterogeneity. Post particular leterogeneity. Post particular leterogeneity. Post particular leterogeneity. Tau* = 0.00; leterogeneity. Tau* = 0.00; let for overall effect. Z = 2.6	-17.8 lie 30 (P = 0.76 ortriptyline -11.3 (Section 1.1) lie 87 (P = 0.00 mitriptyline -17 413.3 -13.6 -13.8 -11.66 -8.9 Chi ² = 4.16,62 (P = 0.00 mipramine	10.73 3) 9 3.0528675 04) e 3.3128157 7.76 9.3 7.2 8.24 4.52 , df = 5 (P = 09)	29 29 29 31 121 62 100 142 76 532 0.53); F	-13.6 -16 -14.2 -16.5 -15.3 -12.64 -11.6 *= 0%	2.58069758 4.04103947 7.76 9.44 7.1 7.97	36 27 27 27 30 64 59 105 144 70	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.64]	
7.2.8 Paroxetine versus lo SIK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 2.8 7.2.10 Sertraline versus a lersani 1994 lobler 1998 loller 1998 loller 1998 loller 2000 letermern 1990 Leternyern 19	-17.8 lie 30 (P = 0.76 ortriptyline -11.3 (Section 1.1) lie 87 (P = 0.00 mitriptyline -17 413.3 -13.6 -13.8 -11.66 -8.9 Chi ² = 4.16,62 (P = 0.00 mipramine	10.73 3) 9 3.0528875 04) e 9.33128157 7.76 9.3 7.2 8.24 4.52 ,df= 5 (P = 199)	29 29 29 31 121 62 100 142 76 532 0.53); F	-13.6 -16 -14.2 -16.5 -15.3 -12.64 -11.6 *= 0%	2.58069758 4.04103947 7.76 9.4 7.1 7.97 11.49	36 27 27 27 30 64 59 105 144 70 472	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5% 20.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.87] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.35] 0.31 [-0.01, 0.84] 0.17 [0.04, 0.29]	 + + + + +
7.2.8 Paroxetine versus lo 1.9.8 (C. 29060/103 1.0.9.10 (195% CI) 1.0.9.2.9 Paroxetine versus n 1.0.9.9 Paroxetine versus a 1.0.9.9 Paroxetine versus i 1.0.9 Paroxetine versu	-17.8 lie 30 (P = 0.76 ortriptyline -11.3 (Sile 87 (P = 0.00 mitriptyline -17 413.3 -13.6 -13.8 -11.66 -8.9 Chi ² = 4.16, 62 (P = 0.00 mipramine -11.7 (-15.85)	10.73 3) 9 3.0528675 04) e 9.33128167 7.76 9.3 7.2 8.24 4.52 ,df= 5 (P = 19) 2.7227835 11.89	31 121 62 100 142 76 532 0.53); F	-13.6 -16.6 -14.2 -16.5 -15.3 -12.64 -11.6	2.58069758 4.04103947 7.76 9.4 7.1 7.97 11.49	36 27 27 30 64 59 105 144 72	2.8% 2.2% 2.2% 3.6% 3.3% 4.1% 3.5% 20.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.67] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.35] 0.31 [-0.01, 0.64] 0.17 [0.04, 0.29]	 + + + + +
7.2.8 Paroxetine versus lo SK_29060/103 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 0.3 7.2.9 Paroxetine versus n lulsant 1999 ubtotal (95% CI) leterogeneity. Not applicab est for overall effect. Z = 2.8 7.2.10 Sertraline versus a lersani 1994 con 1990 loller 1998 loller 1990 leterogeneity. Tau* = 0.00; est for overall effect. Z = 2.8 7.2.11 Sertraline versus in chargava 2012 orienza 2001 leterogeneity. Tau* = 0.00; leterogeneity. Tau* = 0.01; leterogeneity. Tau* = 0.11; leterogeneity. Tau* = 0.11; leterogeneity. Tau* = 0.11;	-17.8 Itel 30 (P = 0.76 30 (P = 0.76 -11.3 3) Itel 87 (P = 0.00 mitriptyline -17 413.8 -13.8 -11.66 -8.9 Chi ² = 4.16,62 (P = 0.00 mipramine -11.7 215.85 Chi ² = 2.60,0	10.73 3) 3.0528675 04) e 3.3128157 7.76 9.3 7.2 8.24 4.52 ,df = 5 (P = 09) 2.7227835 11.89 ,df = 1 (P =	31 121 62 100 142 76 532 0.53); F	-13.6 -16.6 -14.2 -16.5 -15.3 -12.64 -11.6	2.58069758 4.04103947 7.76 9.4 7.1 7.97 11.49	36 27 27 27 30 64 59 105 144 70 472	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5% 20.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.87] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.35] 0.31 [-0.01, 0.84] 0.17 [0.04, 0.29]	 + + + + +
7.2.8 Paroxetine versus lo SK_29060/103 ubtotal (95% CI) eterogeneity. Not applicable est for overall effect. Z = 0.3 7.2.9 Paroxetine versus nulsant 1999 ubtotal (95% CI) eterogeneity. Not applicable est for overall effect. Z = 2.8 7.2.10 Sertraline versus alersani 1994 ohn 1990bioller 1998 loller 2000 elemberr 1990 ER 315 (FDA) eterogeneity. Tau² = 0.00; est for overall effect. Z = 2.8 7.2.11 Sertraline versus in hargava 2012 orlenza 2001 ubtotal (95% CI) leterogeneity. Tau² = 0.01; est for overall effect. Z = 2.8 7.2.11 Sertraline versus in hargava 2012 orlenza 2001 ubtotal (95% CI) leterogeneity. Tau² = 0.11; est for overall effect. Z = 0.11;	-17.8 Itel 30 (P = 0.76 30 (P = 0.76 -11.3 3) Itel 87 (P = 0.00 mitriptyline -17 413.8 -13.8 -11.66 -8.9 Chi ² = 4.16,62 (P = 0.00 mipramine -11.7 215.85 Chi ² = 2.60,0	10.73 3) 3.0528675 04) e 3.3128157 7.76 9.3 7.2 8.24 4.52 ,df = 5 (P = 09) 2.7227835 11.89 ,df = 1 (P =	29 29 31 121 62 100 142 76 532 0.53); F	-13.6 -16.6 -14.2 -16.5 -15.3 -12.64 -11.6	2.58069758 4.04103947 7.76 9.4 7.1 7.97 11.49	36 27 27 27 30 64 59 105 144 472 30 472	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.5% 20.8% 2.3% 4.6%	0.80 [0.25, 1.35] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.07, 0.48] 0.12 [-0.11, 0.35] 0.31 [-0.01, 0.64] 0.17 [0.04, 0.29] 0.54 [0.02, 1.05] -0.07 [-0.80, 0.46] 0.23 [-0.36, 0.83]	
7.2.8 Paroxetine versus lo 1.9.8 (C. 29060/103 1.0.9.10 (195% CI) 1.0.9.2.9 Paroxetine versus n 1.0.9.9 Paroxetine versus a 1.0.9.9 Paroxetine versus i 1.0.9 Paroxetine versu	-17.8 le 30 (P = 0.76 30 (P = 0.76 -11.3 (Section 11) -11.3 (P = 0.00 -17	10.73 3) 9 3.0528675 04) e 3.3128157 7.76 9.3 7.2 8.24 4.52 , df = 5 (P = 09) 2.7227835 11.89 , df = 1 (P = 4)	31 121 162 100 142 76 532 0.53); F	-13.6 -14.2 -16.5 -15.3 -15.3 -11.6 *= 0%	2.58069758 4.04103947 7.76 9.4 7.1 7.97 11.49 3.26046009 10.46	36 27 27 27 30 64 59 105 144 472 30 472	2.8% 2.2% 2.2% 2.4% 3.6% 3.3% 3.8% 4.1% 3.5% 20.8%	-0.07 [-0.51, 0.37] 0.80 [0.25, 1.35] 0.80 [0.25, 1.35] -0.24 [-0.74, 0.27] 0.12 [-0.19, 0.42] 0.31 [-0.05, 0.87] 0.21 [-0.07, 0.48] 0.12 [-0.11, 0.35] 0.31 [-0.01, 0.84] 0.17 [0.04, 0.29]	

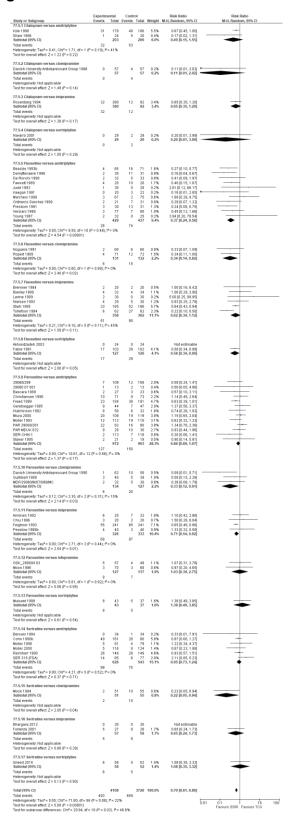
1 Figure 413: Remission (ITT)

Study or Subgroup 77.3.1 Citalopram versus amitriptyline	Experim Events		Contr Events		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Kyle 1998	96	179	99	186	11.3%	1.01 [0.83, 1.22]	
Subtotal (95% CI)	96	179	99	186	11.3%	1.01 [0.83, 1.22]	†
Total events Heterogeneity: Not applicable	90		99				
Test for overall effect: Z = 0.08 (P = 0.94)							
77.3.2 Citalopram versus clomipramine							
Danish University Antidepressant Group 1986	14	57	31	57	4.3%	0.45 [0.27, 0.75]	_
Subtotal (95% CI) Total events	14	57	31	57	4.3%	0.45 [0.27, 0.75]	•
Heterogeneity: Not applicable	14		31				
Test for overall effect: Z = 3.04 (P = 0.002)							
77.3.3 Citalopram versus nortriptyline							
Navarro 2001	20	29	25	29	8.6%	0.80 [0.60, 1.06]	_
Subtotal (95% CI) Total events	20	29	25	29	8.6%	0.80 [0.60, 1.06]	•
Heterogeneity: Not applicable	20		23				
Test for overall effect: Z = 1.54 (P = 0.12)							
77.3.4 Fluoxetine versus amitriptyline							
Beasley 1993b	11	65	15	71	2.6%	0.80 [0.40, 1.62]	
Fawcett 1989 Keegan 1991	4 14	20 20	5 13	20 22	1.1% 5.1%	0.80 [0.25, 2.55] 1.18 [0.75, 1.86]	
Subtotal (95% CI)	14	105	13	113	8.9%	1.03 [0.72, 1.47]	+
Total events	29		33				
Heterogeneity: Tau² = 0.00; Chi² = 1.23, df = 2 (Test for overall effect: Z = 0.15 (P = 0.88)	r = 0.54); l²	= 0%					
77.3.5 Fluoxetine versus imipramine	4.4	00	4.5	00	2.50	0.70 % 44.4.00	
Levine 1989 Tollefson 1994	11 20	30 62	15 14	30 62	3.5% 3.5%	0.73 [0.41, 1.32] 1.43 [0.80, 2.56]	- Ţ-
Subtotal (95% CI)		92		92	7.0%	1.02 [0.53, 1.98]	*
Total events Heterogeneity: Tau² = 0.14; Chi² = 2.51, df = 1 (31 D = 0.11\: R	- enoc	29				
Heterogeniety. Tau* = 0.14, Cri* = 2.51, ut = 1 (Test for overall effect: Z = 0.07 (P = 0.94)	P = 0.11), F	= 00%					
77.3.6 Paroxetine versus amitriptyline Geretsegger 1995	22	44	18	47	4.9%	1.31 [0.82, 2.08]	<u></u>
Hutchinson 1992	38	58	18	32	6.8%	1.16 [0.81, 1.67]	-
Moller 1993	49	112	54	110	8.6%	0.89 [0.67, 1.18]	<u> </u>
Subtotal (95% CI) Total events	109	214	90	189	20.3%	1.05 [0.84, 1.32]	Ť
Heterogeneity: Tau² = 0.01; Chi² = 2.44, df = 2 (= 18%					
Test for overall effect: Z = 0.44 (P = 0.66)							
77.3.7 Paroxetine versus clomipramine							
Danish University Antidepressant Group 1990	12	62	26	58	3.6%	0.43 [0.24, 0.77]	
Guillibert 1989 MDF/29060/III/070/88/MC	20 17	40 32	19 11	39 30	5.2% 3.7%	1.03 [0.66, 1.60] 1.45 [0.82, 2.57]	T.
Subtotal (95% CI)		134		127	12.4%	0.87 [0.45, 1.69]	*
Total events	49	7 700	56				
Heterogeneity: Tau² = 0.27; Chi² = 9.33, df = 2 (Fest for overall effect: Z = 0.41 (P = 0.68)	P = 0.009); I	-= /9%					
77.3.8 Paroxetine versus imipramine Feighner 1993	59	241	63	241	8.0%	0.94 [0.69, 1.27]	4
Subtotal (95% CI)		241		241	8.0%	0.94 [0.69, 1.27]	*
Total events	59		63				
Heterogeneity: Not applicable Test for overall effect: Z = 0.42 (P = 0.68)							
77.3.9 Paroxetine versus lofepramine Moon 1996	33	70	32	68	6.9%	1.00 [0.70, 1.43]	
Subtotal (95% CI)		70	32	68	6.9%	1.00 [0.70, 1.43]	+
Total events	33		32				
Heterogeneity: Not applicable Test for overall effect: Z = 0.01 (P = 0.99)							
77.3.10 Paroxetine versus nortriptyline	40	40	24	27	5.000	0.70 (0.50 4.04)	
Mulsant 1999 Subtotal (95% CI)	19	43 43	21	37 37	5.3% 5.3%	0.78 [0.50, 1.21] 0.78 [0.50, 1.21]	•
Total events	19		21				-
Heterogeneity: Not applicable Test for overall effect: Z = 1.12 (P = 0.26)							
77.3.11 Sertraline versus imipramine							
Forlenza 2001 Subtotal (95% CI)	13	27 27	11	28 28	3.4% 3.4%	1.23 [0.67, 2.24] 1.23 [0.67, 2.24]	-
	13		11			[]	T
Total events							
Total events Heterogeneity: Not applicable							
Total events							
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline							
Total events -leterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline Sneed 2014	14	58 58	19	52 52	3.6%	0.66 [0.37, 1.18]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline	14	58 58	19 19	52 52	3.6% 3.6%	0.66 [0.37, 1.18] 0.66 [0.37, 1.18]	•
Total events -leterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline Sneed 2014 Subtotal (95% CI) Total events -leterogeneity: Not applicable							-
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline Sneed 2014 Subtotal (95% CI) Total events							•
Total events -leterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline Sneed 2014 Subtotal (95% CI) Total events -leterogeneity: Not applicable				52			•
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.66 (P = 0.51) 77.3.12 Sertraline versus nortriptyline Sneed 2014 Subtotal (95% Ct) Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.40 (P = 0.16)	14 486	58 1249	19 509	52	3.6%	0.66 [0.37, 1.18]	0.01 0.1 10 100

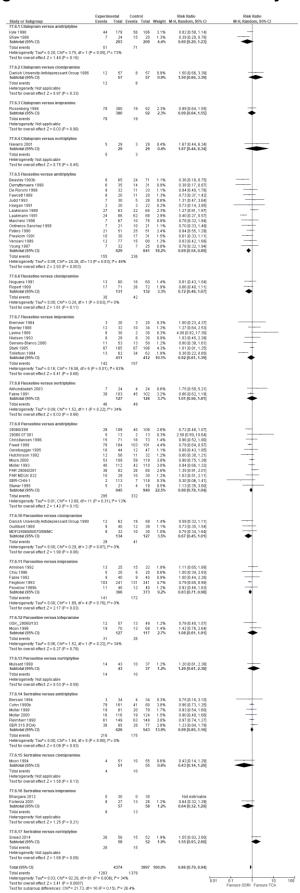
1 Figure 414: Response (ITT)



1 Figure 415: Discontinuation due to SE



1 Figure 416: Discontinuation due to any reason including SE



1 Figure 417: Sleep endpoint

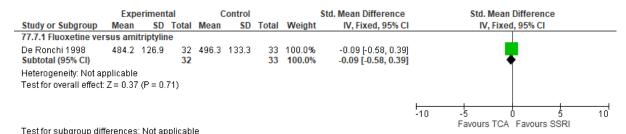
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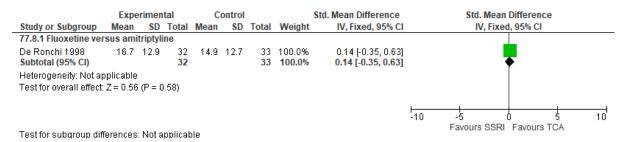
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3 Figure 418: Functional impairment endpoint



6 More severe: Fluoxetine + long-term psychodynamic

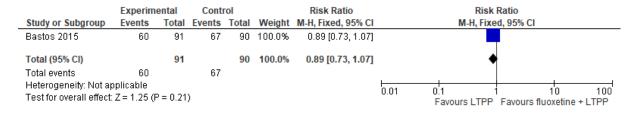
psychotherapy individual versus long-term psychodynamic

8 psychotherapy individual

9 Figure 419: Depression symptomatology endpoint

	Expe	erimen	tal	C	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bastos 2015	4.16	2.52	62	5.28	3.59	73	100.0%	-0.35 [-0.70, -0.01]	
Total (95% CI)			62			73	100.0%	-0.35 [-0.70, -0.01]	•
Heterogeneity: Not ap Test for overall effect:			0.04)						-10 -5 0 5 10 Favours fluoxetine + LTPP Favours LTPP

11 Figure 420: Remission (ITT)



13 Figure 421: Discontinuation due to any reason

	Experim	ental	Contr	rol		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
Bastos 2015	29	91	17	90	100.0%	1.69 [1.00, 2.85]	-	
Total (95% CI)		91		90	100.0%	1.69 [1.00, 2.85]	•	
Total events Heterogeneity: Not a Test for overall effect		° = 0.05	17				0.01 0.1 1 10 Favours fluoxetine + LTPP Favours LTPP	100

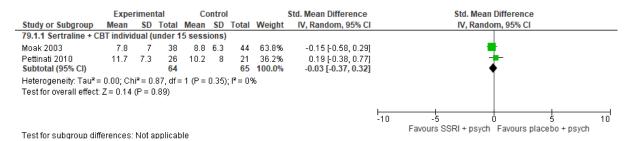
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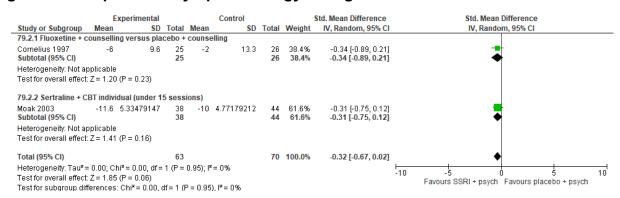
7

2 More severe: SSRI + psych intervention versus placebo +3 psych intervention

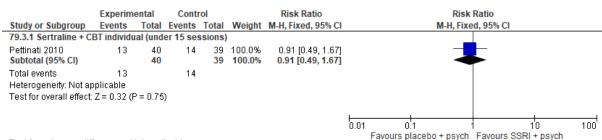
4 Figure 422: Depression symptomatology endpoint



6 Figure 423: Depression symptomatology change score

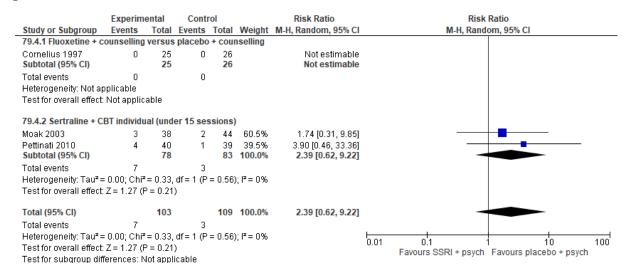


8 Figure 424: Remission (ITT)

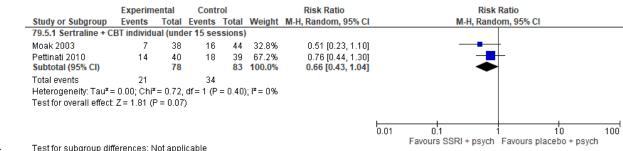


9 Test for subgroup differences: Not applicable

1 Figure 425: Discontinuation due to SE



3 Figure 426: Discontinuation due to any reason including SE



4 Test for subgroup differences: Not applicable

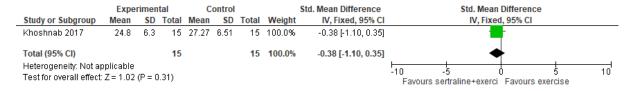
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6 More severe: Sertraline + supervised high intensity exercise

- individual versus supervised high intensity exercise
- individual

9 Figure 427: Depression symptomatology endpoint



11 Figure 428: Depression symptomatology change score

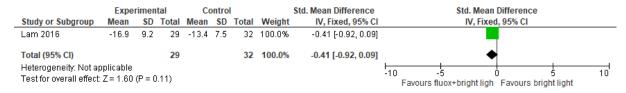
	Exp	eriment	tal	Co	ontro	I		Std. Mean Difference		Std. Mean	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% CI		
Khoshnab 2017	-4.53	12.55	15	-2.13	6.2	15	100.0%	-0.24 [-0.95, 0.48]		-			
Total (95% CI)			15			15	100.0%	-0.24 [-0.95, 0.48]		•	•		
Heterogeneity: Not ap Test for overall effect:	•		52)						-10 - Favours se	t 5 rtraline+exerci	0 Favours exer	t 5 cise	10

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1 More severe: Fluoxetine + bright light therapy versus bright2 light therapy

3 Figure 429: Depression symptomatology change score

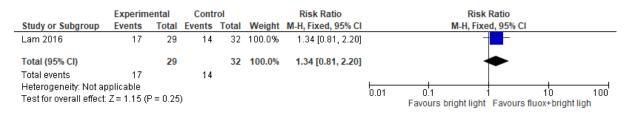


5 Figure 430: Remission (ITT)

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7 Figure 431: Response (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Lam 2016	22	29	16	32	100.0%	1.52 [1.01, 2.27]	-
Total (95% CI)		29		32	100.0%	1.52 [1.01, 2.27]	•
Total events	22		16				
Heterogeneity: Not ap Test for overall effect	• •	P = 0.04)				0.01 0.1 1 10 100 Favours bright light Favours fluox+bright ligh

9 Figure 432: Discontinuation due to SE

	Experim	ental	Contr	rol		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
Lam 2016	1	29	1	32	100.0%	1.10 [0.07, 16.85]		
Total (95% CI)		29		32	100.0%	1.10 [0.07, 16.85]		
Total events	1		1					
Heterogeneity: Not ap Test for overall effect:	•	P = 0.94)				0.01 0.1 1 10 Favours fluox+bright light Favours bright light	100

11 Figure 433: Discontinuation due to any reason including SE

	Experim	ental	Contr	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Lam 2016	2	29	4	32	100.0%	0.55 [0.11, 2.79]	
Total (95% CI)		29		32	100.0%	0.55 [0.11, 2.79]	
Total events	2		4				
Heterogeneity: Not ap Test for overall effect:	•	° = 0.47)				0.01 0.1 1 10 100 Favours fluox+bright ligh Favours bright light

12 13

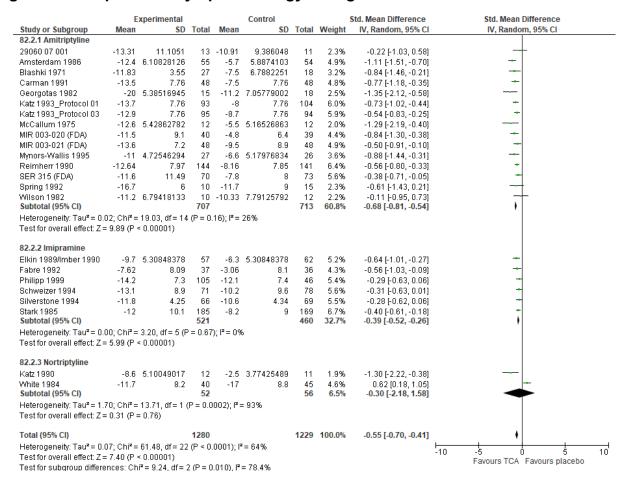
1 More severe: TCAs versus placebo

3

2 Figure 434: Depression symptomatology endpoint

		erimen			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
82.1.1 Amitriptyline									
Amsterdam 1986	12.1	8.59	55	17.7	8.59	54	13.3%	-0.65 [-1.03, -0.26]	*
Blashki 1971	5.73	5.09	27	11.4	9.6	18	6.5%	-0.77 [-1.39, -0.15]	
Georgotas 1982	8.5	8.13	15	17.4	10.18	18	4.9%	-0.93 [-1.66, -0.21]	
McCallum 1975	10.3	8.1	12	16.8	7.8	12	3.8%	-0.79 [-1.63, 0.05]	
Mynors-Wallis 1995	8.1	7.1	27	11.8	7.3	26	7.9%	-0.51 [-1.05, 0.04]	
Spring 1992	8.5	5.3	10	13.1	9.8	15	4.0%	-0.53 [-1.35, 0.28]	
Wilson 1982	14.6	9.73	10	14.67	11.12	12	3.8%	-0.01 [-0.85, 0.83]	.
Subtotal (95% CI)			156			155	44.2%	-0.62 [-0.85, -0.39]	♦
Heterogeneity: Tau² = 0.00	0; Chi²=	3.38, d	f=6 (P	= 0.76)	$ \mathbf{l}^2 = 0\%$	6			
Test for overall effect: Z = 5	5.30 (P <	0.000	01)						
82.1.2 Imipramine									
Barge-Schaapveld 2002	8.9	6.2	23	12.5	6.3	26	7.4%	-0.57 [-1.14, 0.01]	
Byerley 1988	13.7	8.5	24	19.7	6.5	16	5.9%	-0.76 [-1.41, -0.10]	
Elkin 1989/Imber 1990	9.8	7.8	57	13.2	7.8	62	14.3%	-0.43 [-0.80, -0.07]	+
Silverstone 1994	13.5	7.9	66	13.8	7.7	69	15.7%	-0.04 [-0.38, 0.30]	+
Subtotal (95% CI)			170			173	43.3%	-0.38 [-0.68, -0.07]	•
Heterogeneity: Tau ² = 0.04	4: Chi²=	5.46. d	f= 3 (P	= 0.14)	: I² = 45	%			
Test for overall effect: Z = 3									
	•								
82.1.3 Nortriptyline									
Katz 1990	13.1	6.7	12	21.2	5.7	11	3.3%	-1.25 [-2.16, -0.34]	
Subtotal (95% CI)			12			11	3.3%	-1.25 [-2.16, -0.34]	•
Heterogeneity: Not applica	able								
Test for overall effect: Z = 3	2.70 (P =	0.007)	1						
82.1.4 Lofepramine/imipr	amine								
Feighner 1982	11.86	7.24	68	15.86	8.43	21	9.3%	-0.53 [-1.02, -0.03]	.
Subtotal (95% CI)			68			21	9.3%	-0.53 [-1.02, -0.03]	◆
Heterogeneity: Not applica	able								
Test for overall effect: Z = 2	2.08 (P =	0.04)							
Total (95% CI)			406			360	100.0%	-0.52 [-0.69, -0.35]	•
Heterogeneity: Tau ² = 0.02	2: Chi≅=	15 02		(P = 0.1	24): 2 =			[,]	
Test for overall effect: Z = 5				V = 0.2	/, 1 =	2070			-10 -5 _ 0 5 10
Test for subgroup differen				(P = 0	27) 12-	22.7%			Favours TCA Favours placebo
1 COLIGI Sabaloap allielell	oco. Om	- 3.00	, ui – c	, ,, – 0.	217.1 -	22.1 70			

1 Figure 435: Depression symptomatology change score



3 Figure 436: Remission (ITT)

2

	Experim		Contr			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
82.3.1 Amitriptyline							
Mynors-Wallis 1995	16	31	8	30	17.8%	1.94 [0.98, 3.84]	
Subtotal (95% CI)		31		30	17.8%	1.94 [0.98, 3.84]	-
Total events	16		8				
Heterogeneity: Not appli	cable						
Test for overall effect: Z =	= 1.89 (P = 0	0.06)					
82.3.2 Imipramine							
Elkin 1989/Imber 1990	21	63	10	62	18.4%	2.07 [1.06, 4.02]	-
Feighner 1993	63	241	31	244	30.2%	2.06 [1.39, 3.04]	- -
Subtotal (95% CI)		304		306	48.5%	2.06 [1.47, 2.89]	◆
Total events	84		41				
Heterogeneity: Tau ² = 0.0	00; Chi² = 0	.00, df=	1 (P = 0	.99); l ^a :	= 0%		
Test for overall effect: Z=	= 4.20 (P < 0	0.0001)					
82.3.3 Nortriptyline							
Georgotas 1986	13	28	2	30	6.1%	6.96 [1.72, 28.15]	
Nair 1995	12	38	2	35	5.9%	5.53 [1.33, 22.97]	
Reynolds 1999a	14	25	10	22	21.7%	1.23 [0.69, 2.19]	-
Subtotal (95% CI)		91		87	33.6%	3.25 [0.80, 13.18]	
Total events	39		14				
Heterogeneity: Tau ² = 1.1	19; Chi² = 9	.47, df=	2 (P = 0	.009); P	= 79%		
Test for overall effect: Z =	= 1.65 (P = 0	0.10)					
Total (95% CI)		426		423	100.0%	2.08 [1.44, 3.01]	•
Total events	139		63				
Heterogeneity: Tau ² = 0.0	08; Chi² = 8	.25. df=	5 (P = 0	.14); l² :	= 39%		
Test for overall effect: Z=			, -	21.			0.01 0.1 1 10 100 Favours placebo Favours TCA

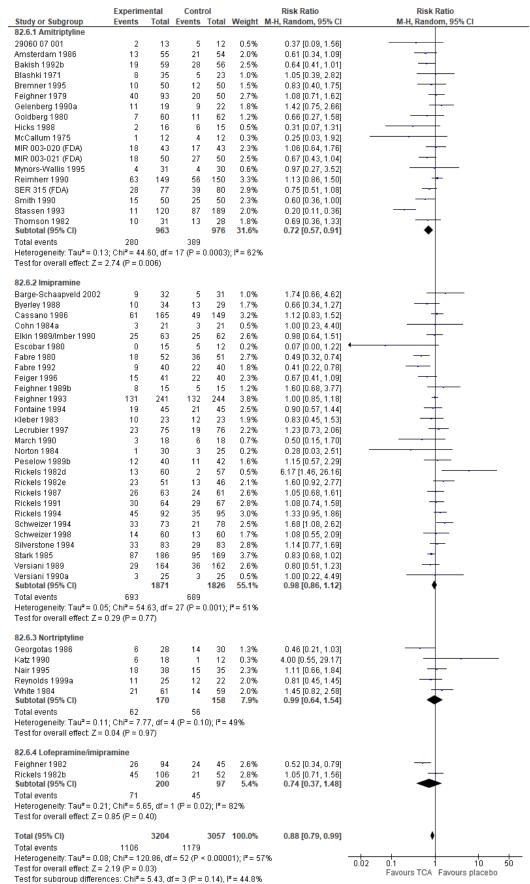
1 Figure 437: Response (ITT)

Study or Subgroup	Experim		Contr		Woight	Risk Ratio	Risk Ratio
Study or Subgroup 32.4.1 Amitriptyline	Events	Total	Events	TOTAL	weight	M-H, Random, 95% CI	M-H, Random, 95% CI
	24	E E	15	E 1	2.00	2.02.04.24.2.241	
Amsterdam 1986	31	55	15	54	3.0%	2.03 [1.24, 3.31]	
lakish 1992b	34	59	20	56	3.2%	1.61 [1.07, 2.44]	
remner 1995	29	50	17	50	3.1%	1.71 [1.08, 2.68]	
elenberg 1990a	6	19	6	22	1.8%	1.16 [0.45, 3.00]	<u> </u>
Foldberg 1980	27	60	27	62	3.2%	1.03 [0.69, 1.54]	\top
Kusalic 1993	10	13	6	15	2.4%	1.92 [0.97, 3.82]	
/IIR 003-020 (FDA)	14	43	5	43	1.9%	2.80 [1.11, 7.09]	
/IIR 003-021 (FDA)	31	50	21	50	3.3%	1.48 [1.00, 2.18]	
Reimherr 1990	86	149	49	150	3.6%	1.77 [1.35, 2.31]	-
3mith 1990	24	50	12	50	2.8%	2.00 [1.13, 3.54]	
Stassen 1993	85	120	65	189	3.7%	2.06 [1.64, 2.59]	🔭
Subtotal (95% CI)		668		741	31.9%	1.72 [1.49, 1.97]	▼
Fotal events	377		243				
Heterogeneity: Tau² = 0.01; C			0 (P = 0.2)	29); l = =	16%		
est for overall effect: Z = 7.6	1 (P < 0.00	1001)					
32.4.2 Imipramine							
Syerley 1988	14	34	4	20	1 704	2 99 14 40 9 021	
Syeney 1988 Cassano 1986	14 65			140	1.7%	2.99 [1.10, 8.07]	<u></u>
		165	51 s	149	3.5%	1.15 [0.86, 1.54]	
Escobar 1980	14	15	6 12	12	2.7%	1.87 [1.04, 3.34]	<u>-</u>
Feiger 1996 Feighner 1990h	25	41	12	40	2.9%	2.03 [1.19, 3.46]	
Feighner 1989b Fontaine 1994	8	15	5	15	2.0%	1.60 [0.68, 3.77]	
Fontaine 1994	22	45 75	14	45	2.9%	1.57 [0.93, 2.66]	<u> </u>
_ecrubier 1997	49	75	48	76	3.6%	1.03 [0.82, 1.31]	T
Peselow 1989a	21	32	14	39	3.0%	1.83 [1.12, 2.98]	
Peselow 1989b	23	40	14	42	2.9%	1.73 [1.04, 2.86]	
Philipp 1999	70	110	29	47	3.6%	1.03 [0.79, 1.35]	Ţ
Rickels 1982d	30	60	29	57	3.4%	0.98 [0.69, 1.41]	
Rickels 1982e	23	51	19	46	3.1%	1.09 [0.69, 1.73]	T
Rickels 1991	26	64	14	67	2.8%	1.94 [1.12, 3.38]	
Rickels 1994	31	92	27	95	3.2%	1.19 [0.77, 1.82]	 -
Rickels 1995_Study 006-1	26	41	23	36	3.4%	0.99 [0.71, 1.39]	†
Rickels 1995_Study 006-2	24	38	15	42	3.0%	1.77 [1.10, 2.84]	
3chweizer 1994	26	73	25	78	3.1%	1.11 [0.71, 1.74]	+
3chweizer 1998	37	60	21	60	3.2%	1.76 [1.18, 2.62]	
Bilverstone 1994	33	83	35	83	3.3%	0.94 [0.65, 1.36]	+
Stark 1985	85	186	39	169	3.5%	1.98 [1.44, 2.72]	-
/ersiani 1989	152	164	157	162	3.9%	0.96 [0.91, 1.01]	1.
Subtotal (95% CI)		1484		1389	64.8%	1.36 [1.13, 1.64]	◆
Fotal events	804		601				
Heterogeneity: Tau² = 0.14; C		•	20 (P < 0	.00001); I² = 86%		
Test for overall effect: $Z = 3.1$	9 (P = 0.00	11)					
22.4.3 Nortriptulino							
32.4.3 Nortriptyline	_	4.0		4.0	0.70/	1.07/0.05 00.00	
Katz 1990	7	18	1	12	0.7%	4.67 [0.65, 33.26]	
Subtotal (95% CI)	_	18		12	0.7%	4.67 [0.65, 33.26]	
Fotal events	7		1				
Heterogeneity: Not applicable		N.					
Test for overall effect: Z = 1.5	4 (F = 0.12	9					
32.4.4 Lofepramine/imipram	nine						
Feighner 1982	53	94	9	45	2.6%	2.82 [1.53, 5.19]	
Subtotal (95% CI)	33	94	9	45	2.6%	2.82 [1.53, 5.19]	•
Fotal events	53	0-7	9	40	2.070	2.02 [1100] 0.10]	
			9				
Heterogeneity: Not applicabl Fest for overall effect: Z = 3.3		ingi					
restrui uveran ellett. Z = 3.3	5 (F = 0.0C	ເດລ)					
Fotal (95% CI)		2264		2187	100.0%	1.51 [1.27, 1.80]	•
Fotal events	1241	2207	854	2.07	7001070	1.01 [1.21, 1.00]	•
		07 df— 1		00004	ان اع – oo∞		
Jotorogopoity: TouZ = 0.000 C			3.3 IF S H				
Heterogeneity: Tau² = 0.20; C Test for overall effect: Z = 4.6		•	JO (1 O	.0000,	,, r = 00 %		0.01 0.1 1 10

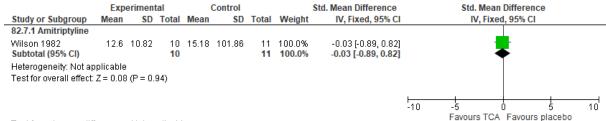
1 Figure 438: Discontinuation due to SE

tudy or Subgroup	Experime Events		Contr		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
2.5.1 Amitriptyline	210110	.oui E	Comes	. Juli	rroigitt	in manuoling 35/8 Cl	m-n, nundom, 35% Ci
9060 07 001	2	13	2	12	1.6%	0.92 [0.15, 5.56]	
msterdam 1986	11	55	3	54	2.9%	3.60 [1.06, 12.20]	<u> </u>
lakish 1992b	10	59	5	56	3.7%	1.90 [0.69, 5.21]	
lashki 1971	7	35	4	23	3.2%	1.15 [0.38, 3.49]	
remner 1995	5	50	2	50	1.9%	2.50 [0.51, 12.29]	
eighner 1979	12	93	3	50	2.9%	2.15 [0.64, 7.27]	
elenberg 1990a	8	19	6	22	4.4%	1.54 [0.65, 3.66]	
oldberg 1980	2	60	2	62	1.4%	1.03 [0.15, 7.10]	
licks 1988	0	16	0	15		Not estimable	
lcCallum 1975	1	12	2	12	1.1%	0.50 [0.05, 4.81]	
IR 003-020 (FDA)	10	43	8	43	4.6%	1.25 [0.55, 2.86]	
IR 003-021 (FDA)	9	50	9	50	4.5%	1.00 [0.43, 2.31]	
lynors-Wallis 1995	3	31	2	30	1.7%	1.45 [0.26, 8.09]	
eimherr 1990	28	149	3	150	3.0%	9.40 [2.92, 30.24]	
ER 315 (FDA)	6	77	6	80	3.3%	1.04 [0.35, 3.08]	
mith 1990	10	50	0	50	0.7%	21.00 [1.26, 348.93]	
homson 1982	7	31	0	28	0.7%	13.59 [0.81, 227.66]	+
ubtotal (95% CI)		843		787	41.6%	1.79 [1.21, 2.66]	•
otal events	131		57				
leterogeneity: Tau² = 0	.20; Chi ² :	= 22.51, 0	f= 15 (P = 0.1	$0); I^2 = 33^4$	%	
est for overall effect: Z			`		· ·		
	,	ŕ					
2.5.2 Imipramine							
yerley 1988	4	34	4	29	2.6%	0.85 [0.23, 3.11]	
assano 1986	17	165	5	149	3.8%	3.07 [1.16, 8.12]	
ohn 1984a	3	21	1	21	1.1%	3.00 [0.34, 26.56]	
scobar 1980	0	15	0	12		Not estimable	
eiger 1996	12	41	0	40	0.7%	24.40 [1.49, 398.83]	
eighner 1989b	5	15	Ō	15	0.7%	11.00 [0.66, 182.87]	
eighner 1993	85	241	21	244	7.3%	4.10 [2.63, 6.38]	
ontaine 1994	6	45	1	45	1.2%	6.00 [0.75, 47.85]	 -
leber 1983	Ō	23	Ó	23		Not estimable	
ecrubier 1997	10	75	4	76	3.2%	2.53 [0.83, 7.72]	 -
larch 1990	0	18	2	18	0.6%	0.20 [0.01, 3.89]	
lorton 1984	Ö	30	ō	25	0.070	Not estimable	
eselow 1989b	3	40	1	42	1.1%	3.15 [0.34, 29.04]	
hilipp 1999	1	110	Ö	47	0.6%	1.30 [0.05, 31.28]	
tickels 1982e	7	51	3	46	2.6%	2.10 [0.58, 7.66]	 -
Rickels 1991	13	64	5	67	3.8%	2.72 [1.03, 7.20]	<u> </u>
Rickels 1994	20	92	8	95	4.9%	2.58 [1.20, 5.57]	
chweizer 1994	18	73	3	78	3.0%	6.41 [1.97, 20.86]	
chweizer 1998	2	60	3	60	1.6%	0.67 [0.12, 3.85]	
ilverstone 1994	10	83	6	83	3.9%	1.67 [0.63, 4.38]	
tark 1985	52	186	8	169	5.3%	5.91 [2.89, 12.07]	
ersiani 1989	7	164	1	162	1.2%	6.91 [0.86, 55.57]	
ersiani 1990a	1	25	Ö	25	0.6%	3.00 [0.13, 70.30]	
ubtotal (95% CI)		1671	Ŭ	1571	50.0%	3.07 [2.27, 4.15]	•
otal events	276		76			[,]	
leterogeneity: Tau² = 0		= 22.76 n		P = 0.2	5): P = 179	96	
est for overall effect: Z				- 0.2	0),1 - 11	,0	
SS. 101 OFFICIAL CHECK Z	1.52 (1	- 5.5000	./				
2.5.3 Nortriptyline							
eorgotas 1986	2	28	0	30	0.6%	5.34 [0.27, 106.70]	
atz 1990	6	18	1	12	1.3%	4.00 [0.55, 29.17]	
air 1995	10	38	1	35	1.3%	9.21 [1.24, 68.31]	
leynolds 1999a	2	25	1	22	1.0%	1.76 [0.17, 18.11]	
ubtotal (95% CI)	-	109	'	99	4.3%	4.47 [1.46, 13.70]	
otal events	20		3			[,]	
eterogeneity: Tau² = 0		= 1.17 df	_	: 0 76)·	J² = 0%		
est for overall effect: Z			- VI -	0.70),	. – 570		
20.101 07014II 01100L.Z	2.02 (1	- 0.000)					
2.5.4 Lofepramine/im	ipramine						
ickels 1982b	22	106	5	52	4.1%	2.16 [0.87, 5.38]	
ubtotal (95% CI)	22	106 106	Ü	52 52	4.170 4.1%	2.16 [0.87, 5.38]	
	22	100	5	JE	-T. 1 /0	2.10 [0.07, 3.30]	
otal events Ieterogeneity: Not anni			9				
leterogeneity: Not appl est for overall effect: Z		- 0.40\					
estioi overali ellett. Z	- 1.00 (P	- 0.10)					
otal (95% CI)		2729		2500	100.0%	2.42 [1.89, 3.10]	_
otal (95% CI) otal events	449	2123	141	2303	100.070	2.72 [1.03, 3.10]	•
otal evelity		- 67 67 -		D = 0 0	43: IZ = 04:5	04.	
otorogopoita: Touz - 0		– ar.ar. 0	n – 40 (r = 0.0	4), r=31'	AU.	0.01 0.1 1 10 1
eterogeneity: Tau² = 0 est for overall effect: Z							Favours TCA Favours placebo

1 Figure 439: Discontinuation due to any reason including SE

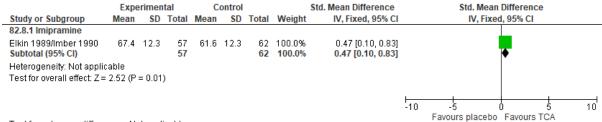


1 Figure 440: Depression symptomatology at 6-month follow-up



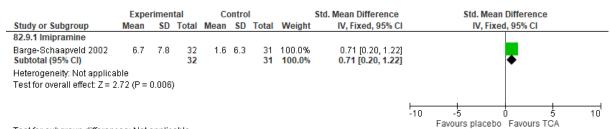
2 Test for subgroup differences: Not applicable

3 Figure 441: Global functioning endpoint



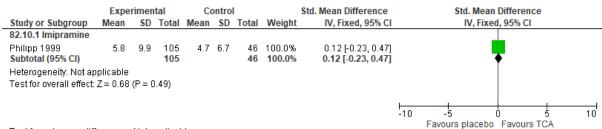
4 Test for subgroup differences: Not applicable

5 Figure 442: Quality of life change score



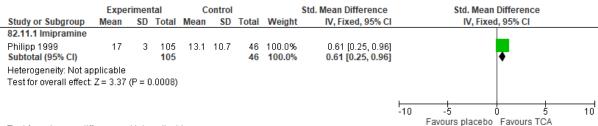
6 Test for subgroup differences: Not applicable

7 Figure 443: Quality of life physical health component endpoint



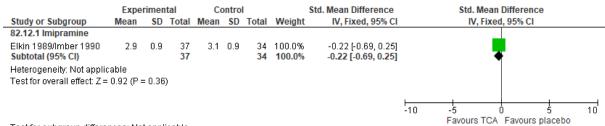
8 Test for subgroup differences: Not applicable

9 Figure 444: Quality of life mental health component endpoint



10 Test for subgroup differences: Not applicable

1 Figure 445: Interpersonal problems endpoint



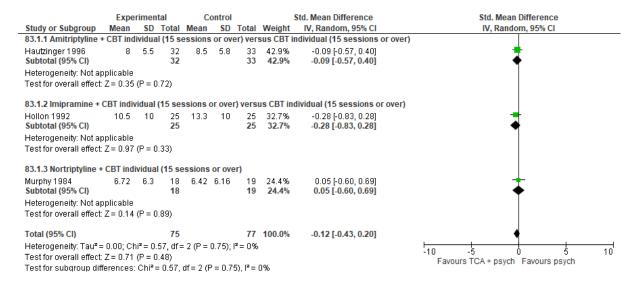
2 Test for subgroup differences: Not applicable

3

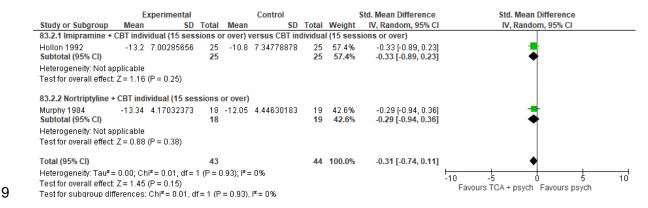
4 More severe: TCA + psych intervention versus psych

5 intervention

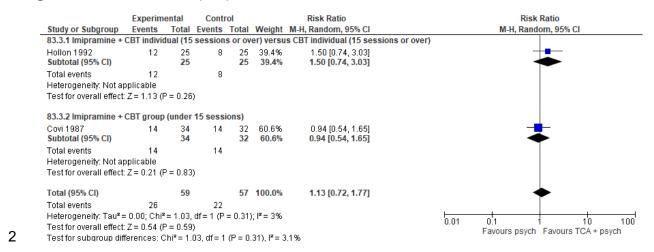
6 Figure 446: Depression symptomatology endpoint



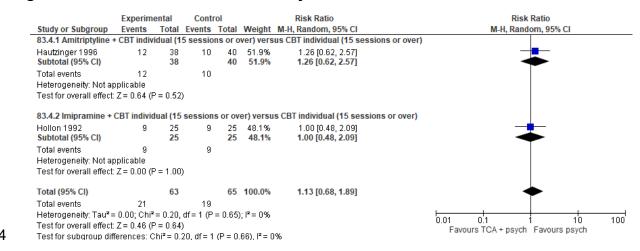
8 Figure 447: Depression symptomatology change score



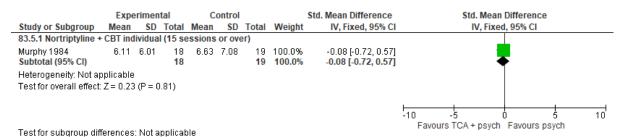
1 Figure 448: Remission (ITT)



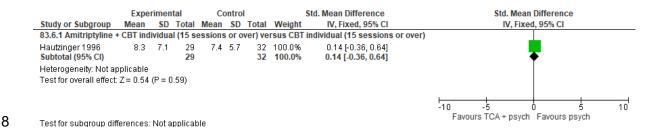
3 Figure 449: Discontinuation due to any reason



5 Figure 450: Depression symptomatology at 1-month follow-up



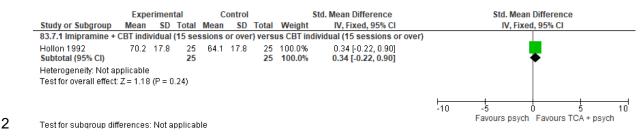
7 Figure 451: Depression symptomatology at 12-month follow-up



1 Figure 452: Global functioning endpoint

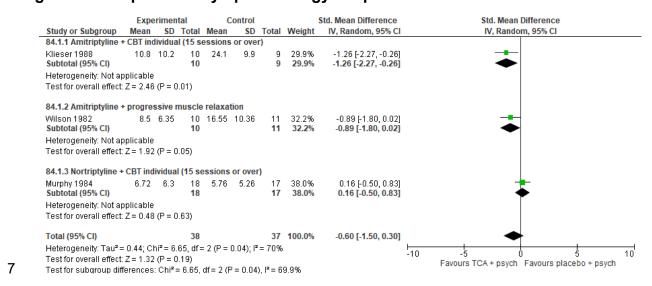
3

9

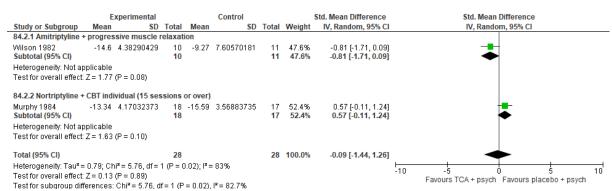


4 More severe: TCA + psych intervention versus placebo +
 5 psych intervention

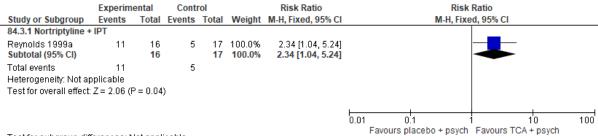
6 Figure 453: Depression symptomatology endpoint



8 Figure 454: Depression symptomatology change score

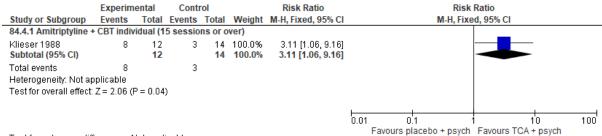


1 Figure 455: Remission (ITT)



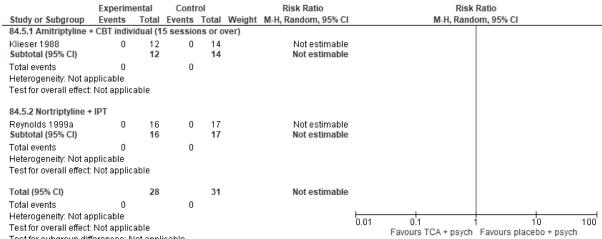
2 Test for subgroup differences: Not applicable

3 Figure 456: Response (ITT)



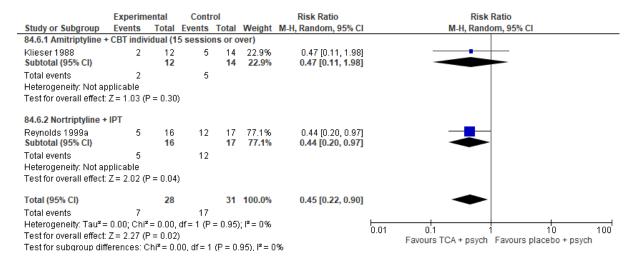
4 Test for subgroup differences: Not applicable

5 Figure 457: Discontinuation due to SE

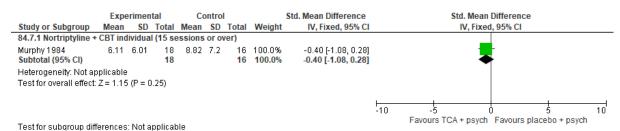


6 Test for subgroup differences: Not applicable

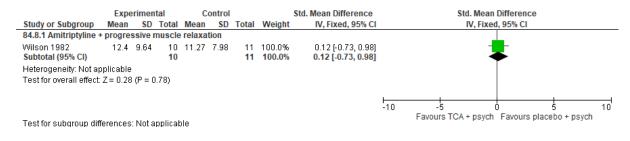
1 Figure 458: Discontinuation due to any reason including SE



3 Figure 459: Depression symptomatology at 1-month follow-up

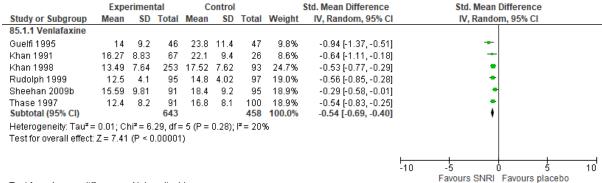


5 Figure 460: Depression symptomatology at 6-month follow-up



8 More severe: SNRIs versus placebo

9 Figure 461: Depression symptomatology endpoint



2

4

6

1 Figure 462: Depression symptomatology change score

		xperimental			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
85.2.1 Duloxetine									
Baldwin 2012	-16.8	9.77	149	-14.8	9.63	145	5.3%	-0.21 [-0.43, 0.02]	*
Boulenger 2014	-21.15	9.3	146	-11.7	9.55	158	5.2%	-1.00 [-1.24, -0.76]	•
Brannan 2005	-10.85	7.93	132	-10.27	7.81	136	5.2%	-0.07 [-0.31, 0.17]	†
Detke 2004	-11.55	4.84	186	-8.8	4.82	93	5.0%	-0.57 [-0.82, -0.31]	•
Eli Lilly HMAT-A	-6.31	6.3	81	-4.78	6.42	89	4.5%	-0.24 [-0.54, 0.06]	*
Higuchi 2009	-10	6.4	74	-8.3	5.8	145	4.7%	-0.28 [-0.56, -0.00]	+
Katona 2012	-15.8	9.7	147	-10.3	9.63	145	5.2%	-0.57 [-0.80, -0.33]	*
Mahableshwarkar 2013	-13.47	9.15	149	-10.5	9.28	149	5.3%	-0.32 [-0.55, -0.09]	-
Nierenberg 2007	-7.61	6.94	273	-5.97	6.79	137	5.5%	-0.24 [-0.44, -0.03]	+
Robinson 2014	-7.42	7.37	201	-7.15	7.51	95	5.1%	-0.04 [-0.28, 0.21]	†
Study F1J-MC-HMAQ - Study Group B Subtotal (95% CI)	-8	6.75	81 1619	-7.1	6.96	72 1364	4.3% 55.4%	-0.13 [-0.45, 0.19] - 0.34 [-0.51, -0.17]	†
Fest for overall effect: Z = 3.88 (P = 0.0) 3 5.2.2 V enlafaxine	,								
Guelfi 1995	-14.2	9.6	46	-4.8	11	47	3.3%	-0.90 [-1.33, -0.47]	-
Hewett 2010	-17	10.56	193	-13.2	10.64	186	5.6%	-0.36 [-0.56, -0.15]	-
Higuchi 2016	-15.17	10.08		-12.41	10.12	182	5.8%	-0.27 [-0.45, -0.09]	-
Khan 1991	-9.07	6.76	67		7.15960893	26	3.0%	-0.73 [-1.20, -0.27]	-
Mendels 1993	-14.8	9.64		-10.53	8.98	75	4.3%	-0.46 [-0.78, -0.13]	-
Schweizer 1994	-15.6	9.8	64	-10.2	9.6	78	4.1%	-0.55 [-0.89, -0.22]	+
Sheehan 2009b		7.32900744			6.86603233	95	4.6%	-0.46 [-0.75, -0.17]	-
/EN 600A-303 (FDA)	-10.14	8.45	69	-9.89	8.45	79	4.3%	-0.03 [-0.35, 0.29]	+
/EN 600A-313 (FDA)	-11.39	8.39	149	-9.49	8.2	75	4.7%	-0.23 [-0.51, 0.05]	+
VEN XR 367 (FDA)	-15.13	10.65	157	-13.1	10.63	81	4.9%	-0.19 [-0.46, 0.08]	-
Subtotal (95% CI)			1261			924	44.6%	-0.38 [-0.50, -0.25]	•
Heterogeneity: Tau² = 0.02; Chi² = 17.9	7, df = 9 ($P = 0.04$); $I^2 =$	50%						
Test for overall effect: $Z = 5.69$ (P < 0.0)	0001)								
Total (95% CI)			2880			2288	100.0%	-0.36 [-0.47, -0.25]	•
Heterogeneity: Tau² = 0.04; Chi² = 69.2	7, df = 20	(P < 0.00001)); I ² = 71	%					1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Test for overall effect: Z = 6.54 (P < 0.0)	0001)								-10 -5 U 5 Favours SNRI Favours placebo
Test for subaroup differences: Chi² = 0	.13. df = 1	$(P = 0.72)$. I^2	= 0%						r avours sivini ir avours placebo

1 Figure 463: Remission (ITT)

	Experim	ental	Contr	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
85.3.1 Duloxetine							
Baldwin 2012	52	157	49	152	4.6%	1.03 [0.75, 1.42]	+
Boulenger 2014	79	147	30	158	4.2%	2.83 [1.98, 4.04]	-
Brannan 2005	30	141	33	141	3.4%	0.91 [0.59, 1.41]	
Cutler 2009	55	151	42	157	4.4%	1.36 [0.98, 1.90]	-
Detke 2002a	55	128	39	139	4.5%	1.53 [1.10, 2.14]	→
Detke 2002b	53	123	18	122	3.1%	2.92 [1.82, 4.68]	
Detke 2004	92	188	28	93	4.3%	1.63 [1.15, 2.29]	
Eli Lilly HMAT-A	23	84	18	90	2.6%	1.37 [0.80, 2.35]	
Goldstein 2002	37	70	22	70	3.6%	1.68 [1.12, 2.54]	
Goldstein 2002	43	91	26	89	3.8%	1.62 [1.10, 2.39]	
Higuchi 2009	26	75	32	146	3.4%	1.58 [1.02, 2.45]	
Katona 2012	51	151	28	145	3.7%		
						1.75 [1.17, 2.61]	
Mahableshwarkar 2013	51	152	33	153	4.0%	1.56 [1.07, 2.27]	
Mahableshwarkar 2015a	38	152	41	161	3.9%	0.98 [0.67, 1.44]	
Nierenberg 2007	75	273	27	137	3.8%	1.39 [0.94, 2.06]	
Perahia 2006	82	196	33	99	4.6%	1.26 [0.91, 1.74]	T
Raskin 2007	55	207	15	104	2.7%	1.84 [1.10, 3.10]	
Robinson 2014	74	249	31	121	4.2%	1.16 [0.81, 1.66]	
Study F1J-MC-HMAQ - Study Group B Subtotal (95% CI)	32	82 2817	21	75 2352	3.3% 72.2 %	1.39 [0.89, 2.19] 1.48 [1.30, 1.70]	<u></u>
Total events	1003		566				
Heterogeneity: Tau² = 0.05; Chi² = 40.6 Test for overall effect: Z = 5.76 (P < 0.00		P = 0.00	(2); I² = 56	6%			
85.3.2 Venlafaxine							
Guelfi 1995	12	46	6	47	1.2%	2.04 [0.84, 4.98]	
Hewett 2009	94	187	63	197	5.5%	1.57 [1.23, 2.02]	-
Hewett 2010							
	108	198	71	187	5.9%	1 44 [1 15 1 80]	-
Levin 2013	108 26	198 51	71 30	187 52	5.9% 4.2%	1.44 [1.15, 1.80] 0.88 [0.62, 1.26]	+
Levin 2013 Nemeroff 2007	26	51	30	52	4.2%	0.88 [0.62, 1.26]	+
Nemeroff 2007	26 31	51 102	30 22	52 102	4.2% 3.1%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26]	
Nemeroff 2007 Rudolph 1999	26 31 35	51 102 100	30 22 17	52 102 98	4.2% 3.1% 2.8%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26] 2.02 [1.21, 3.35]	
Nemeroff 2007 Rudolph 1999 Sheehan 2009b	26 31 35 21	51 102 100 95	30 22 17 14	52 102 98 95	4.2% 3.1% 2.8% 2.2%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26] 2.02 [1.21, 3.35] 1.50 [0.81, 2.77]	
Nemeroff 2007 Rudolph 1999	26 31 35	51 102 100	30 22 17	52 102 98	4.2% 3.1% 2.8%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26] 2.02 [1.21, 3.35]	
Nemeroff 2007 Rudolph 1999 Sheehan 2009b Thase 1997	26 31 35 21	51 102 100 95 95	30 22 17 14	52 102 98 95 102	4.2% 3.1% 2.8% 2.2% 2.9%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26] 2.02 [1.21, 3.35] 1.50 [0.81, 2.77] 1.81 [1.10, 2.96]	
Nemeroff 2007 Rudolph 1999 Sheehan 2009b Thase 1997 Subtotal (95% CI)	26 31 35 21 32 359 34, df = 7 (P	51 102 100 95 95 874	30 22 17 14 19	52 102 98 95 102 880	4.2% 3.1% 2.8% 2.2% 2.9%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26] 2.02 [1.21, 3.35] 1.50 [0.81, 2.77] 1.81 [1.10, 2.96]	- - - - - - •
Nemeroff 2007 Rudolph 1999 Sheehan 2009b Thase 1997 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.02; Chi² = 11.0	26 31 35 21 32 359 34, df = 7 (P	51 102 100 95 95 874	30 22 17 14 19	52 102 98 95 102 880	4.2% 3.1% 2.8% 2.2% 2.9%	0.88 [0.62, 1.26] 1.41 [0.88, 2.26] 2.02 [1.21, 3.35] 1.50 [0.81, 2.77] 1.81 [1.10, 2.96]	- - - - •
Nemeroff 2007 Rudolph 1999 Sheehan 2009b Thase 1997 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.02; Chi² = 11.0 Test for overall effect: Z = 4.13 (P < 0.00)	26 31 35 21 32 359 04, df = 7 (P	51 102 100 95 95 874 = 0.14)	30 22 17 14 19 242 ; ² = 37%	52 102 98 95 102 880	4.2% 3.1% 2.8% 2.2% 2.9% 27.8%	0.88 (0.62, 1.26) 1.41 (0.88, 2.26) 2.02 (1.21, 3.35) 1.50 (0.81, 2.77) 1.81 (1.10, 2.96) 1.46 [1.22, 1.74]	- - - - •
Nemeroff 2007 Rudolph 1999 Sheehan 2009b Thase 1997 Subtotal (95% CI) Total events Heterogeneity: Tau* = 0.02; Chi* = 11.0 Test for overall effect: Z = 4.13 (P < 0.00) Total (95% CI) Total (95% CI) Total events	26 31 35 21 32 359 359 04, df = 7 (P 001)	51 102 100 95 95 874 = 0.14)	30 22 17 14 19 242 ; ₽= 37%	52 102 98 95 102 880	4.2% 3.1% 2.8% 2.2% 2.9% 27.8%	0.88 (0.62, 1.26) 1.41 (0.88, 2.26) 2.02 (1.21, 3.35) 1.50 (0.81, 2.77) 1.81 (1.10, 2.96) 1.46 [1.22, 1.74]	•
Nemeroff 2007 Rudolph 1999 Sheehan 2009b Thase 1997 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.02; Chi² = 11.0 Test for overall effect: Z = 4.13 (P < 0.00)	26 31 35 21 32 359 04, df = 7 (P 001) 1362 '1, df = 26 (l	51 102 100 95 95 874 = 0.14)	30 22 17 14 19 242 ; ₽= 37%	52 102 98 95 102 880	4.2% 3.1% 2.8% 2.2% 2.9% 27.8%	0.88 (0.62, 1.26) 1.41 (0.88, 2.26) 2.02 (1.21, 3.35) 1.50 (0.81, 2.77) 1.81 (1.10, 2.96) 1.46 [1.22, 1.74]	0.01 0.1 10 Favours placebo Favours SNRI

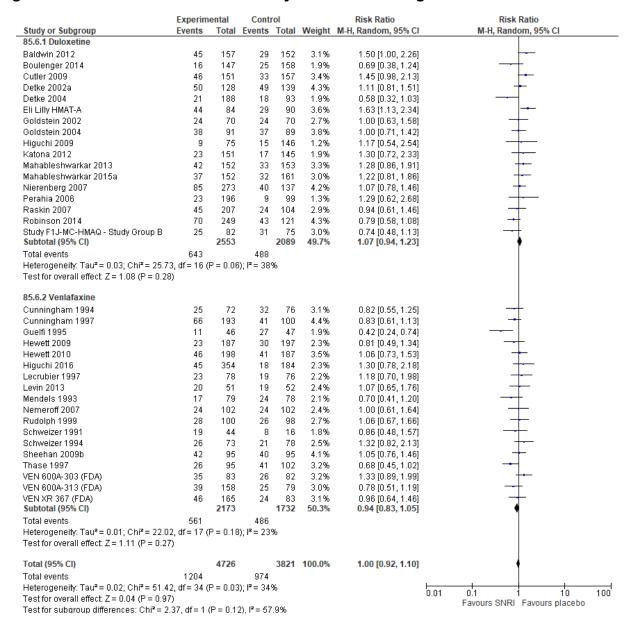
1 Figure 464: Response (ITT)

Study or Subgroup Event 85.4.1 Duloxetine 8 Baldwin 2012 8 Boulenger 2014 10 Brannan 2005 5 Cutler 2009 7 Detke 2002a 8 Detke 2004 12 Eli Lilly HMAT-A 2 Goldstein 2002 4 Goldstein 2004 4 Higuchi 2009 3 Katona 2012 9 Mahableshwarkar 2013 7 Mahableshwarkar 2015a 8 Nierenberg 2007 9 Perahia 2006 12 Raskin 2007 7 Robinson 2014 8 Subtotal (95% CI) 8 Total events 142 Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 1 Test for overall effect: Z = 6.66 (P < 0.00001) 8 85.4.2 Venlafaxine 142	5 157 8 147 5 141 3 151 3 128 5 123 8 188 8 84 2 70 4 91 8 75 3 75 3 152 6 152 0 152 2 273	68 51 54 55 58 33 41 24 33	152 158 141 157 139 122 93 90 70	4.2% 4.0% 3.4% 3.6% 4.1% 3.1% 3.9% 2.0% 3.2%	M-H, Random, 95% CI 1.21 [0.96, 1.52] 2.28 [1.78, 2.91] 1.02 [0.76, 1.37] 1.32 [1.01, 1.74] 1.55 [1.23, 1.96] 2.25 [1.63, 3.12] 1.54 [1.20, 1.98] 1.25 [0.79, 1.97]	M-H, Random, 95% CI
Baldwin 2012 8 Boulenger 2014 100 Brannan 2005 5 Cutter 2009 7 Detke 2002a 8 Detke 2002b 7 Detke 2004 12: Eli Lilly HMAT-A 22: Goldstein 2002 4 Goldstein 2002 4 Higuchi 2009 33 Katona 2012 9 Mahableshwarkar 2013 7 Mahableshwarkar 2015a 8 Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7 Robinson 2014 8 Study F1J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)	8 147 5 141 0 151 3 128 5 123 8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	51 54 55 58 33 41 24 33 27 56	158 141 157 139 122 93 90 70	4.0% 3.4% 3.6% 4.1% 3.1% 3.9% 2.0%	2.28 [1.78, 2.91] 1.02 [0.76, 1.37] 1.32 [1.01, 1.74] 1.55 [1.23, 1.96] 2.25 [1.63, 3.12] 1.54 [1.20, 1.98]	+ + + - - -
Boulenger 2014 10: Brannan 2005 5 Cuttler 2009 7: Detke 2002a 8: Detke 2002b 7: Detke 2004 12: Eli Lilly HMAT-A 2: Goldstein 2002 4: Goldstein 2004 4: Higuchi 2009 3: Katona 2012 9: Mahableshwarkar 2013 7: Mahableshwarkar 2015a 8: Nierenberg 2007 9: Perahia 2006 12: Raskin 2007 7: Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)	8 147 5 141 0 151 3 128 5 123 8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	51 54 55 58 33 41 24 33 27 56	158 141 157 139 122 93 90 70	4.0% 3.4% 3.6% 4.1% 3.1% 3.9% 2.0%	2.28 [1.78, 2.91] 1.02 [0.76, 1.37] 1.32 [1.01, 1.74] 1.55 [1.23, 1.96] 2.25 [1.63, 3.12] 1.54 [1.20, 1.98]	+ + + - -
Brannan 2005 5: Cutter 2009 7: Detke 2002a 8: Detke 2002b 7: Detke 2004 12: Eli Lilly HMAT-A 2: Goldstein 2002 4. Goldstein 2004 4. Higuchi 2009 3: Katona 2012 9: Mahableshwarkar 2013 7: Mahableshwarkar 2015a 8: Nierenberg 2007 9: Perahia 2006 12: Raskin 2007 7: Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% Cl) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	5 141 0 151 3 128 5 123 8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	54 55 58 33 41 24 33 27 56	141 157 139 122 93 90 70	3.4% 3.6% 4.1% 3.1% 3.9% 2.0%	1.02 [0.76, 1.37] 1.32 [1.01, 1.74] 1.55 [1.23, 1.96] 2.25 [1.63, 3.12] 1.54 [1.20, 1.98]	+ + - - -
Cutler 2009 7, Detke 2002a 8 Detke 2002b 7. Detke 2004 12; Eli Lilly HMAT-A 22 Goldstein 2002 4 Goldstein 2004 4 Higuehi 2009 31 Katona 2012 9, Mahableshwarkar 2013 7, Mahableshwarkar 2015a 8, Nierenberg 2007 9, Perahia 2006 12; Raskin 2007 7, Robinson 2014 8 Study F1J-MC-HMAQ - Study Group B 4, Subtotal (95% Cl) Total events 142; Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	0 151 3 128 5 123 8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	55 58 33 41 24 33 27 56	157 139 122 93 90 70	3.6% 4.1% 3.1% 3.9% 2.0%	1.32 [1.01, 1.74] 1.55 [1.23, 1.96] 2.25 [1.63, 3.12] 1.54 [1.20, 1.98]	+ + +
Detke 2002a 8 Detke 2002b 7 Detke 2004 12: Eli Lilly HMAT-A 2: Goldstein 2002 4 Goldstein 2004 4 Higuchi 2009 3 Katona 2012 9 Mahableshwarkar 2013 7: Mahableshwarkar 2015a 8 Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7: Robinson 2014 8 Study F1.J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)	3 128 5 123 8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	58 33 41 24 33 27 56	139 122 93 90 70	4.1% 3.1% 3.9% 2.0%	1.55 [1.23, 1.96] 2.25 [1.63, 3.12] 1.54 [1.20, 1.98]	+
Detke 2002b 7: Detke 2004 12: Eli Lilly HMAT-A 2: Goldstein 2002 4: Goldstein 2004 4: Higuchi 2009 3: Katona 2012 9: Mahableshwarkar 2013 7: Mahableshwarkar 2015a 8: Nierenberg 2007 9: Perahia 2006 12: Raskin 2007 7: Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)	5 123 8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	33 41 24 33 27 56	122 93 90 70	3.1% 3.9% 2.0%	2.25 [1.63, 3.12] 1.54 [1.20, 1.98]	
Detke 2004 12: Eli Lilly HMAT-A 2: Goldstein 2002 4 Goldstein 2004 4 Higuchi 2009 3: Katona 2012 9 Mahableshwarkar 2013 7: Mahableshwarkar 2015a 8 Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7 Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	8 188 8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	41 24 33 27 56	93 90 70	3.9% 2.0%	1.54 [1.20, 1.98]	
Eli Lilly HMAT-A 2: 30 Idstein 2002 4. 30 Idstein 2004 4. Higuchi 2009 3: Katona 2012 9. Mahableshwarkar 2013 7. Mahableshwarkar 2015a 8. Nierenberg 2007 9. Perahia 2006 12: Raskin 2007 7. Robinson 2014 8. Buddy F1J-MC-HMAQ - Study Group B 4. Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	8 84 2 70 4 91 8 75 3 151 6 152 0 152 2 273	24 33 27 56	90 70	2.0%		<u>_</u>
Goldstein 2002 4 Goldstein 2004 4 Higuchi 2009 3 Goldstein 2004 4 Higuchi 2009 3 Goldstein 2012 9 Mahableshwarkar 2013 7 Mahableshwarkar 2015a 8 Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7 Robinson 2014 8 Goldstein 2007 8 Goldstein 2008 8 Gold	2 70 4 91 8 75 3 151 6 152 0 152 2 273	33 27 56	70		1.25 [0.79, 1.97]	
Goldstein 2004 4 Higuchi 2009 3 Katona 2012 9 Mahableshwarkar 2013 8 Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7 Robinson 2014 8 Study F1J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)	4 91 8 75 3 151 6 152 0 152 2 273	27 56		2.204		T-
Higuchi 2009 33 Katona 2012 95 Mahableshwarkar 2013 76 Mahableshwarkar 2015a 86 Nierenberg 2007 97 Perahia 2006 12 Raskin 2007 77 Robinson 2014 86 Study F1J-MC-HMAQ - Study Group B 41 Subtotal (95% CI) Total events 142 Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine 36 Statona 2012 37 Sanda 2013 38 Sanda 2014 38 Sanda 2015 38 Sanda	8 75 3 151 6 152 0 152 2 273	56	89	J.2 N	1.27 [0.93, 1.74]	 -
Katona 2012 9 Mahableshwarkar 2013 7 Mahableshwarkar 2015a 8 Mierenberg 2007 9 Perahia 2006 12 Raskin 2007 7 Robinson 2014 8 Study F1J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) 142 Total events 142 Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Fest for overall effect: Z = 6.66 (P < 0.00001)	3 151 6 152 0 152 2 273			2.6%	1.59 [1.09, 2.33]	
Katona 2012 9 Mahableshwarkar 2013 7 Mahableshwarkar 2015a 8 Mierenberg 2007 9 Perahia 2006 12 Raskin 2007 7 Robinson 2014 8 Study F1J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) 142 Total events 142 Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Fest for overall effect: Z = 6.66 (P < 0.00001)	6 152 0 152 2 273	51	146	3.3%	1.32 [0.98, 1.79]	 •
Mahableshwarkar 2013 7: Mahableshwarkar 2015a 8: Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7 Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	6 152 0 152 2 273		145	3.9%	1.75 [1.36, 2.26]	-
Mahableshwarkar 2015a 81 Nierenberg 2007 9 Perahia 2006 12: Raskin 2007 7 Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 41 Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	0 152 2 273	48	153	3.5%	1.59 [1.20, 2.12]	-
Nierenberg 2007 9 Perahia 2006 12 Raskin 2007 7 Robinson 2014 8 Study F1J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) Fotal events 142 Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Fest for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine	2 273		161	3.9%	1.41 [1.10, 1.81]	-
Perahia 2006 12: Raskin 2007 7: Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% CI) Fotal events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Fest for overall effect: Z = 6.66 (P < 0.00001) 85.4.2 Venlafaxine			137	3.1%	1.28 [0.93, 1.78]	
Raskin 2007 7: Robinson 2014 8: Study F1MC-HMAQ - Study Group B 4: Subtotal (95% CI) Fotal events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 35.4.2 Venlafaxine			99	4.3%	1.28 [1.03, 1.59]	-
Robinson 2014 8: Study F1J-MC-HMAQ - Study Group B 4: Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)		19	104	2.1%		
Study F1J-MC-HMAQ - Study Group B 4 Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001) 35.4.2 Venlafaxine			121	3.5%	1.98 [1.27, 3.09]	
Subtotal (95% CI) Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Test for overall effect: Z = 6.66 (P < 0.00001)					0.93 [0.70, 1.23]	
Total events 142: Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Fest for overall effect: Z = 6.66 (P < 0.00001) 35.4.2 Venlafaxine	0 82 2817		75 2352	2.7% 64.5%	1.31 [0.90, 1.89] 1.44 [1.29, 1.60]	•
Heterogeneity: Tau² = 0.03; Chi² = 46.81, df = 1 Fest for overall effect: Z = 6.66 (P < 0.00001) 3 5.4.2 Venlafaxine		839				l'
Cunningham 1994 4'	7 72	41	76	3.7%	1.21 [0.93, 1.58]	 -
Hewett 2009 12			197	4.7%	1.39 [1.15, 1.67]	-
Hewett 2010 12			187	4.8%	1.32 [1.10, 1.58]	
	5 17		16	0.5%	0.94 [0.33, 2.65]	
= /	9 18	5	15	0.8%	1.50 [0.64, 3.52]	
_ecrubier 1997 6		48	76	4.4%	1.22 [0.99, 1.50]	_
		36	52	3.6%		
					0.91 [0.69, 1.20]	<u></u>
Nemeroff 2007 5			102	3.1%	1.38 [1.00, 1.90]	
Rudolph 1999 5.			98	3.4%	1.29 [0.96, 1.73]	
Schweizer 1994 3:			78	2.4%	1.50 [1.00, 2.24]	
Sheehan 2009b 3:			95	2.1%	1.52 [0.98, 2.37]	
Thase 1997 4			102	1.9%	2.39 [1.47, 3.86]	\ <u></u>
Subtotal (95% CI)	1086		1094	35.5%	1.31 [1.17, 1.45]	•
Fotal events 61: Heterogeneity: Tau² = 0.01; Chi² = 15.84, df = 1 Fest for overall effect: Z = 4.93 (P < 0.00001)		461 5); I² = 31	%			
Total (95% CI)			3446	100.0%	1.39 [1.29, 1.51]	
	3903	1300	0 170	100.070	1100 [1120, 1101]	'
	3903					I
Heterogeneity: Tau² = 0.03; Chi² = 66.23, df = 3 Test for overall effect: Z = 8.21 (P < 0.00001)	4		EEOC		0.0	

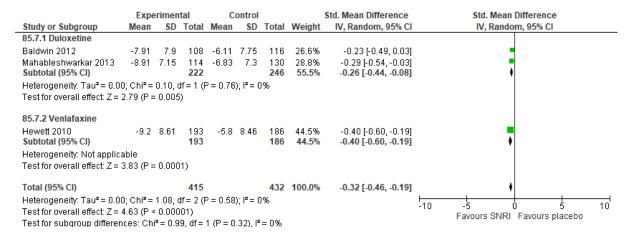
1 Figure 465: Discontinuation due to SE

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
85.5.1 Duloxetine							
Baldwin 2012	19	157	12	152	5.5%	1.53 [0.77, 3.05]	-
Boulenger 2014	7	147	7	158	3.0%	1.07 [0.39, 2.99]	
Brannan 2005	20	141	3	141	2.3%	6.67 [2.03, 21.93]	
Cutler 2009	20	151	7	157	4.2%	2.97 [1.29, 6.82]	_
Detke 2002a	16	128	4	139	2.8%	4.34 [1.49, 12.65]	
Detke 2002b	17	123	3	122	2.3%	5.62 [1.69, 18.69]	
Detke 2004	7	188	3	93	1.9%	1.15 [0.31, 4.36]	
Eli Lilly HMAT-A	13	84	3	90	2.2%	4.64 [1.37, 15.72]	
Goldstein 2002	7	70	3	70	2.0%	2.33 [0.63, 8.66]	
Goldstein 2004	14	91	8	89	4.3%	1.71 [0.76, 3.88]	+-
Higuchi 2009	3	75	5	146	1.7%	1.17 [0.29, 4.76]	
Katona 2012	15	151	6	145	3.6%	2.40 [0.96, 6.02]	
Mahableshwarkar 2013	17	152	7	153	4.0%	2.44 [1.04, 5.73]	-
Mahableshwarkar 2015a	10	152	4	161	2.5%	2.65 [0.85, 8.26]	+
Nierenberg 2007	20	273	8	137	4.5%	1.25 [0.57, 2.77]	
Perahia 2006	4	196	1	99	0.8%	2.02 [0.23, 17.84]	
Raskin 2007	20	207	9	104	4.9%	1.12 [0.53, 2.37]	
Robinson 2014	29	249	7	121	4.5%	2.01 [0.91, 4.46]	 • • •
Subtotal (95% CI)		2735		2277	56.9%	2.07 [1.62, 2.66]	◆
Total events	258		100				
Heterogeneity: Tau ² = 0.03	; Chi² = 19.	35, df=	17 (P = 0)	.31); l²	= 12%		
Test for overall effect: Z = 5	5.78 (P < 0.0	00001)					
85.5.2 Venlafaxine							
Cunningham 1994	13	72	3	76	2.2%	4.57 [1.36, 15.39]	
Cunningham 1997	23	193	2	100	1.7%	5.96 [1.43, 24.76]	
Guelfi 1995	4	46	3	47	1.6%	1.36 [0.32, 5.75]	
Hewett 2009	6	187	9	197	3.0%	0.70 [0.25, 1.93]	
Hewett 2010	16	198	11	187	5.0%	1.37 [0.65, 2.88]	
Higuchi 2016	18	354	2	184	1.6%	4.68 [1.10, 19.94]	
_		67	4	26	3.0%	1.36 [0.49, 3.75]	
Knan 1991	14	n/					
	14 11		-	76	2.7%	2 68 (0 89 8 05)	
Lecrubier 1997	14 11 2	78 51	4	76 52	2.7% 0.4%	2.68 [0.89, 8.05] 5.10 [0.25, 103,61]	
Lecrubier 1997 Levin 2013	11	78	4		0.4%	5.10 [0.25, 103.61]	
Lecrubier 1997 Levin 2013 Mendels 1993	11 2 10	78 51 79	4 0 7	52 78	0.4% 3.6%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007	11	78 51	4	52	0.4%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999	11 2 10 12	78 51 79 102	4 0 7 3	52 78 102	0.4% 3.6% 2.2% 0.8%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994	11 2 10 12 6 12	78 51 79 102 100 73	4 0 7 3 1 3	52 78 102 98	0.4% 3.6% 2.2% 0.8% 2.2%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b	11 2 10 12 6	78 51 79 102 100	4 0 7 3	52 78 102 98 78	0.4% 3.6% 2.2% 0.8%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997	11 2 10 12 6 12 8	78 51 79 102 100 73 95	4 0 7 3 1 3 7 6	52 78 102 98 78 95 102	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA)	11 2 10 12 6 12 8 10	78 51 79 102 100 73 95 95	4 0 7 3 1 3 7 6	52 78 102 98 78 95 102 82	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3% 0.9%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 600A-313 (FDA)	11 2 10 12 6 12 8	78 51 79 102 100 73 95	4 0 7 3 1 3 7 6	52 78 102 98 78 95 102	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 600A-313 (FDA)	11 2 10 12 6 12 8 10 15	78 51 79 102 100 73 95 95 83 158	4 0 7 3 1 3 7 6 1 5	52 78 102 98 78 95 102 82 79	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3% 0.9% 3.3%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62]	
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 800A-313 (FDA) VEN XR 367 (FDA) Subtotal (95% CI) Total events	11 2 10 12 6 12 8 10 15 17 15	78 51 79 102 100 73 95 95 83 158 165 2196	4 0 7 3 1 3 7 6 1 5 3	52 78 102 98 78 95 102 82 79 83 1742	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3% 0.9% 3.3% 2.2% 43.1%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44] 2.52 [0.75, 8.44]	•
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 500A-313 (FDA) VEN XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.11	11 2 10 12 6 12 8 10 15 17 15 212 ; Chi ^z = 22.	78 51 79 102 100 73 95 95 83 158 165 2196 42, df=	4 0 7 3 1 3 7 6 1 5 3	52 78 102 98 78 95 102 82 79 83 1742	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3% 0.9% 3.3% 2.2% 43.1%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44] 2.52 [0.75, 8.44]	•
Khan 1991 Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 600A-313 (FDA) VEN KOOA-313 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.11 Test for overall effect: Z = 4	11 2 10 12 6 12 8 10 15 17 15 212 ; Chi ^z = 22.	78 51 79 102 100 73 95 95 83 158 165 2196 42, df=	4 0 7 3 1 3 7 6 1 5 3	52 78 102 98 78 95 102 82 79 83 1742	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 0.9% 3.3% 2.2% 43.1% = 24%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44] 2.52 [0.75, 8.44] 2.13 [1.55, 2.93]	•
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 600A-313 (FDA) VEN XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.11 Test for overall effect: Z = 4	11 2 10 12 6 12 8 10 15 17 15 212 ; Chi ^z = 22.	78 51 79 102 100 73 95 95 83 158 165 2196 42, df=	4 0 7 3 1 3 7 6 1 5 3 74 17 (P = 0	52 78 102 98 78 95 102 82 79 83 1742	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3% 0.9% 3.3% 2.2% 43.1%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44] 2.52 [0.75, 8.44]	•
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 600A-313 (FDA) VEN XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.11 Test for overall effect: Z = 4 Total (95% CI) Total events	11 2 10 12 6 12 8 10 15 17 15 212 ; Chi ^z = 22.	78 51 79 102 100 73 95 83 158 165 2196 42, df= 000001)	4 0 7 3 1 3 7 6 1 5 3 74 17 (P = C	52 78 102 98 78 95 102 82 79 83 1742 1.17); I ²	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 3.3% 0.9% 3.3% 2.2% 43.1% = 24%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44] 2.52 [0.75, 8.44] 2.13 [1.55, 2.93]	•
Lecrubier 1997 Levin 2013 Mendels 1993 Nemeroff 2007 Rudolph 1999 Schweizer 1994 Sheehan 2009b Thase 1997 VEN 600A-303 (FDA) VEN 600A-313 (FDA) VEN XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.11 Test for overall effect: Z = 4	11 2 10 12 6 12 8 10 15 17 15 212 ; Chi ² = 22. i.65 (P < 0.0	78 51 79 102 100 73 95 83 158 165 2196 42, df= 000001) 4931 66, df=	4 0 7 3 1 3 7 6 1 5 3 74 17 (P = C	52 78 102 98 78 95 102 82 79 83 1742 1.17); I ²	0.4% 3.6% 2.2% 0.8% 2.2% 3.3% 0.9% 3.3% 2.2% 43.1% = 24%	5.10 [0.25, 103.61] 1.41 [0.57, 3.52] 4.00 [1.16, 13.75] 5.88 [0.72, 47.95] 4.27 [1.26, 14.54] 1.14 [0.43, 3.03] 1.79 [0.68, 4.73] 14.82 [2.00, 109.62] 1.70 [0.65, 4.44] 2.52 [0.75, 8.44] 2.13 [1.55, 2.93]	0.01 0.1 10 100

1 Figure 466: Discontinuation due to any reason including SE



3 Figure 467: Functional impairment change score

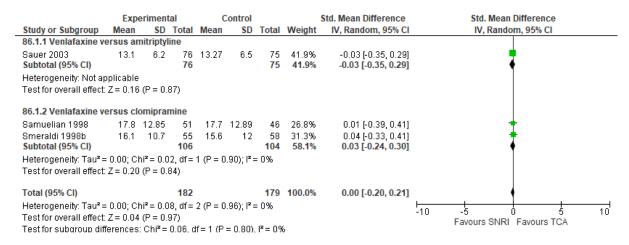


4

2

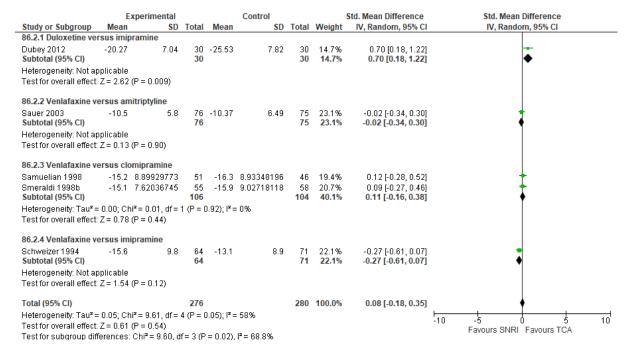
1 More severe: SNRIs versus TCAs

2 Figure 468: Depression symptomatology endpoint

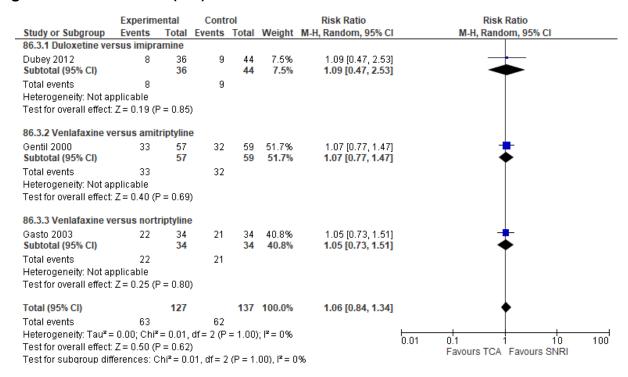


4 Figure 469: Depression symptomatology change score

3



1 Figure 470: Remission (ITT)



3 Figure 471: Response (ITT)

2

	Experim		Conti			Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
86.4.1 Duloxetine ve		amine					
Dubey 2012 Subtotal (95% CI)	22	36 36	24	44 44	8.4% 8.4%	1.12 [0.77, 1.63] 1.12 [0.77, 1.63]	*
Fotal events	22		24				
Heterogeneity: Not a	pplicable						
Test for overall effect	:: Z = 0.59 (F	P = 0.55)				
36.4.2 Venlafaxine v	ersus amit	triptylin	е				
Gentil 2000	43	57	44	59	26.8%	1.01 [0.82, 1.25]	†
Subtotal (95% CI)		57		59	26.8%	1.01 [0.82, 1.25]	•
Fotal events	43		44				
Heterogeneity: Not a							
Test for overall effect	:: Z = 0.11 (F	P = 0.91)				
36.4.3 Venlafaxine v	ersus clon	niprami	ne				
Bamuelian 1998	21	52	17	50	4.6%	1.19 [0.71, 1.97]	-
3meraldi 1998b	26	55	28	58	7.9%	0.98 [0.67, 1.44]	+
Subtotal (95% CI)		107		108	12.5%	1.05 [0.77, 1.43]	•
Total events	47		45				
Heterogeneity: Tau² :				= 0.55)); I² = 0%		
Test for overall effect	Z = 0.32 (F)	P = 0.75)				
86.4.4 Venlafaxine v	ersus imip	ramine					
Benkert 1996	44	85	50	82	16.4%	0.85 [0.65, 1.11]	-=
Lecrubier 1997	60	78	49	75	28.2%	1.18 [0.96, 1.45]	<u>+</u>
Bchweizer 1994	35	73	26	73	7.8%	1.35 [0.91, 1.99]	 -
Subtotal (95% CI)		236		230	52.3%	1.09 [0.84, 1.40]	•
Fotal events	139		125				
Heterogeneity: Tau ² :				= 0.08)); I ^z = 60%	·	
Test for overall effect	:: Z = 0.64 (F	° = 0.52)				
Total (95% CI)		436		441	100.0%	1.06 [0.95, 1.19]	,
Total events	251		238				
Heterogeneity: Tau² :	= 0.00; Chi²	= 5.71,	df=6 (P	= 0.46)); I² = 0%		0.01 0.1 1 10 10
Test for overall effect	,		•				Favours TCA Favours SNRI
Test for subaroup dit	fferences: C	$hi^2 = 0.$	30, df = 3	P = 0	.96), $I^2 = 0$	1%	. avodio 10/1 1 avodio Olviti

1 Figure 472: Discontinuation due to SE

	Experime	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
86.5.1 Duloxetine ve	rsus imipra	mine					
Dubey 2012 Subtotal (95% CI)	1	36 36	4	44 44	4.1% 4.1 %	0.31 [0.04, 2.61] 0.31 [0.04, 2.61]	
Total events	1		4				
Heterogeneity: Not ap							
Test for overall effect:	: Z = 1.08 (P	= 0.28)					
86.5.2 Venlafaxine v	oreue amitr	rintuline					
Gentil 2000	6 6	1 pty 11116	3	59	9.3%	2.07 [0.54, 7.88]	
Subtotal (95% CI)	U	57	3	59	9.3%	2.07 [0.54, 7.88]	
Total events	6	٠.	3		0.070	2.07 [0.0 1, 7.00]	
Heterogeneity: Not a	_		Ū				
Test for overall effect		= 0.29)					
86.5.3 Venlafaxine v		-			47.00	0.07.00.00.4.00	_
Samuelian 1998	7	52	10	50	17.0%	0.67 [0.28, 1.63]	
Smeraldi 1998b Subtotal (95% CI)	3	55 107	4	58 108	8.1% 25.1%	0.79 [0.19, 3.37] 0.70 [0.33, 1.50]	
Total events	10	101	14	100	25.170	0.70 [0.55, 1.50]	
Heterogeneity: Tau ² =		= 0.03.		= 0.85)	: I² = 0%		
Test for overall effect				0.00,	,. 02		
	,						
86.5.4 Venlafaxine v	-						
Benkert 1996	6	21	8	82	15.6%	2.93 [1.14, 7.53]	
Lecrubier 1997	11	78	10	75	19.4%	1.06 [0.48, 2.34]	_
Schweizer 1994	12	73 172	18	73 230	24.0% 58.9%	0.67 [0.35, 1.28]	
Subtotal (95% CI) Total events	29	1/2	36	230	30.9%	1.20 [0.53, 2.73]	
Heterogeneity: Tau² =		- 6 41		= 0.04)	· I² = 60%		
Test for overall effect:				- 0.04,	,,	,	
		,					
86.5.5 Venlafaxine v							
Gasto 2003	1	34	1	34	2.6%	1.00 [0.07, 15.34]	
Subtotal (95% CI)		34		34	2.6%	1.00 [0.07, 15.34]	
Total events	1 nalisahla		1				
Heterogeneity: Not ap Test for overall effect:		= 1.003					
restror overall effect.	. 2 - 0.00 (1	- 1.00,					
Total (95% CI)		406		475	100.0%	1.01 [0.64, 1.60]	*
Total events	47		58				
Heterogeneity: Tau ² =			,	= 0.21)	; I²= 28%	5	0.01 0.1 1 10 100
Test for overall effect	,						Favours SNRI Favours TCA
Test for subgroup dif	terences: Cl	hi* = 3.0	31, df = 4	(P=0.	51), $ ^2 = 0$	1%	

2

1 Figure 473: Discontinuation due to any reason including SE

	Experim		Contr			Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
86.6.1 Duloxetine ve	•						
Dubey 2012 Subtotal (95% CI)	6	36 36	14	44 44	5.3% 5.3%	0.52 [0.22, 1.22] 0.52 [0.22, 1.22]	•
Total events	6		14				
Heterogeneity: Not ap Test for overall effect	•	P = 0.14))				
86.6.2 Venlafaxine v	ersus amit	riptyline	e				
Gentil 2000 Subtotal (95% CI)	9	57 57	8	59 59	4.9% 4.9 %	1.16 [0.48, 2.81] 1.16 [0.48, 2.81]	•
Total events	9		8				
Heterogeneity: Not as	oplicable						
Test for overall effect	Z = 0.34 (F	P = 0.73)				
86.6.3 Venlafaxine v	ersus clon	nipramii	ne				
Samuelian 1998	18	52	18	50	13.9%	0.96 [0.57, 1.63]	+
Smeraldi 1998b	20	55	18	58	14.2%	1.17 [0.70, 1.97]	
Subtotal (95% CI)		107		108	28.1%	1.06 [0.73, 1.54]	•
Total events	38		36				
Heterogeneity: Tau ² = Test for overall effect:			•	= 0.60)); I² = 0%		
86.6.4 Venlafaxine v	ersus imip	ramine					
Benkert 1996	21	85	31	82	17.8%	0.65 [0.41, 1.04]	
Lecrubier 1997	23	78	23	75	16.4%	0.96 [0.59, 1.56]	_
Schweizer 1994 Subtotal (95% CI)	26	73 236	33	73 230	24.1% 58.4 %	0.79 [0.53, 1.17] 0.79 [0.61, 1.02]	•
Total events	70		87				
Heterogeneity: Tau ² = Test for overall effect:				= 0.53)); I² = 0%		
86.6.5 Venlafaxine v	ersus nort	riptyline					
Gasto 2003 Subtotal (95% CI)	5	34 34	6	34 34	3.2% 3.2%	0.83 [0.28, 2.47] 0.83 [0.28, 2.47]	
Total events	5	34	6	54	J.Z70	0.03 [0.20, 2.47]	
Heterogeneity: Not as	_		ŭ				
Test for overall effect	•	0.74)				
Total (95% CI)		470		475	100.0%	0.86 [0.70, 1.04]	•
Total events	128		151				
Heterogeneity: Tau ² =		= 5.04,	df = 7 (P	= 0.65)	; I² = 0%		0.01 0.1 1 10 100
Test for overall effect							Favours SNRI Favours TCA
Test for subgroup dif	ferences: C	hi² = 3.4	49. df = 4	(P = 0.	48), $I^2 = 0$	0%	. around office a decound for

1 More severe: SNRIs versus SSRIs

2 Figure 474: Depression symptomatology endpoint

		eriment			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean		Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
87.1.1 Duloxetine v									
Mowla 2016 Subtotal (95% CI)	18.66	3.2	26 26	17.43	3.1	28 28	3.6% 3.6%	0.39 [-0.15, 0.92] 0.39 [-0.15, 0.92]	★
Heterogeneity: Not a	applicable	!							
Test for overall effec	t: Z = 1.40) (P = 0.1	16)						
87.1.2 Venlafaxine	versus ci	taloprar	n						
Allard 2004 Subtotal (95% CI)	9.6	7.9	73 73	9.6	8.3	75 75	8.1% 8.1%	0.00 [-0.32, 0.32] 0.00 [-0.32, 0.32]	
Heterogeneity: Not a	applicable	!							
Test for overall effec	t: Z = 0.00	(P = 1.0	00)						
87.1.3 Venlafaxine	versus flu	oxetine	•						
Basterzi 2009	11.2	8.1	21	12.1	8.1	22	3.0%	-0.11 [-0.71, 0.49]	+
Chang 2015	8.7	8.3	54	8	7.7	58	6.6%	0.09 [-0.28, 0.46]	+
Clerc 1994	12	12.3	33	20	15	34	4.2%	-0.58 [-1.06, -0.09]	-
Costa 1998	9	8.4	196	9.1	7.8	185	14.5%	-0.01 [-0.21, 0.19]	†
Dierick 1996	10.7	9.9	153	12.4	8.88	161	13.1%	-0.18 [-0.40, 0.04]	-
Heller 2009	5	3.67	15	7.33	4.92	14	2.0%	-0.52 [-1.27, 0.22]	-
Rudolph 1999	12.5	4.1	95	14.2	4.14	103	9.8%	-0.41 [-0.69, -0.13]	+
Sheehan 2009b	15.59	9.81	91	18.09	8.89	99	9.6%	-0.27 [-0.55, 0.02]	+
Subtotal (95% CI)			658			676	62.7%	-0.20 [-0.35, -0.05]	•
Heterogeneity: Tau² Test for overall effec				= 7 (P =	0.14); l²	'= 36%	ı		
87.1.4 Venlafaxine	versus pa	aroxetin	е						
Casabona 2004	12.1	7	58	14	8.7	56	6.7%	-0.24 [-0.61, 0.13]	-
Hackett 1996	10.74	10.19		13.45	10.48	80	10.4%	-0.26 [-0.53, 0.01]	-
Subtotal (95% CI)			219			136	17.1%	-0.25 [-0.47, -0.04]	•
Heterogeneity: Tau²			•	1 (P = 0)	.92); l²=	- 0%			
Test for overall effec	t: Z = 2.30) (P = 0.0	02)						
87.1.5 Venlafaxine	versus se	ertraline)						
Shelton 2006 Subtotal (95% CI)	9.7	6.4	76 76	10.8	6.4	82 82	8.5% 8.5%	-0.17 [-0.48, 0.14] - 0.17 [-0.48, 0.14]	
Heterogeneity: Not a Test for overall effec			28)						
Total (95% CI)			1052			997	100.0%	-0.17 [-0.28, -0.06]	•
Heterogeneity: Tau ²	= 0.01; C	hi² = 16.	73, df	= 12 (P :	= 0.16);	l² = 28°	%		-10 -5 0 5
Test for overall effec			•	•	<i>"</i>				
Test for subgroup d		•		If = 1 /P	- 0.21)	P - 32	0%		Favours SNRI Favours SSRI

1 Figure 475: Depression symptomatology change score

	E	xperimental			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	-	Total	Mean		Total	Weight	IV, Random, 95% CI	
87.2.1 Duloxetine versus escitalopram	1								
Khan 2007	-19.3	9.1	91	-19.2	8.6	110	5.3%	-0.01 [-0.29, 0.27]	†
Nierenberg 2007 Subtotal (95% CI)	-7.61	6.94	273 364	-7.22	6.62	274 384	7.7% 13.0%	-0.06 [-0.23, 0.11] - 0.05 [-0.19, 0.10]	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.08,	df = 1 (F	P = 0.78\: P = 0				304	13.0%	-0.03 [-0.13, 0.10]	
Test for overall effect: Z = 0.62 (P = 0.54		- 0.70),1 - 0	,0						
87.2.2 Duloxetine versus fluoxetine	_				_				
Study F1J-MC-HMAQ - Study Group B Subtotal (95% CI)	-8	6.75	81 81	-7.63	7	37 37	3.6% 3.6%	-0.05 [-0.44, 0.34] - 0.05 [-0.44, 0.34]	
Heterogeneity: Not applicable			٠.			01	0.070	-0.00 [-0.74, 0.04]	Ī
Test for overall effect: Z = 0.27 (P = 0.79)								
07.2.2 Dulamatica management									
87.2.3 Duloxetine versus paroxetine Detke 2004	-11.55	4.84	186	-11.7	4.61	85	5.7%	0.03 [-0.23, 0.29]	<u> </u>
Eli Lilly HMAT-A	-6.31	6.3	81	-7.4	6.44	87	4.8%	0.03 [-0.23, 0.29]	
Hao 2014	-13.8	6.6	127	-12	7.1	132	5.9%	-0.26 [-0.51, -0.02]	
Higuchi 2009	-10	6.4	74	-9.4	6.9	148	5.2%	-0.09 [-0.37, 0.19]	+
Subtotal (95% CI)	-16 O (F	0.450-19. 4	468			452	21.7%	-0.05 [-0.23, 0.13]	1
Heterogeneity: Tau ² = 0.01; Chi ² = 5.35, Test for overall effect: Z = 0.53 (P = 0.60		'= 0.15); I*= 4	4%						
restror overall effect. 2 = 0.33 (r = 0.00)	,								
87.2.4 Duloxetine versus sertraline									
Mowla 2016	-9.3	2.48394847	26	-9.97	2.5855367	28	2.2%	0.26 [-0.28, 0.80]	
Subtotal (95% CI)			26			28	2.2%	0.26 [-0.28, 0.80]	T
Heterogeneity: Not applicable Test for overall effect: Z = 0.95 (P = 0.34	١								
1001101 0101411 011002 2 = 0.00 (1 = 0.0)	,								
87.2.5 Venlafaxine versus citalopram									
Allard 2004	-18	5.71926569	73	-17.4	6.08522802	75	4.5%	-0.10 [-0.42, 0.22]	1
Subtotal (95% CI)			73			75	4.5%	-0.10 [-0.42, 0.22]	T T
Heterogeneity: Not applicable Test for overall effect: Z = 0.61 (P = 0.54	١								
87.2.6 Venlafaxine versus escitalopra									
Bielski 2004 Subtotal (95% CI)	-13.6	9.6	98 98	-15.9	10.3	97 97	5.2% 5.2 %	0.23 [-0.05, 0.51] 0.23 [-0.05, 0.51]	
Heterogeneity: Not applicable			30			31	3.2/0	0.23 [-0.03, 0.31]	ľ
Test for overall effect: Z = 1.60 (P = 0.11))								
07.2.7 Venlatavina varava fluovetina									
87.2.7 Venlafaxine versus fluoxetine Basterzi 2009	160	5.48497949	21	126	5.94432503	22	1.9%	-0.29 [-0.89, 0.31]	
Chang 2015		5.49454275	54		5.09362347	58	3.8%	-0.17 [-0.54, 0.20]	
Clerc 1994		9.16733331	33		11.7260394	34	2.6%	-0.67 [-1.16, -0.17]	
Costa 1998	-21.4	5.5569776	196		5.18844871	185	6.9%	-0.15 [-0.35, 0.05]	
DeNayer 2002	-14.4	7.6	64	-10.4	8.6	67	4.1%	-0.49 [-0.84, -0.14]	
Dierick 1996 Heller 2009		7.29931504 2.55984374	153		6.40721468 3.39863208	161 14	6.4% 1.3%	-0.31 [-0.53, -0.08] -0.34 [-1.07, 0.40]	
Sheehan 2009b		7.32900744	91		6.46107963	99	5.1%	-0.42 [-0.70, -0.13]	
Subtotal (95% CI)			627			640	32.1%	-0.30 [-0.41, -0.19]	
Heterogeneity: Tau ² = 0.00; Chi ² = 6.55,		P = 0.48); $P = 0.48$	%						
Test for overall effect: Z = 5.29 (P < 0.00	UU1)								
87.2.8 Venlafaxine versus paroxetine									
Owens 2008	-17.3	8.99	41	-16.7	8.59	40	3.1%	-0.07 [-0.50, 0.37]	
VEN XR 367 (FDA)	-15.13	10.65	157	-11.26	10.55	80	5.4%	-0.36 [-0.63, -0.09]	
Subtotal (95% CI) Heterogeneity: Tau ² = 0.01; Chi ² = 1.28,	df = 1 /F	2 = 0.26\· IZ = 21	198			120	8.5%	-0.27 [-0.54, 0.01]	₹
Test for overall effect: Z = 1.92 (P = 0.05		- 0.20), 1 - 2.	2.70						
	•								
87.2.9 Venlafaxine versus sertraline	40-	4.0400401	70	44.0	4.0400401	00	4.000	0.001.004.00	
Shelton 2006 Sir 2005	-12.7 -14.3		76 79	-11.3 -15.9	4.6400431 8.44	82 79	4.6% 4.7%	-0.30 [-0.61, 0.01] 0.19 [-0.12, 0.50]	
Subtotal (95% CI)	-14.3	0.33	155	-10.8	0.44	161	9.3%	-0.06 [-0.54, 0.43]	
Heterogeneity: Tau² = 0.09; Chi² = 4.70,		P = 0.03); IP = 79	9%					•	
Test for overall effect: $Z = 0.22$ (P = 0.82))								
Total (95% CI)			2090			1994	100.0%	-0.14 [-0.23, -0.04]	
Heterogeneity: Tau ² = 0.02; Chi ² = 39.98	i, df = 21	(P = 0.008): I ²				1004	100.070	-0.1-1 [-0.23, -0.04]	
Test for overall effect: Z = 2.92 (P = 0.00		,y ₁ ,	70						-10 -5 0 5 10 Favours SNRI Favours SSRI
Test for subgroup differences: Chi² = 20).55, df=	8 (P = 0.008),	$I^2 = 61$	1%					I GVOGIO OIVINI PAVOGIO CONI

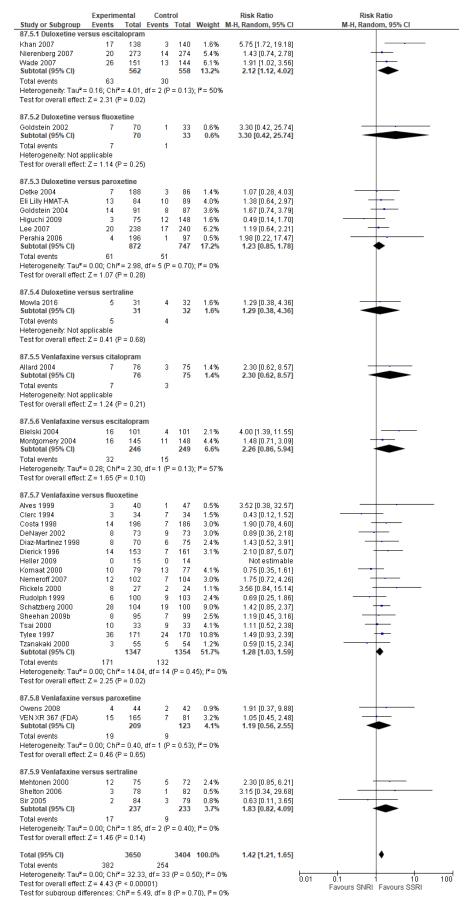
1 Figure 476: Remission (ITT)

i7.3.1 Duloxetine versus escitalopran (han 2007 lierenberg 2007 Vade 2007 iubtotal (95% CI) fotal events leterogeneity: Tau² = 0.00; Chi² = 1.31, est for overall effect: Z = 0.69 (P = 0.48	75 102 223	138 273 151 562	54 69 103	140 274 144	3.2% 3.9% 12.2%	0.86 [0.63, 1.18] 1.09 [0.82, 1.44] 0.94 [0.81, 1.10]	+
lierenberg 2007 Vade 2007 Subtotal (95% CI) Total events Jeterogeneity: Tau² = 0.00; Chi² = 1.31,	75 102	273 151	69	274 144	3.9%	1.09 [0.82, 1.44]	<u>+</u>
Vade 2007 subtotal (95% CI) fotal events Heterogeneity: Tau² = 0.00; Chi² = 1.31,	102	151		144			Ī
i <mark>ubtotal (95% CI)</mark> fotal events Heterogeneity: Tau² = 0.00; Chi² = 1.31,			103		12.2%		
otal events Heterogeneity: Tau² = 0.00; Chi² = 1.31,	223	JUE		558	19.3%	0.96 [0.85, 1.08]	1
leterogeneity: Tau² = 0.00; Chi² = 1.31,			226	550	13.370	0.50 [0.05, 1.00]	ľ
		: 0.52); l²					
7.3.2 Duloxetine versus fluoxetine							
Foldstein 2002	37	70	10	33	1.0%	1.74 [0.99, 3.06]	
Study F1J-MC-HMAQ - Study Group B	32	82	11	37	1.0%	1.31 [0.75, 2.31]	+
Subtotal (95% CI)		152		70	2.0%	1.51 [1.02, 2.25]	•
'otal events Heterogeneity: Tau² = 0.00; Chi² = 0.49, 'est for overall effect: Z = 2.04 (P = 0.04		: 0.48); l²	21 = 0%				
7.3.3 Duloxetine versus paroxetine							
etke 2004	92	188	38	86	4.0%	1.11 [0.84, 1.46]	+
Eli Lilly HMAT-A	23	84	31	89	1.6%	0.79 [0.50, 1.23]	+
Foldstein 2004	43	91	31	87	2.5%	1.33 [0.93, 1.89]	
lao 2014	51	140	42	141	2.8%	1.22 [0.87, 1.71]	
liguchi 2009 .ee 2007	26 117	75 238	49 121	148 240	2.1% 9.0%	1.05 [0.71, 1.54]	Ţ
ee 2007 Perahia 2006	82	230 196	42	97	3.9%	0.98 [0.81, 1.17] 0.97 [0.73, 1.28]	+
Subtotal (95% CI)		1012		888	26.0%	1.04 [0.93, 1.16]	•
otal events	434		354				
Heterogeneity: Tau² = 0.00; Chi² = 5.13, Test for overall effect: Z = 0.69 (P = 0.49		: 0.53); I²	= 0%				
7.3.4 Venlafaxine versus citalopram							
llard 2004	11	76	14	75	0.6%	0.78 [0.38, 1.60]	
Subtotal (95% CI)		76		75	0.6%	0.78 [0.38, 1.60]	-
otal events	11		14				
Heterogeneity: Not applicable Test for overall effect: Z = 0.69 (P = 0.49	3)						
7.3.5 Venlafaxine versus escitalopra	ım						
Bielski 2004	36	101	40	101	2.5%	0.90 [0.63, 1.28]	+
fontgomery 2004	99	145	102	148	11.7%	0.99 [0.85, 1.16]	1
Subtotal (95% CI)	405	246	4.40	249	14.2%	0.98 [0.85, 1.12]	T
otal events leterogeneity: Tau² = 0.00; Chi² = 0.26, est for overall effect: Z = 0.34 (P = 0.73		: 0.61); l²	142 = 0%				
7.3.6 Venlafaxine versus fluoxetine							
lves 1999	15	40	16	47	1.0%	1.10 [0.63, 1.94]	
costa 1998	118	196	112	186	10.7%	1.00 [0.85, 1.18]	<u>†</u>
0eNayer 2002 Kornaat 2000	38 26	73 79	27 19	73 77	2.3% 1.3%	1.41 [0.97, 2.04] 1.33 [0.81, 2.20]	
Jemeroff 2007	31	102	28	104	1.7%	1.13 [0.73, 1.74]	
Rickels 2000	9	27	10	24	0.6%	0.80 [0.39, 1.63]	
Rudolph 1999	35	100	23	103	1.6%	1.57 [1.00, 2.45]	
Schatzberg 2000	25	104	20	100	1.2%	1.20 [0.71, 2.02]	+
Sheehan 2009b	21	95	15	99	0.9%	1.46 [0.80, 2.66]	
Sai 2000	12	33	12	33	0.8%	1.00 [0.53, 1.89]	
ylee 1997 zanakaki 2000	52 18	171 55	53 15	170 54	3.1% 1.0%	0.98 [0.71, 1.34] 1.18 [0.66, 2.09]	_
zanakaki 2000 Subtotal (95% CI)	10	1075	10	1070	26.2%	1.18 [0.86, 2.09] 1.10 [0.99, 1.23]	, and the second
otal events leterogeneity: Tau² = 0.00; Chi² = 8.60, est for overall effect: Z = 1.76 (P = 0.08			350 ²= 0%				
7.3.7 Venlafaxine versus paroxetine							
casabona 2004	18	58	20	56	1.2%	0.87 [0.52, 1.46]	
)wens 2008	26	44	18	42	1.8%	1.38 [0.90, 2.11]	
Subtotal (95% CI)		102		98	2.9%	1.12 [0.71, 1.77]	*
otal events	44	_	38				
Heterogeneity: Tau² = 0.05; Chi² = 1.84, Test for overall effect: Z = 0.50 (P = 0.62		: 0.18); l²	= 46%				
7.3.8 Venlafaxine versus sertraline							
lehtonen 2000	40	75	27	72	2.4%	1.42 [0.99, 2.05]	 -
Shelton 2006	37	78	29	82	2.3%	1.34 [0.92, 1.95]	
3ir 2005	43	84 237	47	79 233	4.1% 8.7%	0.86 [0.65, 1.14]	T
	400	ZJI	103	233	0.770	1.16 [0.82, 1.63]	
i <mark>ubtotal (95% CI)</mark> iotal events Heterogeneity: Tau² = 0.06; Chi² = 6.09,		: 0.05); l²	= 67%				
iubtotal (95% CI) otal events	, df = 2 (P =	= 0.05); I²	= 67%				
i <mark>ubtotal (95% CI)</mark> iotal events Heterogeneity: Tau² = 0.06; Chi² = 6.09,	, df = 2 (P =	= 0.05); I ²	= 67%	3241	100.0%	1.05 [0.99, 1.11]	
iubtotal (95% CI) fotal events leterogeneity: Tau² = 0.06; Chi² = 6.09, fest for overall effect: Z = 0.84 (P = 0.40	, df = 2 (P =)) 1436	3462	1248		100.0%	1.05 [0.99, 1.11]	

1 Figure 477: Response (ITT)

Study or Subgroup	Events	Total	Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	M-H, Random, 95% CI
7.4.1 Duloxetine versus escitaloprar	n 10	4.0	16	16	870	1 00 to 00 4 4 27	1
iang 2017 (han 2007	10 62	10 138	16 83	140	4.7% 2.8%	1.00 [0.86, 1.17] 0.76 [0.60, 0.95]	
lierenberg 2007	92	273	94	274	2.7%	0.98 [0.78, 1.24]	
Vade 2007	112	151	115	144	5.8%	0.93 [0.82, 1.05]	4
Subtotal (95% CI)	112	572	113	574	16.1%	0.93 [0.83, 1.03]	•
otal events	276		308			5155 [5155] 1155]	j
Heterogeneity: Tau² = 0.00; Chi² = 4.65		: 0.20\:12					
est for overall effect: Z = 1.39 (P = 0.16		0.20,,					
7.4.2 Duloxetine versus fluoxetine							
Foldstein 2002	42	70	17	33	1.2%	1.16 [0.79, 1.71]	 -
Study F1J-MC-HMAQ - Study Group B	40	82	15	37	0.9%	1.20 [0.77, 1.88]	+
Subtotal (95% CI)		152		70	2.1%	1.18 [0.88, 1.58]	♦
otal events	82		32				
leterogeneity: Tau² = 0.00; Chi² = 0.01		= 0.91); l²	= 0%				
est for overall effect: Z = 1.12 (P = 0.2)	0)						
7.4.3 Duloxetine versus paroxetine	120	100	6.4	06	4 604	0.04 (0.70.4.07)	_
Detke 2004	128 28	188	64 38	86 89	4.6% 1.2%	0.91 [0.78, 1.07]	
:li Lilly HMAT-A Foldstein 2004	44	84 91		87	1.5%	0.78 [0.53, 1.15]	<u></u>
Hao 2014	86	140	34 74	141	3.3%	1.24 [0.88, 1.73] 1.17 [0.95, 1.44]	_
liguchi 2009	38	75	78	148	2.2%	0.96 [0.73, 1.26]	
.ee 2007	144	238	157	240	5.3%	0.92 [0.81, 1.06]	4
ee 2007 Perahia 2006	129	196	59	97	3.7%	1.08 [0.90, 1.31]	+
Subtotal (95% CI)	123	1012	53	888	21.7%	1.00 [0.91, 1.10]	•
otal events	597		504		/*	[1
otal events leterogeneity: Tau² = 0.00; Chi² = 8.53		: 0.20\· I=					
est for overall effect: Z = 0.07 (P = 0.9)		2.20/,1	50 10				
7.4.4 Venlafaxine versus citalopram							
llard 2004	54	76	55	75	3.4%	0.97 [0.79, 1.18]	+
Subtotal (95% CI)		76		75	3.4%	0.97 [0.79, 1.18]	*
otal events	54		55				
leterogeneity: Not applicable	-						
est for overall effect: Z = 0.31 (P = 0.7)	J)						
7.4.5 Venlafaxine versus escitalopra		4.04	F7	4.04	2.20	0.00 to 60 4.00	
Bielski 2004	47	101	57 113	101	2.2%	0.82 [0.63, 1.08]	1
Rielski 2004 Nontgomery 2004		145	57 113	148	5.9%	1.02 [0.90, 1.16]	-
Bielski 2004 Montgomery 2004 Bubtotal (95% CI)	47 113		113				•
itelski 2004 fontgomery 2004 subtotal (95% CI) fotal events leterogeneity: Tau² = 0.01; Chi² = 2.24	47 113 160 , df=1 (P=	145 246	113 170	148	5.9%	1.02 [0.90, 1.16]	•
Bielski 2004 fontgomery 2004 B ubtotal (95% CI) Total events	47 113 160 , df=1 (P=	145 246	113 170	148	5.9%	1.02 [0.90, 1.16]	•
Dielski 2004 fontgomery 2004 subtotal (95% CI) otal events leterogeneity: Tau² = 0.01; Chi² = 2.24 est for overall effect: Z = 0.51 (P = 0.61) 7.4.6 Venlafaxine versus fluoxetine	47 113 160 , df = 1 (P =	145 246 = 0.13); I ²	113 170 = 55%	148 249	5.9% 8.0%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17]	•
itelski 2004 fontgomery 2004 subtotal (95% CI) fotal events leterogeneity: Tau² = 0.01; Chi² = 2.24 rest for overall effect: Z = 0.51 (P = 0.61) 17.4.6 Venlafaxine versus fluoxetine ulves 1999	47 113 160 , df = 1 (P = 1)	145 246 = 0.13); ² 40	113 170 = 55%	148 249 47	5.9% 8.0% 1.6%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51]	•
itielski 2004 fontgomery 2004 iouthotal (95% CI) fotal events leterogeneity: Tau² = 0.01; Chi² = 2.24 fest for overall effect: Z = 0.51 (P = 0.61) for the street of the street of the street overall effect overall eff	47 113 160 , df = 1 (P = 1) 26 23	145 246 = 0.13); ² 40 34	113 170 = 55% 28 17	148 249 47 34	5.9% 8.0% 1.6% 1.1%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04]	- •
idelski 2004 fontgomery 2004 subtotal (95% CI) fotal events leterogeneity: Tau² = 0.01; Chi² = 2.24 fest for overall effect: Z = 0.51 (P = 0.6) for.4.6 Venlafaxine versus fluoxetine lives 1999 clerc 1994 costa 1998	47 113 160 , df = 1 (P = 1) 26 23 158	145 246 = 0.13); * 40 34 196	113 170 = 55% 28 17 156	148 249 47 34 186	5.9% 8.0% 1.6% 1.1% 7.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06]	+
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Melski 2004 Montgomery 2004 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 2.24 Fest for overall effect: Z = 0.51 (P = 0.6° T.4.6 Venlafaxine versus fluoxetine Mes 1999 Her 1994 Denayer 2002 Diaz-Martinez 1998 Dierick 1996 Mornaat 2000 Hemeroff 2007 Rudolph 1999 Schatzberg 2000 Scheban 2009b Sai 2000 Mylee 1997 Zanakaki 2000 Subtotal (95% CI)	47 113 160 , df = 1 (P = 1)) 26 23 158 37 37 107 33 51 54 59 35 24 81 30	145 246 = 0.13); P 40 34 196 73 70 153 79 102 100 104 95 33 171	113 170 = 55% 28 17 156 27 45 95 33 45 52 52 27 22 98 82	47 34 186 73 75 161 77 104 103 100 99 33 170	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.0% 3.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.89, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01]	+ + + + + + + + + + + + + + + + + + +
Melski 2004 Montgomery 2004 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 2.24 Fest for overall effect: Z = 0.51 (P = 0.6° F.4.6 Venlafaxine versus fluoxetine Moves 1999 Here 1994 Dosta 1998 Denayer 2002 Diaz-Martinez 1998 Dierick 1996 Cornaat 2000 Hemeroff 2007 Rudolph 1999 Schalzberg 2000 Sheehan 2009b Sai 2000 Ylee 1997 Zanakaki 2000 Stotal events	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 35 24 81 30	145 246 = 0.13); P 40 34 196 73 70 153 79 102 100 104 95 33 171 535 1305	113 170 = 55% 28 17 156 27 45 95 33 45 52 52 27 22 98 28 725	148 249 47 34 186 73 75 161 77 104 103 100 99 33 170 54 1316	1.6% 1.1% 7.3% 1.2% 4.3% 1.3% 2.4% 1.0% 1.6% 3.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.89, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50]	+ + + + + + + + + + + + + + + + + + +
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Moleski 2004 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2003 Montgomery 2004 Montgomery 2006 Montgomery 2007 Montgomery 2008 Montgomery 2009 M	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 24 81 30 755 5, df = 13 (3)	145 246 = 0.13); P 40 34 196 73 70 153 79 102 100 104 95 33 171 535 1305	113 170 = 55% 28 17 156 27 45 95 33 45 52 52 27 22 98 28 725	148 249 47 34 186 73 75 161 77 104 103 100 99 33 170 54 1316	1.6% 1.1% 7.3% 1.2% 4.3% 1.3% 2.4% 1.0% 1.6% 3.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.89, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50]	+ + + + + + + + + + + +
detski 2004 dentgomery 2004 dentgomery 2004 deutstal (95% CI) fotal events deterogeneity: Tau² = 0.01; Chi² = 2.24 fest for overall effect: Z = 0.51 (P = 0.6* deterogeneity: Tau² = 0.01; Chi² = 2.24 fest for overall effect: Z = 0.51 (P = 0.6* deterogeneity: Tau² = 0.51 (P = 0.6* deterogeneity: Tau² = 0.01; Chi² = 17.9 detero	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 35 24 81 30 755 5, df = 13 (3)	145 246 = 0.13); F 40 34 196 73 70 153 79 102 100 104 95 33 171 53 171 95 1305	113 170 = 555% 28 17 156 27 45 96 33 34 55 52 27 72 22 98 28 725; F= 28'	148 249 47 34 186 73 75 161 77 104 103 33 170 99 33 175 4 1316	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.06% 3.3% 1.4% 32.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.36 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.06] 1.19 [1.00, 1.40] 0.97 [0.68, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.89, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.97, 1.14]	+ + + + + + + + + + + + + + + +
Rielski 2004 fontgomery 2004 subtotal (95% CI) rotal events leterogeneity: Tau² = 0.01; Chi² = 2.24 est for overall effect: Z = 0.51 (P = 0.6* 17.4.6 Venlafaxine versus fluoxetine lives 1999 clore 1994 costa 1998 cenayer 2002 clore Anathinez 1998 cerick 1996 cornaat 2000 demeroff 2007 Rudolph 1999 chatzberg 2000 sheehan 2009b fsai 2000 gibtotal (95% CI) rotal events leterogeneity: Tau² = 0.01; Chi² = 17.9 rest for overall effect: Z = 1.19 (P = 0.25* 17.4.7 Venlafaxine versus paroxetine casabona 2004	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 35 24 81 30 755 5, df = 13 (3)	145 246 = 0.13); F 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16)	113 170 = 555% 28 17 156 27 45 95 33 45 52 27 22 29 8 28	148 249 47 34 186 73 75 161 77 104 103 100 93 31 170 54 1316	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.4% 1.6% 3.3% 1.4% 32.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.95, 1.40] 1.35 [0.89, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.77, 1.14]	
Melski 2004 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2000 Mo	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 35 24 81 30 755 5, df = 13 (3)	145 246 = 0.13); IF 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16)	113 170 = 55% 28 17 1566 27 45 95 52 52 27 22 98 28 725 2; F = 28'	148 249 47 34 186 73 75 161 17 77 104 103 33 170 99 33 170 54 1316 %	1.6% 1.1% 7.3% 2.0% 4.3% 1.9% 2.3% 2.4% 3.3% 2.4% 3.2.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.68, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.99, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.74, 1.50]	+ + + + + + + + + + +
Melski 2004 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2004 Melst events Meterogeneity: Tau² = 0.01; Chi² = 2.24 Mest for overall effect: Z = 0.51 (P = 0.6° Montgomery 2004 Mest 1999 Merc 1994 Montgomery 2002 Melst 1998 Ment 1999 Ment 1999 Ment 1999 Ment 1999 Ment 1997 Ment 1997 Ment 1998 Ment 1997 Ment 1997 Ment 1998 Ment 1997 Ment 199	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 35 24 81 30 755 5, df = 13 (3)	145 246 = 0.13); IF 40 34 196 73 70 153 79 102 100 104 95 33 171 5 1305 P = 0.16)	113 170 = 555% 28 17 156 27 45 95 33 45 52 27 22 29 8 28	148 249 47 34 186 73 75 161 103 100 99 33 170 54 1316 %	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.6% 3.3% 1.4% 3.2.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.36 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.96, 1.55] 1.07 [0.82, 1.39] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.74, 1.50] 1.05 [0.97, 1.14]	+ + + + + + + + + + + + + + + +
Rielski 2004 fontgomery 2004 subtotal (95% CI) fotal events leterogeneity: Tau* = 0.01; Chi* = 2.24 fest for overall effect: Z = 0.51 (P = 0.6* for. 4.6 Venlafaxine versus fluoxetine lives 1999 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Cornaat 2000 lemeroff 2007 Rudolph 1999 Cohatzberg 2000 Sheehan 2009b Sai 2000 Sylee 1997 Canakaki 2000 Subtotal (95% CI) Total events leterogeneity: Tau* = 0.01; Chi* = 17.9 fest for overall effect: Z = 1.19 (P = 0.2; for. 4.7 Venlafaxine versus paroxetine Casabona 2004 Wavang 2004 Wavang 2008 Subtotal (95% CI)	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 35 24 81 30 755, df = 13 (3) 3)	145 246 = 0.13); IF 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16)	113 170 = 555% 28 17 156 27 45 95 33 35 45 22 72 22 98 28 725 27 27 22 29 48 26	148 249 47 34 186 73 75 161 17 77 104 103 33 170 99 33 170 54 1316 %	1.6% 1.1% 7.3% 2.0% 4.3% 1.9% 2.3% 2.4% 3.3% 2.4% 3.2.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.68, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.99, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.74, 1.50]	
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Rielski 2004 fontgomery 2004 subtotal (95% CI) fotal events leterogeneity: Tau* = 0.01; Chi* = 2.24 fest for overall effect: Z = 0.51 (P = 0.6* for. 4.6 Venlafaxine versus fluoxetine lives 1999 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Cornaat 2000 lemeroff 2007 Rudolph 1999 Cohatzberg 2000 Sheehan 2009b Sai 2000 Sylee 1997 Canakaki 2000 Subtotal (95% CI) Total events leterogeneity: Tau* = 0.01; Chi* = 17.9 fest for overall effect: Z = 1.19 (P = 0.2; for. 4.7 Venlafaxine versus paroxetine Casabona 2004 Wavang 2004 Wavang 2008 Subtotal (95% CI)	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 24 81 30 765 5, df = 13 (3) 3)	145 246 = 0.13); F 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16)	113 170 = 55% 28 17 1566 27 45 95 33 45 52 27 22 98 28 725 29 17 29 48 26	148 249 47 34 186 73 75 161 177 7104 103 100 99 93 31 170 54 1316 8	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.6% 3.3% 1.4% 3.2.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.36 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.96, 1.55] 1.07 [0.82, 1.39] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.74, 1.50] 1.05 [0.97, 1.14]	
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Montgomery 2004 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2000 Montgomery 2001 Montgomery 2001 Montgomery 2001 Montgomery 2004 Montgomery 2008 Montgomery 200	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 35 24 81 35 24 81 35 36 37 37 107 33 51 54 59 35 24 81 35 24 81 37 37 37 37 47 47 47 47 47 47 47 47 47 47 47 47 47	145 246 = 0.13); F 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16) 58 52 44 154 = 0.01); F	113 170 = 55% 28 17 1566 27 45 95 52 52 27 22 98 28 725 ; F = 28' 29 48 26 103 = 77%	148 249 47 34 1866 73 75 101 100 99 33 1700 54 1316 %	1.6% 1.1% 7.3% 2.0% 4.3% 1.9% 2.3% 2.4% 3.3% 1.6% 3.3,4% 3.2.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.84, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.35 [0.99, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.97, 1.14] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49]	
Moleski 2004 Montgomery 2005 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2000 Montgomery 2001 Montgomery 2004 Montgomery 2006 Montgomery 2007 M	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 24 81 30 755 24 81 30 755 5, df = 13 (3) 29 43 43 29	145 246 = 0.13); F 40 34 196 73 70 163 79 102 100 104 95 33 171 55 1305 P = 0.16) 58 52 44 154 = 0.01); F	113 170 = 555% 28 17 156 95 33 45 52 52 22 98 28 725 (1° = 28' 29 48 26 103 = 77%	148 249 47 34 186 73 75 161 177 104 103 100 54 1316 %	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.6% 3.3% 1.4% 32.8%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.36 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.85, 1.40] 1.36 [0.89, 2.05] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.77, 1.14] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49]	
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Montgomery 2004 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2002 Montgomery 2007 Montgomery 2007 Montgomery 2007 Montgomery 2007 Montgomery 2009 Montgomery 200	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 24 81 30 755 24 81 30 755 5, df = 13 (3) 29 43 43 29	145 246 = 0.13); F 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16) 58 52 44 154 = 0.01); F	113 170 = 555% 28 17 156 95 33 45 52 52 22 98 28 725 (1° = 28' 29 48 26 103 = 77%	148 249 47 34 1866 73 75 161 17 75 104 103 17 104 1316 56 53 42 151	1.6% 1.1% 7.3% 2.0% 4.3% 1.9% 2.3% 2.4% 3.3.4% 32.8% 1.9% 4.8% 1.7% 8.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.79, 1.50] 1.05 [0.79, 1.14] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49] 1.15 [0.88, 1.49] 1.29 [0.97, 1.72] 0.94 [0.76, 1.16]	
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Rielski 2004 fontgomery 2004 fontgomery 2004 fubtotal (95% CI) fotal events Reterogeneity: Tau² = 0.01; Chi² = 2.24 rest for overall effect: Z = 0.51 (P = 0.6* r. 4.6 Venlafaxine versus fluoxetine r. 4.6 Venlafaxine versus fluoxetine r. 5.6 Venlafaxine versus fluoxetine r. 6.6 Venlafaxine versus fluoxetine r. 7.4.6 Venlafaxine versus r. 8.6 Venlafaxine versus r. 8.7 Venlafaxine versus r. 8.7 Venlafaxine versus r. 8.7 Venlafaxine versus r. 8.8 Venlafaxine r.	47 113 160 , df = 1 (P = 1) 26 23 31 158 37 37 107 33 51 54 48 59 35 24 81 30 755, df = 13 (3) 30 43 43 29 43 43 43 29 48 56	145 246 = 0.13); F 40 34 196 73 70 153 79 102 100 104 95 33 171 51 1305 P = 0.16) 58 52 44 154 = 0.01); F 78 84 237	113 170 = 555% 28 17 156 95 33 45 52 27 72 29 8 28 725 51 F = 28' 29 48 26 103 = 777% 41 39 56 136 137 138 139 149 149 149 149 149 149 149 14	148 249 47 34 1866 73 75 161 17 75 104 103 17 104 1316 56 53 42 151	1.6% 1.1% 7.3% 2.0% 4.3% 1.9% 2.3% 2.4% 3.3.4% 32.8% 1.9% 4.8% 1.7% 8.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.79, 1.50] 1.05 [0.79, 1.14] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49] 1.15 [0.88, 1.49] 1.29 [0.97, 1.72] 0.94 [0.76, 1.16]	+ + + + + + + + + +
Montgomery 2004 Montgomery 2005 Montgomery 2007 Montgomery 2008 Montgomery 2009 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2008 Montgomery 2009 Montgomery 200	47 113 160 , df = 1 (P = 1) 26 23 31 158 37 37 107 33 51 54 48 59 35 24 81 30 755, df = 13 (3) 30 43 43 29 43 43 43 29 48 56	145 246 = 0.13); F 40 34 196 73 70 163 79 102 100 104 95 33 171 55 1305 P = 0.16) 58 52 44 154 = 0.01); F 75 78 88 84 237	113 170 = 555% 28 17 156 95 33 45 52 27 72 29 8 28 725 51 F = 28' 29 48 26 103 = 777% 41 39 56 136 137 138 139 149 149 149 149 149 149 149 14	148 249 47 34 186 73 75 161 17 71 104 103 100 99 33 170 41 1316 % 566 53 42 151	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.0% 3.3% 1.4% 3.2.8% 1.9% 4.8% 1.7% 8.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.36 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.82, 1.39] 1.09 [0.85, 1.40] 1.36 [0.88, 1.45] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.74, 1.50] 1.06 [0.77, 1.44] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49] 1.15 [0.88, 1.49] 1.29 [0.97, 1.72] 0.94 [0.76, 1.16] 1.10 [0.90, 1.33]	+ + + + + + + + +
Rielski 2004 fontgomery 2004 subtotal (95% CI) fotal events leterogeneity: Tau* = 0.01; Chi* = 2.24 fest for overall effect: Z = 0.51 (P = 0.6* for the events of the events of the events leterogeneity: Tau* = 0.01; Chi* = 2.24 fest for overall effect: Z = 0.51 (P = 0.6* for 1994 losta 1998 loenayer 2002 loener 1994 losta 1998 loenayer 2002 loener 1996 fornaat 2000 lemeroff 2007 Rodolph 1999 lohatzberg 2000 loener 2000 loen	47 113 160 df = 1 (P = 1) 26 23 3158 37 37 37 37 37 35 51 54 45 36 24 81 30 755 5, df = 13 (3 3) 43 43 29 41 45 48 56 48 56	145 246 = 0.13); F 40 34 196 73 70 153 79 102 100 104 95 33 171 51 1305 P = 0.16) 58 52 44 154 = 0.01); F 78 84 237	113 170 = 555% 28 17 156 95 33 45 52 27 72 29 88 28 725; F = 28' 29 48 26 103 = 77% 41 39 56 136 137 138 139 149 149 149 149 149 149 149 14	148 249 47 34 186 73 75 161 17 71 104 103 100 99 33 170 41 1316 % 566 53 42 151	1.6% 1.1% 7.3% 2.0% 4.3% 1.9% 2.3% 2.4% 3.3.4% 32.8% 1.9% 4.8% 1.7% 8.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.35 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.88, 1.41] 1.16 [0.86, 1.55] 1.07 [0.82, 1.39] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.79, 1.50] 1.05 [0.79, 1.14] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49] 1.15 [0.88, 1.49] 1.29 [0.97, 1.72] 0.94 [0.76, 1.16]	+ + + + + + + + + + + + + + + + + + +
Montgomery 2004 Montgomery 2005 Montgomery 2007 Montgomery 2008 Montgomery 2009 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2004 Montgomery 2008 Montgomery 2009 Montgomery 200	47 113 160 , df = 1 (P = 1) 26 23 158 37 37 107 33 51 54 59 35 24 81 30 755 5, df = 13 (3) 43 43 29 115 , df = 2 (P = 5)	145 246 = 0.13); F 40 34 196 73 70 102 100 104 95 33 171 55 1305 P = 0.16) 58 52 44 154 154 = 0.01); F 75 78 84 237 = 0.17); F	113 170 = 55% 28 17 1566 27 45 95 33 46 52 27 22 29 88 725 ; F = 28' 29 48 26 103 = 77% 41 39 56 136 437 448 449 449 449 449 449 449 449	148 249 47 34 1866 73 75 101 100 99 33 1700 54 1316 56 53 42 151	1.6% 1.1% 7.3% 1.2% 2.0% 4.3% 1.9% 2.3% 2.4% 1.0% 3.3% 1.4% 3.2.8% 1.9% 4.8% 1.7% 8.3%	1.02 [0.90, 1.16] 0.95 [0.76, 1.17] 1.09 [0.79, 1.51] 1.36 [0.90, 2.04] 0.96 [0.88, 1.06] 1.37 [0.94, 1.99] 0.88 [0.66, 1.18] 1.19 [1.00, 1.40] 0.97 [0.82, 1.39] 1.09 [0.85, 1.40] 1.36 [0.88, 1.45] 1.09 [0.79, 1.50] 0.82 [0.67, 1.01] 1.05 [0.74, 1.50] 1.05 [0.74, 1.50] 1.06 [0.77, 1.44] 1.43 [1.07, 1.92] 0.91 [0.78, 1.06] 1.06 [0.77, 1.46] 1.10 [0.81, 1.49] 1.15 [0.88, 1.49] 1.29 [0.97, 1.72] 0.94 [0.76, 1.16] 1.10 [0.90, 1.33]	+ + + + + + + + + + + + + + + + + + +

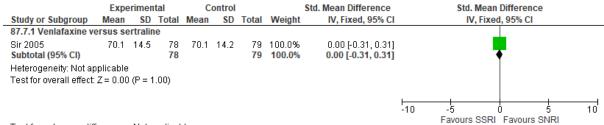
1 Figure 478: Discontinuation due to SEs



1 Figure 479: Discontinuation due to any reason including SE

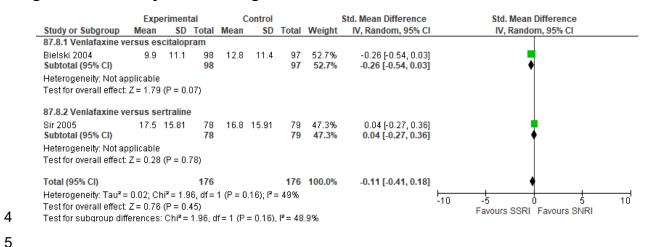
7.6.1 Duloxetine versus escitaloprar	Experim Events		Conti Events		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
7.6.1 Duloxeune versus eschaloprar Than 2007	47	138	30	140	4.1%	1.59 [1.07, 2.35]	
lierenberg 2007	85	273	66	274	7.2%	1.29 [0.98, 1.70]	 -
Vade 2007	37	151	32	144	3.7%	1.10 [0.73, 1.67]	+
Subtotal (95% CI)		562		558	15.0%	1.31 [1.08, 1.60]	◆
Total events	169		128				
Heterogeneity: Tau² = 0.00; Chi² = 1.60 Fest for overall effect: Z = 2.70 (P = 0.00		= 0.45); F	= 0%				
37.6.2 Duloxetine versus fluoxetine							
Goldstein 2002	24	70	12	33	2.2%	0.94 [0.54, 1.64]	
Study F1J-MC-HMAQ - Study Group B	25	82	14	37	2.4%	0.81 [0.48, 1.36]	
Subtotal (95% CI)	40	152		70	4.6%	0.87 [0.59, 1.27]	\blacksquare
Total events	49 at = 1.70 -	. 0.000-0	26				
Heterogeneity: Tau² = 0.00; Chi² = 0.16 Fest for overall effect: Z = 0.73 (P = 0.41		· 0.69), r	= 076				
37.6.3 Duloxetine versus paroxetine							
Detke 2004	21	188	10	86	1.4%	0.96 [0.47, 1.95]	
Eli Lilly HMAT-A	44	84	31	89	4.9%	1.50 [1.06, 2.13]	 -
3oldstein 2004	38	91	38	87	5.2%	0.96 [0.68, 1.34]	<u> </u>
Hao 2014	32	140	36	141	3.7%	0.90 [0.59, 1.36]	<u></u>
Higuchi 2009	9 72	75 238	22 57	148 240	1.3% 6.4%	0.81 [0.39, 1.67]	-
.ee 2007 Perahia 2006	23	196	11	97	1.5%	1.27 [0.95, 1.72] 1.03 [0.53, 2.03]	
Subtotal (95% CI)	-23	1012		888	24.5%	1.12 [0.95, 1.32]	*
Total events	239		205			- · · ·	
Heterogeneity: Tau² = 0.00; Chi² = 6.44 Test for overall effect: Z = 1.31 (P = 0.19		= 0.38); F	= 7%				
37.6.4 Duloxetine versus sertraline							
Mowla 2016	5	31	4	32	0.5%	1.29 [0.38, 4.36]	
Subtotal (95% CI)	3	31	4	32 32	0.5%	1.29 [0.38, 4.36]	
Fotal events	5		4				
Heterogeneity: Not applicable Fest for overall effect: Z = 0.41 (P = 0.68							
87.6.5 Venlafaxine versus citalopram							
Allard 2004	18	76	16	75	2.0%	1.11 [0.61, 2.01]	
Subtotal (95% CI)		76		75	2.0%	1.11 [0.61, 2.01]	•
Fotal events	18		16				
Heterogeneity: Not applicable Fest for overall effect: Z = 0.35 (P = 0.73	3)						
3 7.6.6 Venlafaxine versus escitalopr a Bielski 2004	33	101	24	101	3.3%	1.38 [0.88, 2.15]	
Jontgomery 2004	20	145	22	148	2.2%	0.93 [0.53, 1.63]	
Subtotal (95% CI)		246		249	5.4%	1.17 [0.80, 1.71]	*
Fotal events Heterogeneity: Tau² = 0.01; Chi² = 1.16		0.28); f	46 = 14%				
Fest for overall effect: Z = 0.82 (P = 0.41	1)						
37.6.7 Venlafaxine versus fluoxetine	10	40	9	47	1.1%	1.31 [0.59, 2.89]	
Alves 1999					1.0%		I I
Alves 1999 Basterzi 2009	7	21	7	22		1.05 [0.44, 2.48]	
		34	12	34	1.0%	1.05 [0.44, 2.48] 0.50 [0.21, 1.18]	
Basterzi 2009	7						
Basterzi 2009 Clerc 1994	7 6	34	12 18 29	34 186 73	1.0%	0.50 [0.21, 1.18]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998	7 6 29 24 15	34 196 73 70	12 18 29 20	34 186 73 75	1.0% 2.2% 3.5% 2.0%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996	7 6 29 24 15 38	34 196 73 70 153	12 18 29 20 40	34 186 73 75 161	1.0% 2.2% 3.5% 2.0% 4.2%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47]	+
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009	7 6 29 24 15 38 3	34 196 73 70 153	12 18 29 20 40 5	34 186 73 75 161	1.0% 2.2% 3.5% 2.0% 4.2% 0.5%	0.50 (0.21, 1.18) 1.53 (0.88, 2.66) 0.83 (0.54, 1.28) 0.80 (0.45, 1.44) 1.00 (0.68, 1.47) 0.56 (0.16, 1.92)	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heiller 2009 Kornaat 2000	7 6 29 24 15 38 3	34 196 73 70 153 15 79	12 18 29 20 40 5	34 186 73 75 161 14 77	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Vemeroff 2007	7 6 29 24 15 38 3 15 24	34 196 73 70 153 15 79 102	12 18 29 20 40 5 24	34 186 73 75 161 14 77	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999	7 6 29 24 15 38 3 15 24	34 196 73 70 153 15 79 102 100	12 18 29 20 40 5 24 18 35	34 186 73 75 161 14 77 104 103	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b	7 6 29 24 15 38 3 15 24 28	34 196 73 70 153 15 79 102 100 95	12 18 29 20 40 5 24 18 35 32	34 186 73 75 161 14 77 104 103 99	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7% 4.6%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999	7 6 29 24 15 38 3 15 24	34 196 73 70 153 15 79 102 100	12 18 29 20 40 5 24 18 35	34 186 73 75 161 14 77 104 103	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b Esai 2000	7 6 29 24 15 38 3 15 24 28 42	34 196 73 70 153 15 79 102 100 95 33	12 18 29 20 40 5 24 18 35 32	34 186 73 75 161 14 77 104 103 99 33	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7% 4.6% 2.4%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.66 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Vemeroff 2007 Rudolph 1999 Sheehan 2009b Fsai 2000 Fylee 1997 Tzanakaki 2000	7 6 29 24 15 38 3 15 24 28 42 14	34 196 73 70 153 15 79 102 100 95 33	12 18 29 20 40 5 24 18 35 32 16 46	34 186 73 75 161 14 77 104 103 99 33 170	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7% 4.6% 2.4% 5.0%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Remeroff 2007 Rudolph 1999 Sheehan 2009b Tylee 1997 Tyanakaki 2000 Subtotal (95% CI) Total events	7 6 29 24 15 38 3 15 24 28 42 14 47 12	34 196 73 70 153 15 79 102 100 95 33 171 55 1237	12 18 29 20 40 5 24 18 35 32 16 46 12	34 186 73 75 161 14 77 104 103 99 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 4.6% 2.4% 5.0%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99]	
lasterzi 2009 Ilerc 1994 Jerc 1994 Josta 1998 Jelvayer 2002 Jiaz-Martinez 1998 Jelierick 1996 Jelieller 2009 Jelierick 2007 Jelieller 2007 Jelieller 2007 Jelieller 2009 Jelieller 2009 Jelieller 2009 Jelieller 2000 Je	7 6 29 24 15 38 3 15 24 28 42 14 47 12 314 3, df=14 (34 196 73 70 153 15 79 102 100 95 33 171 55 1237	12 18 29 20 40 5 24 18 35 32 16 46 12	34 186 73 75 161 14 77 104 103 99 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 4.6% 2.4% 5.0%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b Tsai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.80) 87.6.8 Venlafaxine versus paroxetine	7 6 29 24 15 38 3 15 24 28 42 14 47 12 314 3, df = 14 (i)	34 196 73 70 153 15 79 102 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 24 18 35 32 16 46 42 323 ; F= 9%	34 186 73 75 161 14 77 104 103 99 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 4.6% 2.4% 5.0% 1.4%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dielrick 1996 Heller 2009 Gornad 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b Isai 2000 Iylee 1997 Izanakaki 2000 Subtotal (95% CI) Total events Hesterogeneity: Tau² = 0.01; Chi² = 15.4 Test for overall effect: Z = 0.25 (P = 0.80) 37.6.8 Veniafaxine versus paroxetine Hwang 2004	7 6 29 24 15 38 3 15 24 28 42 14 42 17 12 314 3, df = 14 ())	34 196 73 70 153 15 79 102 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 5 24 18 35 32 16 46 46 12 323 (; F = 9%	34 186 73 75 161 14 77 104 103 99 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.3% 3.7% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dielrick 1996 Heller 2009 Kornaat 2000 Wemeroff 2007 Rudolph 1999 Sheehan 2009b Fsai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.8) 637.6.8 Venlafaxine versus paroxetine Hwang 2004 Dwens 2008	7 6 29 24 15 38 3 15 24 28 42 14 47 12 314 3, df = 14 (i))	34 196 73 70 153 15 79 102 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 24 18 35 16 46 12 323 3; F= 9%	34 186 73 75 161 14 77 104 103 99 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.3% 3.7% 4.6% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Vemeroff 2007 Rudolph 1999 Sheehan 2009b (Sai 2000 Fylee 1997 Fzanakaki 2000 Subtotal (95% CI) Fotal events Heterogeneily: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.80 87.6.8 Venlafaxine versus paroxetine Hwang 2004 Dwens 2008 KEN XS 367 (FDA)	7 6 29 24 15 38 3 15 24 28 42 14 42 17 12 314 3, df = 14 ())	34 196 73 70 153 15 79 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 5 24 18 35 32 16 46 46 12 323 (; F = 9%	34 186 73 75 161 14 77 104 103 99 33 1700 54 1252	1.0% 2.2% 3.5% 4.2% 0.5% 2.3% 3.7% 4.6% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.07 [0.72, 1.44] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19]	
Basterzi 2009 Clerc 1994 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Cornaat 2000 Vemeroff 2007 Rudolph 1999 Sheehan 2009b Sai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Test for overall effect: Z = 0.25 (P = 0.80 St7.6.8 Veniafaxine versus paroxetine Twang 2004 Dwens 2008 ENIX R 367 (FDA) Subtotal (95% CI)	7 6 29 24 15 38 3 3 15 5 24 42 14 47 12 314 3, df = 14 (J) 3 12 46	34 196 73 70 153 15 79 102 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 24 18 35 16 46 12 323 3; F= 9%	34 186 73 75 161 14 77 104 103 99 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.3% 3.7% 4.6% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13]	
Basterzi 2009 Clerc 1994 Clerc 1994 Dosta 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Cornaat 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b Tsai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Test for overall effect: Z = 0.25 (P = 0.86 ST.6.8 Venlafaxine versus paroxetine Hwang 2004 Wens 2008 (EN XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.00; Chi² = 0.74	7 6 29 24 15 38 3 15 24 47 12 314 3, df = 14 (J) 31 12 46 61 , df = 2 (P =	34 196 73 70 153 15 79 102 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 24 18 35 32 16 46 12 323 3; IF = 9%	34 186 73 75 161 14 77 104 103 99 33 1700 54 1252	1.0% 2.2% 3.5% 4.2% 0.5% 2.3% 3.7% 4.6% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.07 [0.72, 1.44] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19]	
Basterzi 2009 Clerc 1994 Clerc 1994 Des 1998 DeNayer 2002 Diaz-Martinez 1998 Dielrick 1996 Heller 2009 Gornad 2000 Wemeroff 2007 Rudolph 1999 Sheehan 2009b Fsai 2000 Tylee 1997 Fzanakaki 2000 Subtotat (95% CI) Fotal events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.80 S7.6.8 Venlafaxine versus paroxetine Hwang 2004 Dwens 2008 ZEN XR 367 (FDA) Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45	7 6 29 24 15 38 3 15 24 47 12 314 3, df = 14 (J) 31 12 46 61 , df = 2 (P =	34 196 73 70 153 15 79 102 100 95 33 171 55 1237 P = 0.35	12 18 29 20 40 5 24 18 35 32 16 46 12 323 3; IF = 9%	34 186 73 75 161 14 77 104 103 99 33 1700 54 1252	1.0% 2.2% 3.5% 4.2% 0.5% 2.3% 3.7% 4.6% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.07 [0.72, 1.44] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19]	
Basterzi 2009 Clerc 1994 Clerc 1994 Dosta 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b [Sai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.86 B7.6.8 Venlafaxine versus paroxetine Hwang 2004 Dwens 2008 /EN XR 367 (FDA) Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45 B7.6.9 Venlafaxine versus sertraline	7 6 29 24 15 38 3 15 24 42 14 47 12 314 3, df = 14 ()) 31 12 46 61 , df = 2 (P = 5)	34 196 73 70 153 15 79 102 100 95 33 171 155 1237 P= 0.35	12 18 29 20 40 5 5 24 18 35 32 16 46 12 323 10 28 41 1 = 0%	34 186 73 75 161 14 77 104 103 99 33 170 54 1252 81 176	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 4.6% 2.3% 4.6% 2.4% 5.4% 5.37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.07 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23]	
Basterzi 2009 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Delerick 1996 Heller 2009 Gornad 2000 Vemeroff 2007 Rudolph 1999 Shehehan 2009b Isai 2000 Iylee 1997 Izanakaki 2000 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Test for overall effect: Z = 0.25 (P = 0.80 37.6.8 Veniafaxine versus paroxetine Hwang 2004 Dwens 2008 ENI XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45 37.6.9 Veniafaxine versus sertraline Methonen 2000	7 6 6 29 24 15 38 8 3 15 5 24 42 28 42 114 47 12 314 3, df = 14 (i)) 3 12 46 61 , df = 2 (P : 5)	34 1966 73 70 153 155 79 1002 95 33 171 155 1237 P = 0.35	12 18 29 20 40 40 40 40 18 35 5 24 18 32 16 6 46 12 2 323 10 8 10 28 41 12 2 323 10 28 41 12 12 12 12 12 12 12 12 12 12 12 12 12	34 186 73 75 161 14 77 104 103 33 170 54 1252 81 176	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7% 5.0% 3.7.1% 0.3% 1.3% 4.2% 5.0%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.56, 1.19] 0.88 [0.63, 1.23]	
Basterzi 2009 Clerc 1994 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Gornad 2000 Wemeroff 2007 Rudolph 1999 Sheehan 2009b Fsai 2000 Tylee 1997 Fzanakaki 2000 Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.8) B7.6.8 Veniafaxine versus paroxetine Herogeneity: Tau² = 0.00; Chi² = 0.74 Evens 2008 JEN XR 387 (FDA) Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45) B7.6.9 Veniafaxine versus sertraline Methonen 2000 Shelton 2006 Shelton 2006	7 6 6 29 24 15 38 8 3 15 24 28 42 14 47 12 314 33 df = 14 (0))	34 1966 73 70 153 70 155 157 99 102 100 95 33 31 155 1237 P= 0.35 261 60 609); F	12 18 29 20 40 40 5 5 24 18 35 32 16 46 12 2 12 19 10 28 41 12 12 12 12 12 12 12 12 12 12 12 12 12	34 186 73 75 161 147 104 103 99 33 170 54 1252 53 42 81 176	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7% 4.8% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23]	
Basterzi 2009 Clerc 1994 Clerc 1994 Dosta 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Kornaat 2000 Nemeroff 2007 Rudolph 1999 Sheehan 2009b [Sai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.86 87.6.8 Venlafaxine versus paroxetine Hwang 2004 Dwens 2008 /EN XR 367 (FDA) Subtotal (95% CI) Fotal events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.48 87.6.9 Venlafaxine versus sertraline Mehtonen 2000 Shelton 2006 Bir 2005	7 6 6 29 24 15 38 8 3 15 5 24 42 28 42 114 47 12 314 3, df = 14 (i)) 3 12 46 61 , df = 2 (P : 5)	34 1966 73 70 153 155 179 100 95 33 171 155 1237 P = 0.35 261 261 260 75 78 84	12 18 29 20 40 40 40 40 18 35 5 24 18 32 16 6 46 12 2 323 10 8 10 28 41 12 2 323 10 28 41 12 12 12 12 12 12 12 12 12 12 12 12 12	34 186 73 75 161 144 77 104 103 9 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.3% 3.7% 4.6% 2.4% 5.0% 37.1% 0.3% 1.3% 5.8%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23] 1.28 [0.65, 2.51] 0.61 [0.31, 1.20] 1.81 [1.00, 3.28]	
Basterzi 2009 Clerc 1994 Clerc 1994 Dosta 1998 DeNayer 2002 Diaz-Martinez 1998 Delerick 1996 Heller 2009 Gornad 2000 Vemeroff 2007 Rudolph 1999 Sheehan 2009b Ssai 2000 Fylee 1997 Tzanakaki 2000 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.01; Chi² = 15.4 Fest for overall effect: Z = 0.25 (P = 0.80 37.6.8 Veniafaxine versus paroxetine Hwang 2004 Dwens 2008 VEN XR 367 (FDA) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.00; Chi² = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45 Sir 1005 Sir 1005 Sir 2005 Sir 2005 Subtotal (95% CI)	7 6 6 29 24 15 38 8 3 15 5 24 42 28 42 14 47 12 314 3, df = 14 (i)) 3 12 46 61 (if f = 2 (P = 5))	34 1966 73 70 153 70 155 157 99 102 100 95 33 31 155 1237 P= 0.35 261 60 609); F	12 18 29 20 40 40 40 40 41 88 35 5 32 16 46 46 42 12 323 100 80 41 12 12 19 13 13	34 186 73 75 161 147 104 103 99 33 170 54 1252 53 42 81 176	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.2% 2.3% 3.7% 4.8% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23]	
Rasterzi 2009 Flerc 1994 Flerc 1994 Flerc 1998 DeNayer 2002 Flarc 1998 DeNayer 2002 Flarc 1998 Delerk 1996 Fleller 2009 Flerc 1996 Fleller 2009 Flerc 1907	7 6 6 299 24 15 38 3 15 24 42 14 47 12 314 3, df = 14 () 11 25 52 , df = 2 (P = 52 , df = 2	34 1966 73 70 153 70 155 1237 P= 0.35 261 75 78 84 237	12 18 18 29 20 40 40 40 40 40 40 40 40 40 40 40 40 40	34 186 73 75 161 144 77 104 103 9 33 170 54 1252	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.3% 3.7% 4.6% 2.4% 5.0% 37.1% 0.3% 1.3% 5.8%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23] 1.28 [0.65, 2.51] 0.61 [0.31, 1.20] 1.81 [1.00, 3.28]	
Basterzi 2009 Clerc 1994 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Gornad 2000 Gornad 200	7 6 6 299 24 15 38 3 15 24 42 14 47 12 314 3, df = 14 () 11 25 52 , df = 2 (P = 52 , df = 2	34 1966 73 70 153 165 79 102 100 95 33 31 155 1237 P= 0.35 261 44 165 261 261 27 75 78 84 237	12 18 18 29 20 40 40 40 40 40 40 40 40 40 40 40 40 40	34 186 73 75 161 11 11 11 11 11 11 11 11 11 11 11 11	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 4.8% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23] 1.28 [0.65, 2.51] 0.61 [0.31, 1.20] 1.81 [1.00, 3.28] 1.14 [0.60, 2.14]	
Basterzi 2009 Clerc 1994 Clerc 1994 Dosta 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 -teller 2009 Gornad 2000 Wemeroff 2007 Rudolph 1999 Sheehan 2009b Fsai 2000 Tylee 1997 Tzanakaki 2000 Subtotal (95% CI) Total events -telerogeneity. Tau" = 0.01; Chi" = 15.4 Fest for overall effect: Z = 0.25 (P = 0.80 87.6.8 Venlafaxine versus paroxetine- twang 2004 Dwens 2008 ZEN XR 367 (FDA) Subtotal (95% CI) Total events -telerogeneity: Tau" = 0.00; Chi" = 0.74 Fest for overall effect: Z = 0.76 (P = 0.45 87.6.9 Venlafaxine versus sertraline Mehtonen 2000 Sir 2005 Subtotal (95% CI) Total events -teletogeneity: Tau" = 0.00; Chi" = 5.73 Fest for overall effect: Z = 0.40 (P = 0.65 Fotal events -teletogeneity: Tau" = 0.20; Chi" = 5.73 Fest for overall effect: Z = 0.40 (P = 0.65 Fotal (95% CI)	7 6 6 29 24 15 38 3 15 24 42 14 47 12 314 3, df = 14 (3) 46 61 12 5) 16 52 (df = 2 (P = 3))	34 1966 73 70 153 70 155 1237 P= 0.35 261 75 78 84 237	12 18 29 20 40 40 40 40 40 41 81 35 32 32 31 60 42 19 90 81 19 90	34 186 73 75 161 11 11 11 11 11 11 11 11 11 11 11 11	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 2.3% 3.7% 4.6% 2.4% 5.0% 37.1% 0.3% 1.3% 5.8%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.54, 1.25] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23] 1.28 [0.65, 2.51] 0.61 [0.31, 1.20] 1.81 [1.00, 3.28]	
Basterzi 2009 Clerc 1994 Clerc 1994 Costa 1998 DeNayer 2002 Diaz-Martinez 1998 Dierick 1996 Heller 2009 Gornad 2000 Gornad 200	7 6 6 29 24 15 38 8 3 15 24 42 14 47 12 314 47 12 46 61 , df = 2 (P = 5) 16 11 25 , df = 2 (P = 3)	34 1966 73 70 153 155 79 1002 95 33 171 155 1237 P = 0.35 261 75 261 75 78 84 237	12 18 29 20 40 40 40 40 41 81 83 55 24 41 81 81 81 81 81 81 81 81 81 81 81 81 81	34 186 73 75 161 14 77 104 103 33 1700 54 1252 53 42 81 176 72 82 233 3533	1.0% 2.2% 3.5% 2.0% 4.2% 0.5% 4.8% 2.4% 5.0% 1.4% 37.1%	0.50 [0.21, 1.18] 1.53 [0.88, 2.66] 0.83 [0.54, 1.28] 0.80 [0.45, 1.44] 1.00 [0.68, 1.47] 0.56 [0.16, 1.92] 0.61 [0.35, 1.07] 1.36 [0.79, 2.35] 0.82 [0.54, 1.25] 1.37 [0.95, 1.97] 0.88 [0.51, 1.97] 0.88 [0.51, 1.49] 1.02 [0.72, 1.44] 0.98 [0.48, 1.99] 0.98 [0.85, 1.13] 1.02 [0.22, 4.82] 1.15 [0.55, 2.36] 0.81 [0.55, 1.19] 0.88 [0.63, 1.23] 1.28 [0.65, 2.51] 0.61 [0.31, 1.20] 1.81 [1.00, 3.28] 1.14 [0.60, 2.14]	

1 Figure 480: Quality of life endpoint



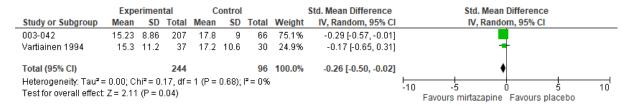
2 Test for subgroup differences: Not applicable

3 Figure 481: Quality of life change score

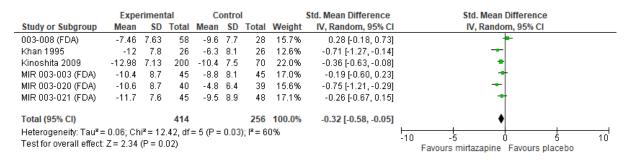


6 More severe: Mirtazapine versus placebo

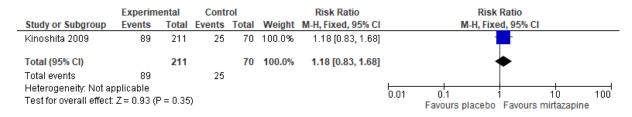
7 Figure 482: Depression symptomatology at endpoint



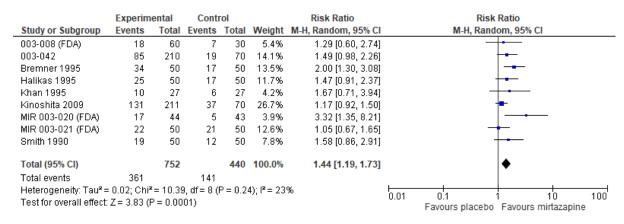
9 Figure 483: Depression symptomatology change score



1 Figure 484: Remission (ITT)



3 Figure 485: Response (ITT)



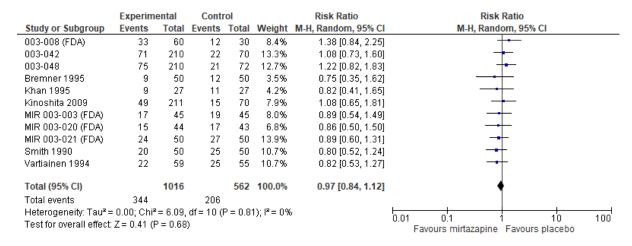
5 Figure 486: Discontinuation due to SE

	Experimental		Cont	rol		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Events Total Events Total Weight M-H, Rando		M-H, Random, 95% CI		M-H, Random, 95% CI				
003-008 (FDA)	19	60	4	30	11.8%	2.38 [0.89, 6.36]		-		
003-042	36	210	5	70	13.8%	2.40 [0.98, 5.88]		-		
003-048	23	210	3	72	8.8%	2.63 [0.81, 8.49]		 -		
Bremner 1995	3	50	2	50	4.3%	1.50 [0.26, 8.60]		- •		
Halikas 1995	7	50	3	50	7.4%	2.33 [0.64, 8.51]		 • 		
Khan 1995	1	27	1	27	1.9%	1.00 [0.07, 15.18]				
Kinoshita 2009	11	211	2	70	5.8%	1.82 [0.41, 8.03]		- •		
MIR 003-003 (FDA)	9	45	11	45	17.0%	0.82 [0.38, 1.78]				
MIR 003-020 (FDA)	6	44	8	43	12.1%	0.73 [0.28, 1.94]				
MIR 003-021 (FDA)	9	50	9	50	15.3%	1.00 [0.43, 2.31]				
Smith 1990	7	50	0	50	1.7%	15.00 [0.88, 255.78]		-	→	
Total (95% CI)		1007		557	100.0%	1.49 [1.02, 2.17]		•		
Total events	131		48							
Heterogeneity: Tau ² =	-		0.01	0.1 1 10	100					
Test for overall effect:	Z - 2.00 (r = 0.04	/					Favours mirtazapine Favours placebo		

6

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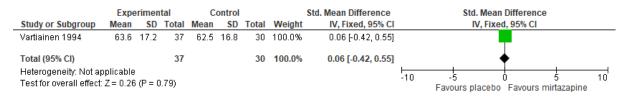
1 Figure 487: Discontinuation due to any reason including SE



3 Figure 488: Global functioning endpoint

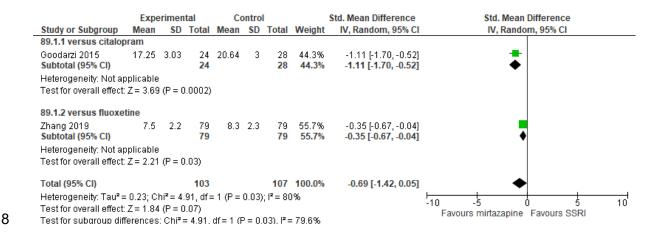
2

4 5

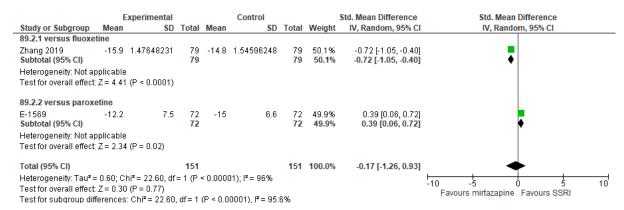


6 More severe: Mirtazapine versus SSRIs

7 Figure 489: Depression symptomatology endpoint

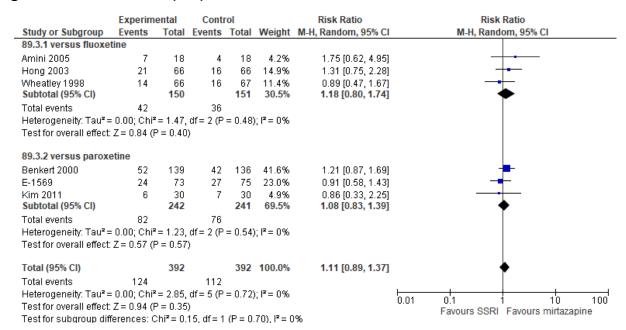


1 Figure 490: Depression symptomatology change score



3 Figure 491: Remission (ITT)

2



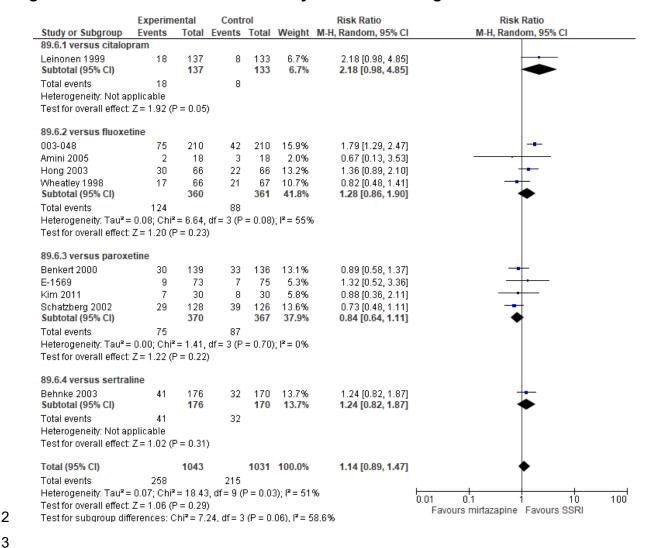
1 Figure 492: Response (ITT)

	Experim		Contr			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
89.4.1 versus citalo							
Leinonen 1999 Subtotal (95% CI)	116	137 137	117	133 133	25.2% 25.2%	0.96 [0.88, 1.06] 0.96 [0.88, 1.06]	•
Total events	116		117				
Heterogeneity: Not a	pplicable						
Test for overall effect	Z = 0.79 (F	P = 0.43)				
89.4.2 versus fluoxe	etine						
Amini 2005	12	18	8	18	2.1%	1.50 [0.81, 2.76]	+
Hong 2003	35	66	30	66	5.7%	1.17 [0.82, 1.65]	 -
Wheatley 1998	38	66	34	67	6.7%	1.13 [0.83, 1.55]	 -
Zhang 2019	55	79	43	79	9.6%	1.28 [1.00, 1.64]	 -
Subtotal (95% CI)		229		230	24.1%	1.23 [1.04, 1.45]	•
Total events	140		115				
Heterogeneity: Tau²:	= 0.00; Chi²	= 0.84,	df=3 (P	= 0.84); I² = 0%		
Test for overall effect	:: Z= 2.45 (F	P = 0.01))				
89.4.3 versus parox	etine						
Benkert 2000	74	139	66	136	10.6%	1.10 [0.87, 1.38]	+
E-1569	40	73	48	75	8.6%	0.86 [0.65, 1.12]	-
Kim 2011	19	30	20	30	5.1%	0.95 [0.66, 1.38]	
Schatzberg 2002 Subtotal (95% CI)	81	128 370	69	126 367	12.4% 36.7%	1.16 [0.94, 1.42] 1.04 [0.90, 1.19]	
Total events	214		203				
Heterogeneity: Tau²:		= 3.45		= 0.33	r P = 13%	<u> </u>	
Test for overall effect				0.00,	,,	•	
89.4.4 versus sertra	iline						
Behnke 2003	93	176	101	170	14.1%	0.89 [0.74, 1.07]	-
Subtotal (95% CI)		176		170	14.1%	0.89 [0.74, 1.07]	•
Total events	93		101				
Heterogeneity: Not a	pplicable						
Test for overall effect	:: Z = 1.23 (F	P = 0.22)				
Total (95% CI)		912		900	100.0%	1.04 [0.95, 1.13]	
Total events	563		536				
Heterogeneity: Tau ² :	= 0.01; Chi²	= 13.23	df = 9 (f	P = 0.1	5); I² = 32	%	
Test for overall effect							'0.01 0.1 1 10 10 Favours SSRI Favours mirtazapine
Test for subgroup di				(P = 0)	$(04), \mathbf{l}^2 = 6$	64.0%	ravours somi ravours minazapine

1 Figure 493: Discontinuation due to SE

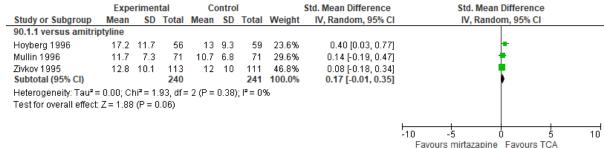
Study or Subarous	Experim		Conti		Majaht	Risk Ratio	Risk Ratio
Study or Subgroup 89.5.1 versus citalop	Events	TOTAL	Events	Total	weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Leinonen 1999	8	137	4	133	8.3%	1.94 [0.60, 6.30]	
Subtotal (95% CI)	0	137	4	133	8.3%	1.94 [0.60, 6.30]	-
Total events	8		4				
Heterogeneity: Not ap							
Test for overall effect:	Z = 1.11 (F	P = 0.27)				
89.5.2 versus fluoxet	ine						
003-048	23	210	12	210	13.8%	1.92 [0.98, 3.75]	
Amini 2005	1	18	2	18	3.1%	0.50 [0.05, 5.04]	
Hong 2003	13	66	8	66	12.0%	1.63 [0.72, 3.66]	+-
Wheatley 1998	7	66	9	67	10.7%	0.79 [0.31, 2.00]	
Subtotal (95% CI)		360		361	39.6%	1.40 [0.88, 2.23]	•
Total events	44		31				
Heterogeneity: Tau² =				= 0.36)); I² = 6%		
Test for overall effect:	Z = 1.43 (F	P = 0.15)				
89.5.3 versus paroxe	tine						
Benkert 2000	12	139	10	136	12.1%	1.17 [0.52, 2.63]	
E-1569	5	73	6	75	8.6%	0.86 [0.27, 2.68]	
Kim 2011	2	30	3	30	5.0%	0.67 [0.12, 3.71]	
Schatzberg 2002	19	128	33	126	16.0%	0.57 [0.34, 0.94]	-
Subtotal (95% CI)		370		367	41.7%	0.71 [0.48, 1.05]	•
Total events	38		52				
Heterogeneity: Tau² =	0.00; Chi ²	= 2.37,	df = 3 (P	= 0.50)); I² = 0%		
Test for overall effect:	Z = 1.70 (F	P = 0.09)				
89.5.4 versus sertral	ine						
Behnke 2003	21	176	5	170	10.4%	4.06 [1.57, 10.51]	
Subtotal (95% CI)		176		170	10.4%	4.06 [1.57, 10.51]	-
Total events	21		5				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 2.88 (F	P = 0.00	4)				
Total (95% CI)		1043		1031	100.0%	1.22 [0.78, 1.89]	*
Total events	111		92				
Heterogeneity: Tau² =	0.25; Chi ²	= 19.80	i, df = 9 (i	P = 0.03	2); I² = 55	%	0.01 0.1 1 10 100
Test for overall effect:	Z = 0.88 (F	P = 0.38)				Favours mirtazapine Favours SSRI
Test for subgroup diff	erences: C	hi²=13	1.88, df=	3 (P = 1	0.003), I²:	= 78.4%	r avours mintazapine i avours conti

1 Figure 494: Discontinuation due to any reason including SE



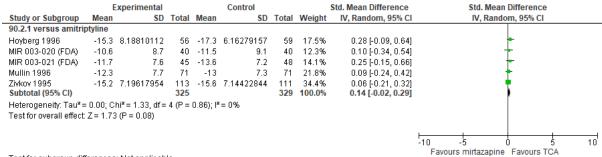
4 More severe: Mirtazapine versus TCAs

5 Figure 495: Depression symptomatology endpoint



6 Test for subgroup differences: Not applicable

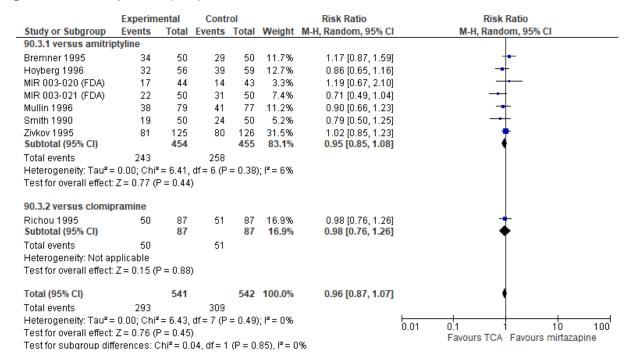
1 Figure 496: Depression symptomatology change score



2 Test for subgroup differences: Not applicable

4

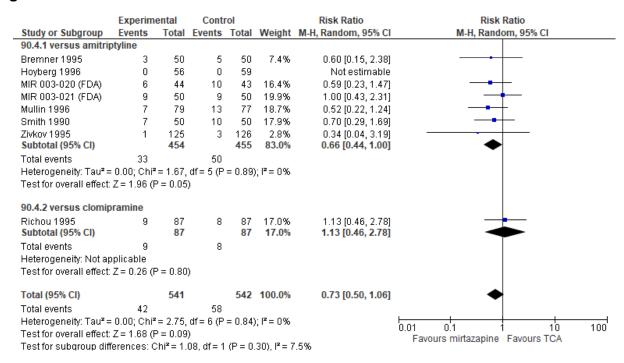
3 Figure 497: Response (ITT)



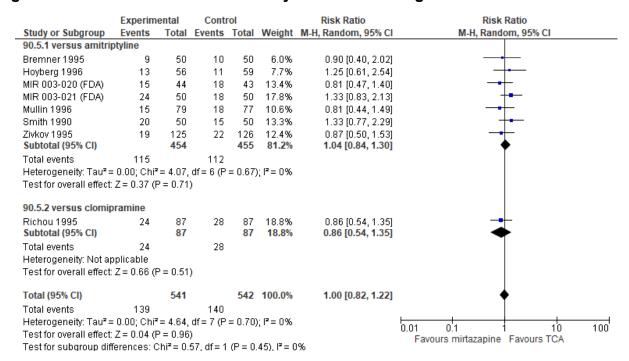
1 Figure 498: Discontinuation due to SE

2

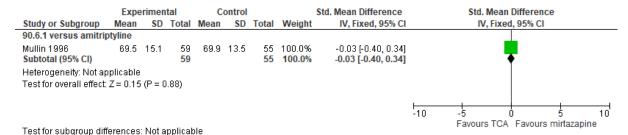
4



3 Figure 499: Discontinuation due to any reason including SE

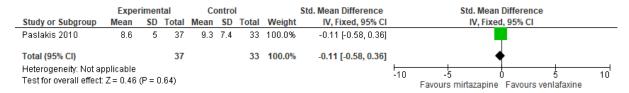


1 Figure 500: Global functioning endpoint

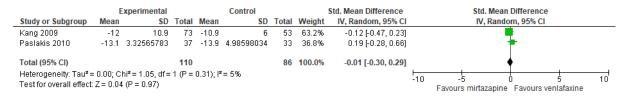


3 More severe: Mirtazapine versus venlafaxine

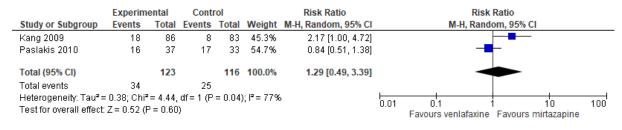
4 Figure 501: Depression symptomatology endpoint



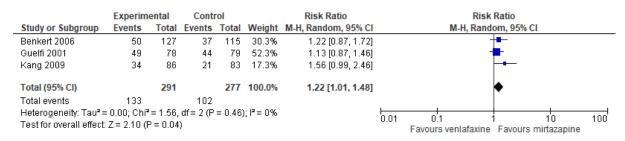
6 Figure 502: Depression symptomatology change score



8 Figure 503: Remission (ITT)



10 Figure 504: Response (ITT)



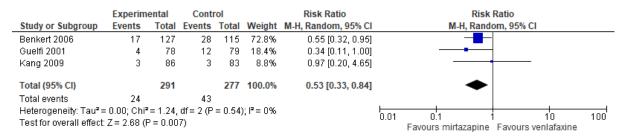
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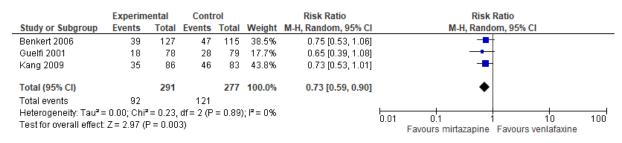
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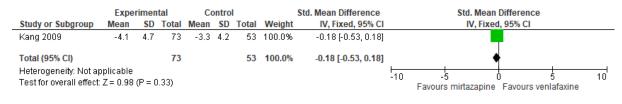
1 Figure 505: Discontinuation due to SE



3 Figure 506: Discontinuation due to any reason including SE



5 Figure 507: Sleeping difficulties change score

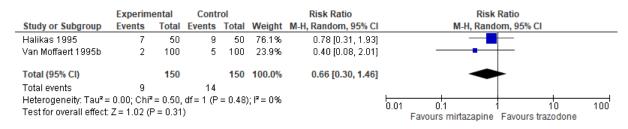


8 More severe: Mirtazapine versus trazodone

9 Figure 508: Response (ITT)

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Rand	om, 95% CI	
Halikas 1995	25	50	20	50	24.2%	1.25 [0.81, 1.94]		-	-	
Van Moffaert 1995b	61	100	51	100	75.8%	1.20 [0.93, 1.53]			=	
Total (95% CI)		150		150	100.0%	1.21 [0.97, 1.50]			*	
Total events	86		71							
Heterogeneity: Tau² =	0.00; Chi²	= 0.03,	df=1 (P	= 0.86)	; I² = 0%		0.01	n 1	1 10	100
Test for overall effect:	Z = 1.72 (F	P = 0.08)				0.01	0.1	Favours mirtazapine	100

11 Figure 509: Discontinuation due to SE



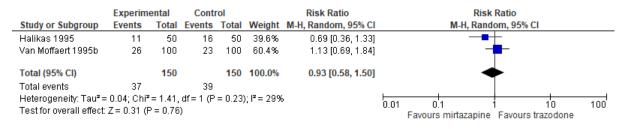
12

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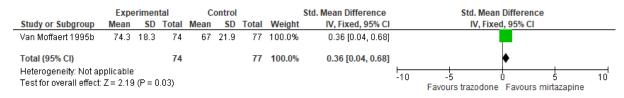
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1 Figure 510: Discontinuation due to any reason including SE



3 Figure 511: Global functioning endpoint



6 More severe: Trazodone versus placebo

7 Figure 512: Depression symptomatology endpoint

	Expe	rimen	tal	Control				Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	t IV, Random, 95% CI IV, Random, 95% CI				
Sheehan 2009a	11.8	8	202	13.2	8.1	204	50.9%	-0.17 [-0.37, 0.02]]			
Zhang 2014	10.8	6.4	183	13.8	6.9	180	49.1%	-0.45 [-0.66, -0.24]	i			
Total (95% CI)			385			384	100.0%	-0.31 [-0.58, -0.04]	1 ♦			
Heterogeneity: Tau² = Test for overall effect:				1 (P =	0.06)	; I² = 72		-10 -5 0 5 10 Favours trazodone Favours placebo				

9 Figure 513: Depression symptomatology change score

	Exper	imen	tal	Co	Control Std. Mean Difference				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Sheehan 2009a	-11.4	8.2	202	-9.3	7.9	204	52.4%	-0.26 [-0.46, -0.06]	
Zhang 2014	-11.07	6.5	183	-8.29	6.5	180	47.6%	-0.43 [-0.63, -0.22]	•
Total (95% CI)			385			384	100.0%	-0.34 [-0.50, -0.18]	•
Heterogeneity: Tau² = Test for overall effect:			-10 -5 0 5 10 Favours trazodone Favours placebo						

11 Figure 514: Remission (ITT)

	Experim	ental	Conti	rol		Risk Ratio		Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	/eight M-H, Random, 95% CI M-H, Random, 95% CI					
Sheehan 2009a	72	206	65	206	53.7%	1.11 [0.84, 1.46]			-		
Zhang 2014	65	192	40	190	46.3%	1.61 [1.15, 2.26]			-		
Total (95% CI)		398		396	100.0%	1.32 [0.91, 1.90]			•		
Total events	137		105								
Heterogeneity: Tau ² = Test for overall effect:				= 0.09)); I²= 65%	5	0.01	0.1 Favours placebo	1 10 Favours trazodo	100 ne	

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4 5

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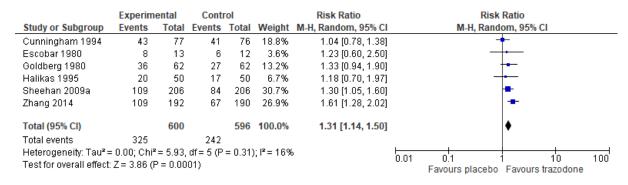
1 Figure 515: Response (ITT)

2

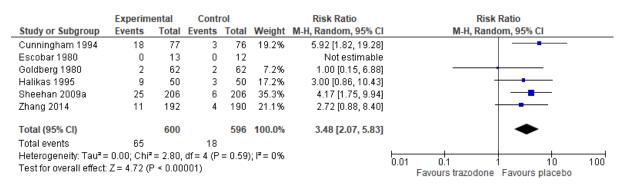
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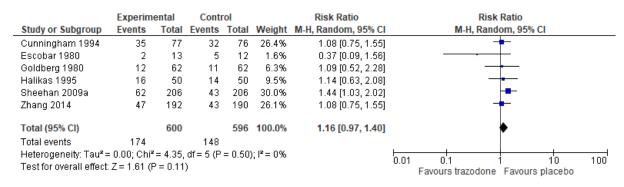
8 9



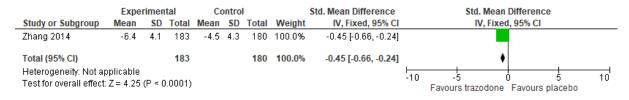
3 Figure 516: Discontinuation due to SE



5 Figure 517: Discontinuation due to any reason including SE

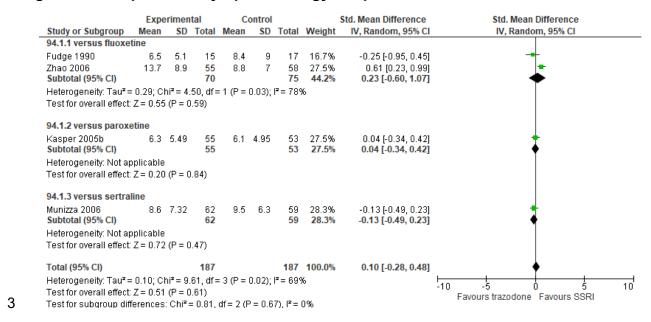


7 Figure 518: Sleeping difficulties change score

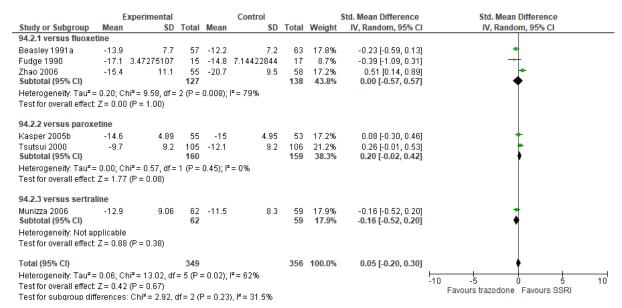


1 More severe: Trazodone versus SSRIs

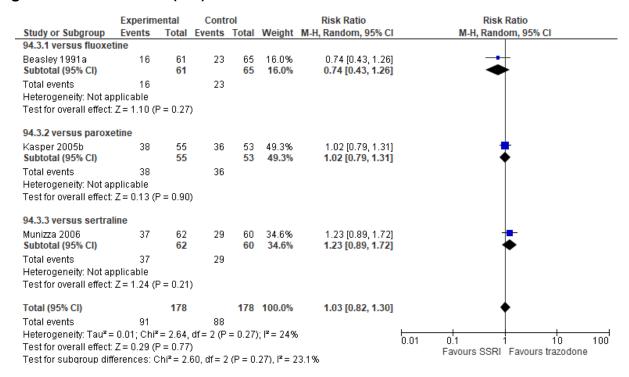
2 Figure 519: Depression symptomatology endpoint



4 Figure 520: Depression symptomatology change score



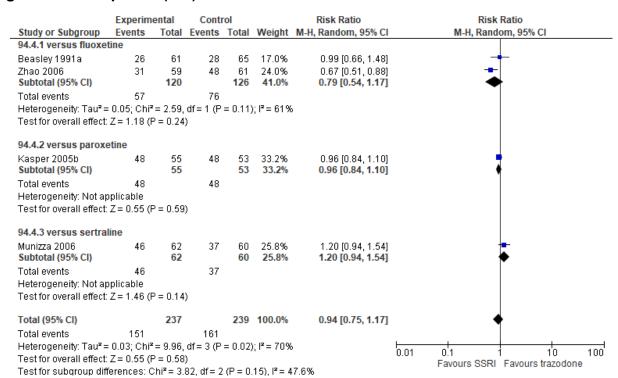
1 Figure 521: Remission (ITT)



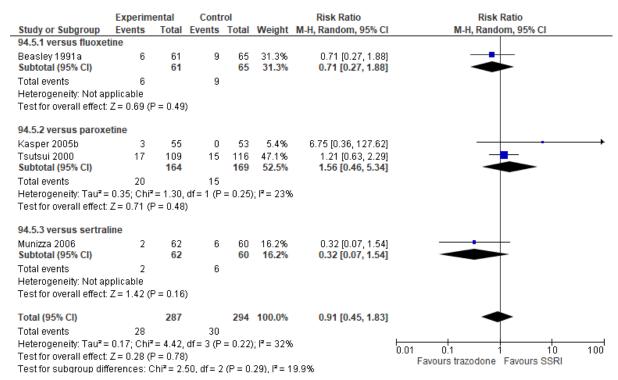
3 Figure 522: Response (ITT)

2

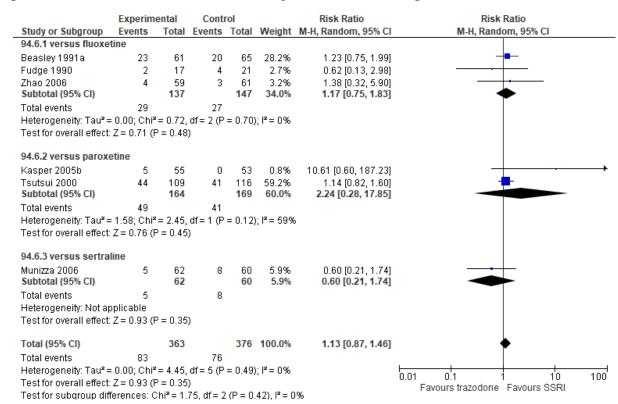
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1 Figure 523: Discontinuation due to SE



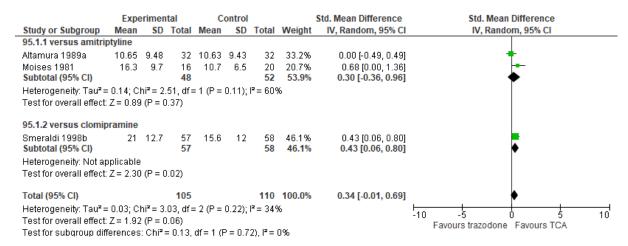
3 Figure 524: Discontinuation due to any reason including SE



4

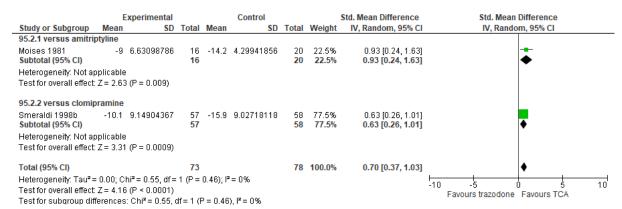
1 More severe: Trazodone versus TCAs

2 Figure 525: Depression symptomatology at endpoint

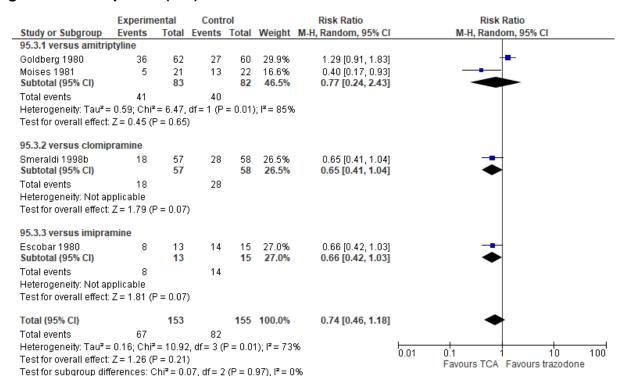


4 Figure 526: Depression symptomatology change score

3

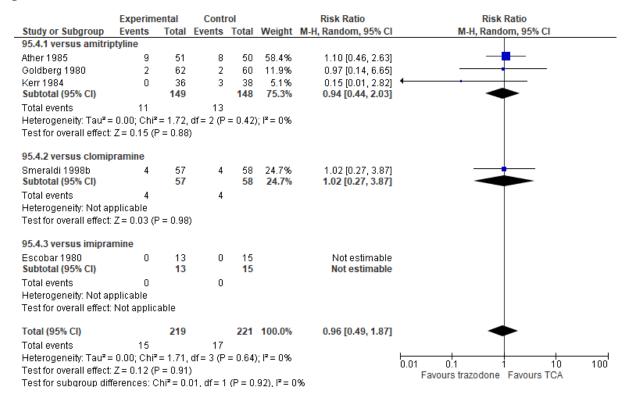


1 Figure 527: Response (ITT)

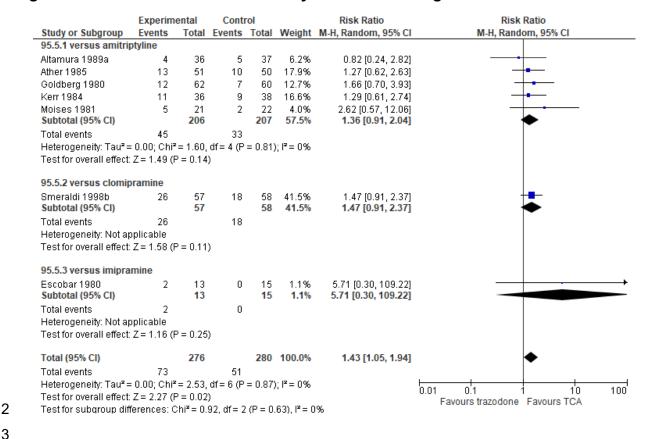


3 Figure 528: Discontinuation due to SE

2

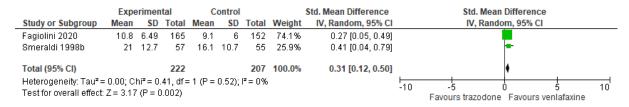


1 Figure 529: Discontinuation due to any reason including SE

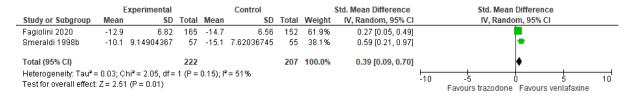


4 More severe: Trazodone versus venlafaxine

5 Figure 530: Depression symptomatology endpoint

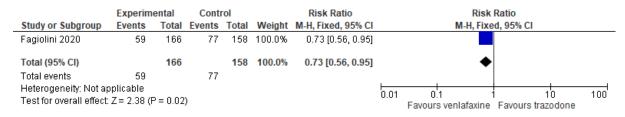


7 Figure 531: Depression symptomatology change score



6

1 Figure 532: Remission (ITT)



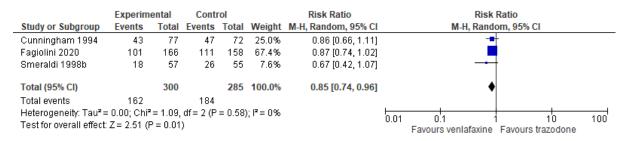
3 Figure 533: Response (ITT)

2

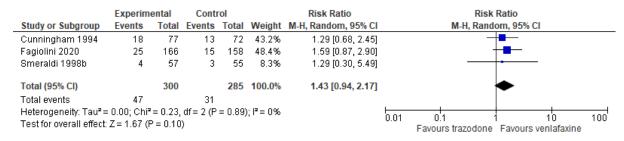
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8 9

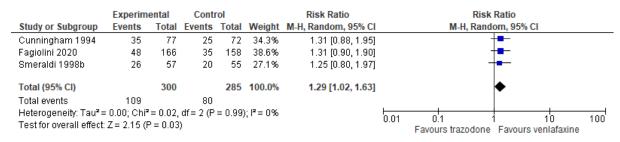
13



5 Figure 534: Discontinuation due to SE

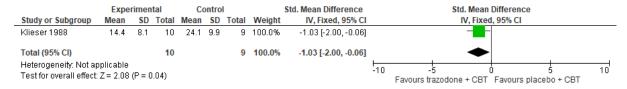


7 Figure 535: Discontinuation due to any reason including SE



10 More severe: Trazodone + CBT individual versus placebo +11 CBT individual

12 Figure 536: Depression symptomatology endpoint

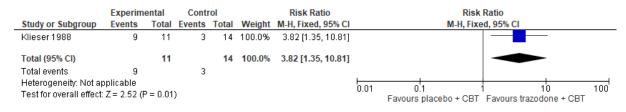


1 Figure 537: Response (ITT)

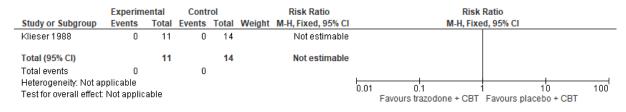
2

4

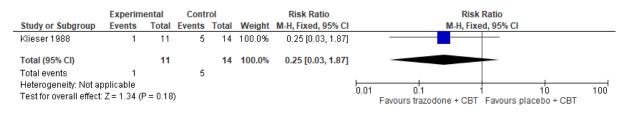
6 7



3 Figure 538: Discontinuation due to SE



5 Figure 539: Discontinuation due to any reason including SE

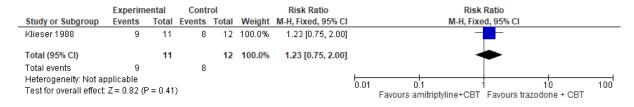


8 More severe: Trazodone + CBT individual versus9 amitriptyline + CBT individual

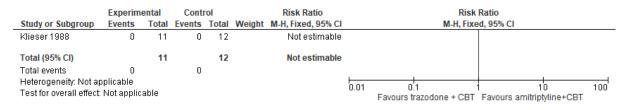
10 Figure 540: Depression symptomatology endpoint

	Expe	rimen	ital	C	ontrol			Std. Mean Difference	Std. Mean Differ	ence
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95%	CI
Klieser 1988	14.4	8.1	10	10.8	10.2	10	100.0%	0.37 [-0.51, 1.26]	-	
Total (95% CI)			10			10	100.0%	0.37 [-0.51, 1.26]	•	
Heterogeneity: Not ap Test for overall effect:		(P = 0	0.41)) -5 0 Favours trazodone + CBT Favo	5 10 urs amitriptyline+CBT

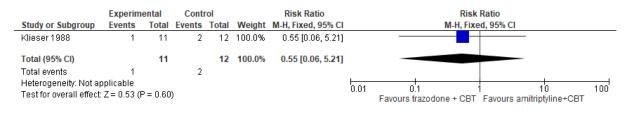
12 Figure 541: Response (ITT)



1 Figure 542: Discontinuation due to SE



3 Figure 543: Discontinuation due to any reason including SE



6 More severe: Supervised high intensity exercise individual versus no treatment

8 Figure 544: Depression symptomatology endpoint

	Expe	erimen	tal	C	ontrol			Std. Mean Difference		Std. Mean I	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Randoi	m, 95% CI		
Hemat-Far 2012	16.6	6.9	10	22.8	4.9	10	9.8%	-0.99 [-1.93, -0.05]		-			
Huipeng 2013	8.7	4.4	35	11.8	3.8	33	35.8%	-0.74 [-1.24, -0.25]		-			
Jinchun 2015	5.01	3.31	35	7.26	4.42	35	38.0%	-0.57 [-1.05, -0.09]		-			
Khoshnab 2017	27.27	6.51	15	30	4.37	15	16.4%	-0.48 [-1.21, 0.25]			-		
Total (95% CI)			95			93	100.0%	-0.66 [-0.95, -0.36]		•			
Heterogeneity: Tau ² = Test for overall effect:					0.81);	I* = 0%			-10	-5 0 Favours exercise	Favours no	treatment	10

10 Figure 545: Depression symptomatology change score



12 Figure 546: Remission (ITT)

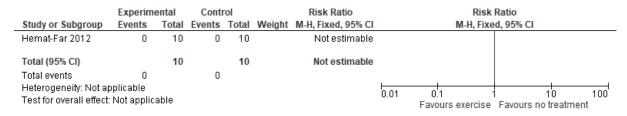
	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Huipeng 2013	16	35	9	33	100.0%	1.68 [0.86, 3.26]	+
Total (95% CI)		35		33	100.0%	1.68 [0.86, 3.26]	◆
Total events	16		9				
Heterogeneity: Not ap Test for overall effect:	•	° = 0.13)				0.01 0.1 1 10 100 Favours no treatment Favours exercise

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1 Figure 547: Discontinuation due to any reason



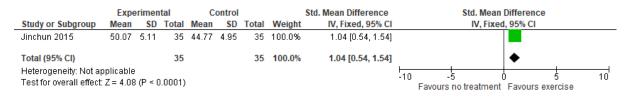
3 Figure 548: Quality of life endpoint

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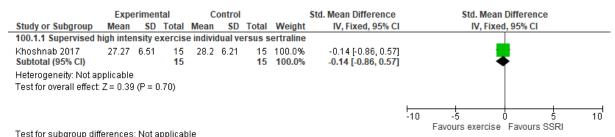
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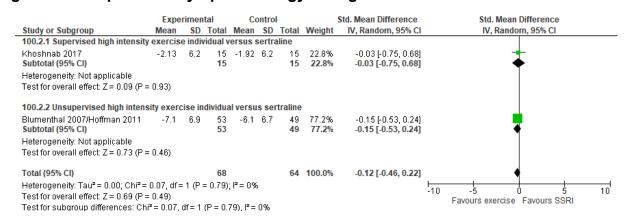


6 More severe: Exercise individual versus SSRI

7 Figure 549: Depression symptomatology endpoint



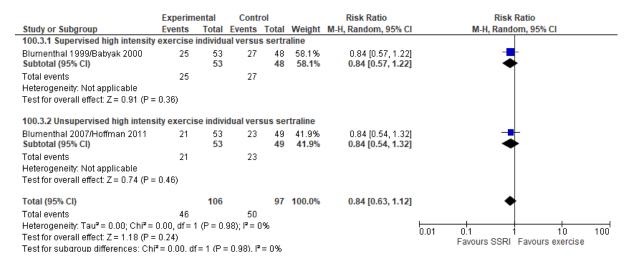
9 Figure 550: Depression symptomatology change score



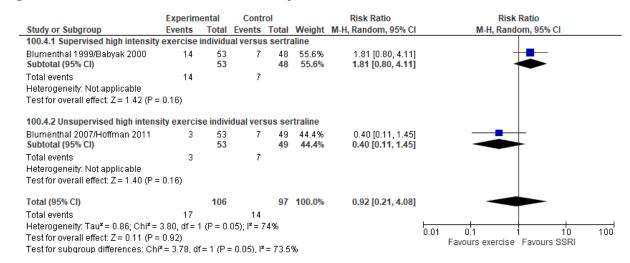
1 Figure 551: Remission (ITT)

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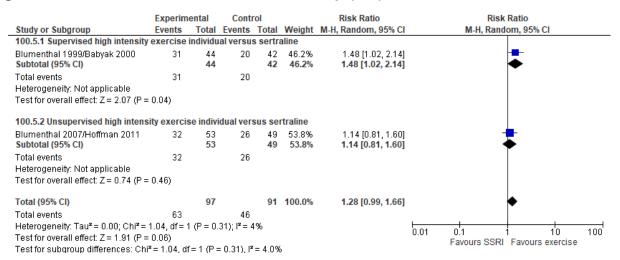
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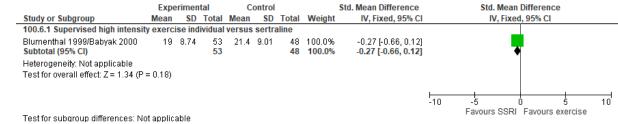
3 Figure 552: Discontinuation due to any reason



5 Figure 553: Remission at 6-12 month follow-up (ITT)



1 Figure 554: Quality of life endpoint

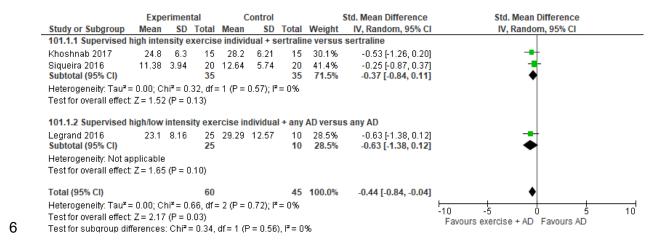


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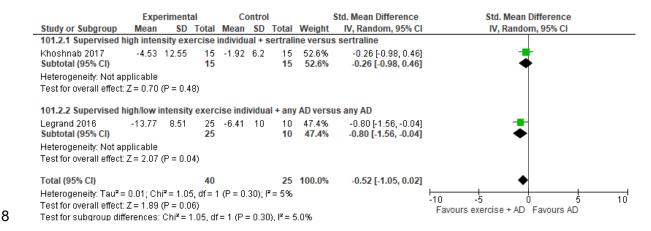
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4 More severe: Exercise individual + AD versus AD

5 Figure 555: Depression symptomatology endpoint



7 Figure 556: Depression symptomatology change score

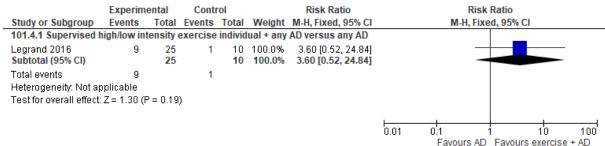


1 Figure 557: Remission (ITT)



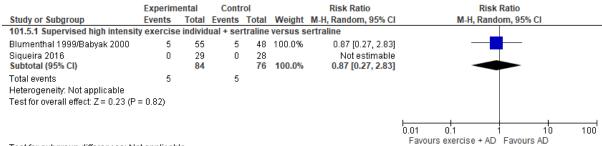
2 Test for subgroup differences: Not applicable

3 Figure 558: Response (ITT)



4 Test for subgroup differences: Not applicable

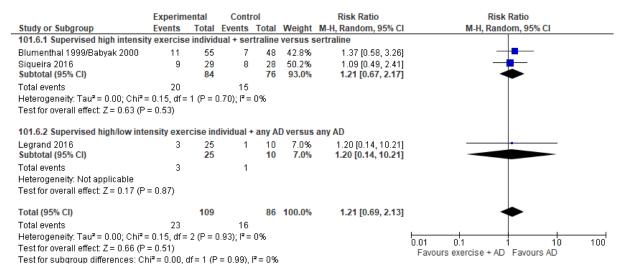
5 Figure 559: Discontinuation due to SE



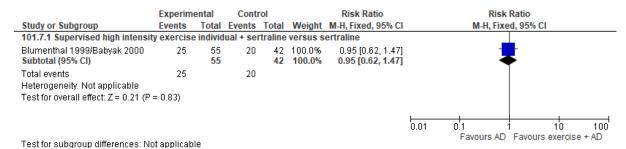
6 Test for subgroup differences: Not applicable

8

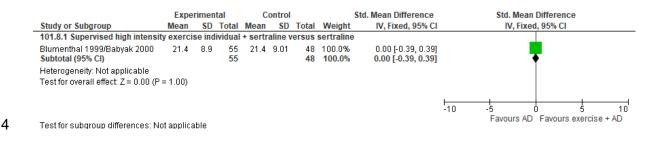
7 Figure 560: Discontinuation due to any reason including SE



1 Figure 561: Remission at 6-month follow-up (ITT)

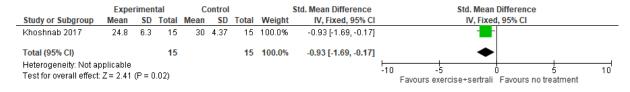


3 Figure 562: Quality of life endpoint

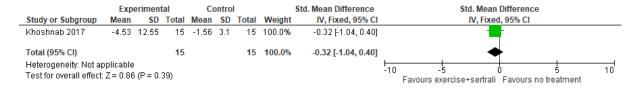


6 More severe: Supervised high intensity exercise individual + 7 sertraline versus no treatment

8 Figure 563: Depression symptomatology endpoint



10 Figure 564: Depression symptomatology change score



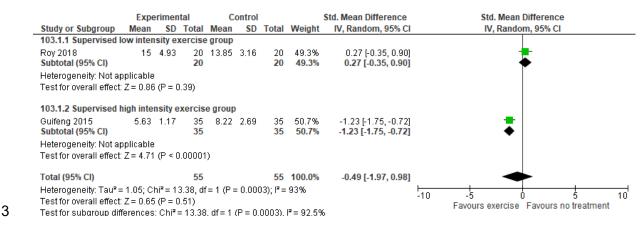
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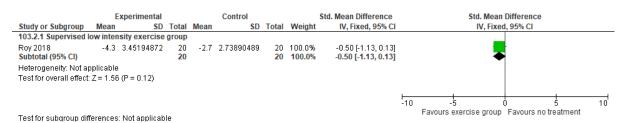
5

1 More severe: Exercise group versus no treatment

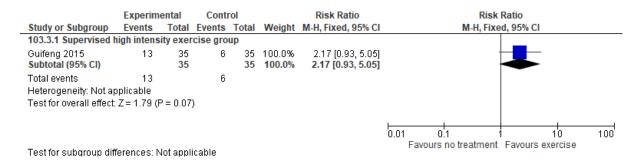
2 Figure 565: Depression symptomatology endpoint



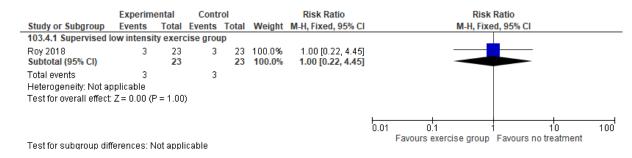
4 Figure 566: Depression symptomatology change score



6 Figure 567: Response (ITT)



8 Figure 568: Discontinuation due to any reason



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1 More severe: Supervised low/high intensity exercise group

2 versus TAU

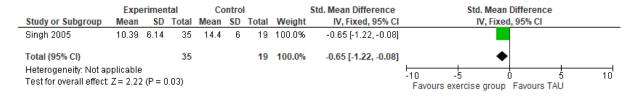
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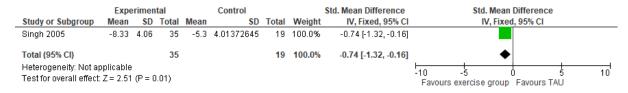
8

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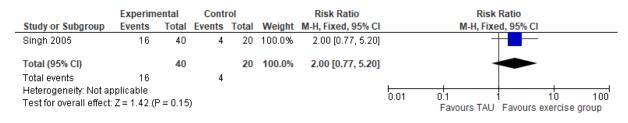
3 Figure 569: Depression symptomatology endpoint



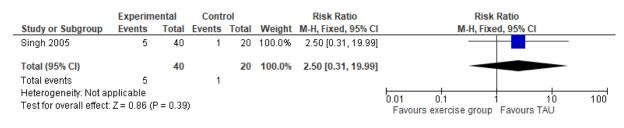
5 Figure 570: Depression symptomatology change score



7 Figure 571: Response (ITT)



9 Figure 572: Discontinuation due to any reason



12 More severe: Supervised high intensity exercise group

13 versus sertraline

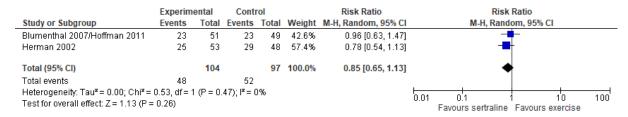
14 Figure 573: Depression symptomatology change score



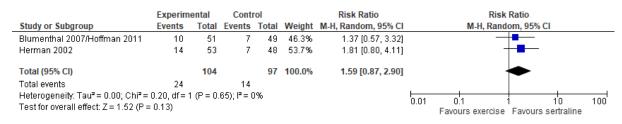
1 Figure 574: Remission (ITT)

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3 Figure 575: Discontinuation due to any reason



5 Figure 576: Remission at 12-month follow-up (ITT)

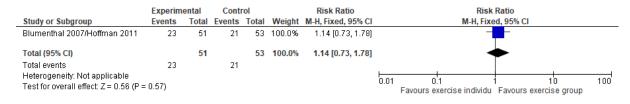


8 More severe: Supervised high intensity exercise group versus unsupervised high intensity exercise individual

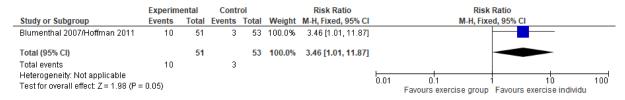
10 Figure 577: Depression symptomatology change score

	Exper	rimen	tal	Co	ontro	I		Std. Mean Difference		Std. Mear	Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% CI	
Blumenthal 2007/Hoffman 2011	-7.2	6.9	51	-7.1	6.9	53	100.0%	-0.01 [-0.40, 0.37]				
Total (95% CI)			51			53	100.0%	-0.01 [-0.40, 0.37]		•	•	
Heterogeneity: Not applicable Test for overall effect: Z = 0.07 (P =	: 0.94)								-10	-5 Favours exercise group	0 Favours exerci:	5 10 se individu

12 Figure 578: Remission (ITT)



1 Figure 579: Discontinuation due to any reason



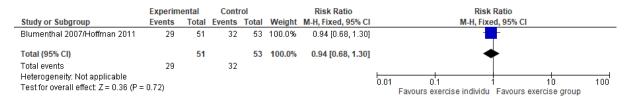
3 Figure 580: Remission at 12-month follow-up (ITT)

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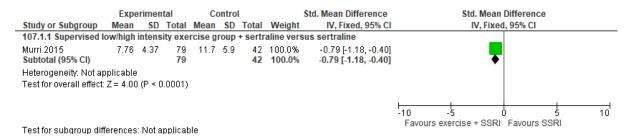
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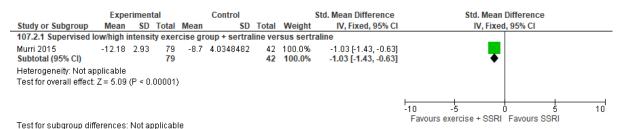


6 More severe: Exercise group + SSRI versus SSRI

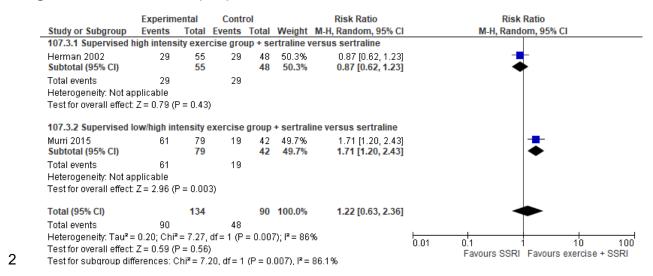
7 Figure 581: Depression symptomatology endpoint



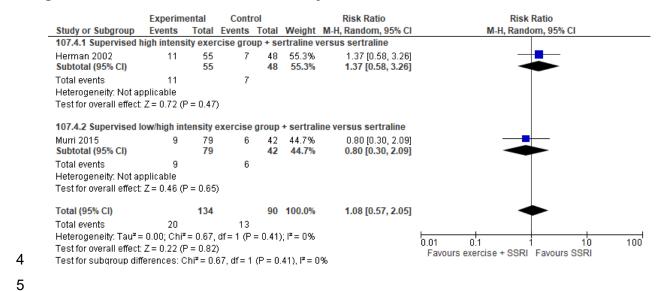
9 Figure 582: Depression symptomatology change score



1 Figure 583: Remission (ITT)

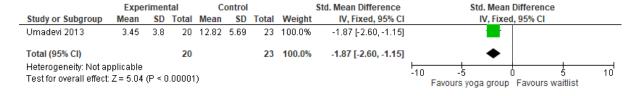


3 Figure 584: Discontinuation due to any reason

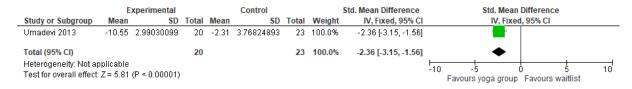


6 More severe: Yoga group versus waitlist

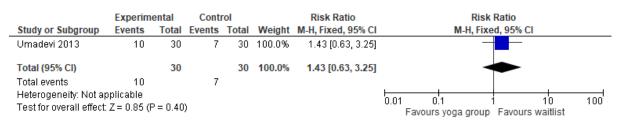
7 Figure 585: Depression symptomatology endpoint



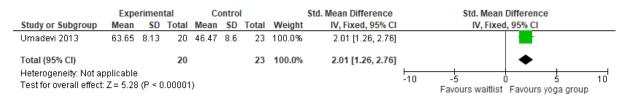
1 Figure 586: Depression symptomatology change score



3 Figure 587: Discontinuation due to any reason



5 Figure 588: Quality of life endpoint



8 More severe: Yoga group versus imipramine

9 Figure 589: Depression symptomatology endpoint

	Expe	rimen	ital	Co	ontro	I		Std. Mean Difference		Std. M	ean Differei	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, F	ixed, 95% C	1	
Janakiramaiah 2000	8.3	8.6	15	6.3	7.9	15	100.0%	0.24 [-0.48, 0.95]			-		
Total (95% CI)			15			15	100.0%	0.24 [-0.48, 0.95]		1	•		
Heterogeneity: Not app Test for overall effect: 2		P = 0.6	52)						-10	-5 Favours yoga gro	oup Favour	5 rs imipramii	10 ne

11 Figure 590: Depression symptomatology change score

	E	xperimental			Control			Std. Mean Difference		Std. Mear	Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% CI		
Janakiramaiah 2000	-16.8	5.68858506	15	-16.4	5.23020076	15	100.0%	-0.07 [-0.79, 0.64]		•	-		
Total (95% CI)			15			15	100.0%	-0.07 [-0.79, 0.64]			•		
Heterogeneity: Not app Test for overall effect: Z		P = 0.85)							-10	-5 Favours yoga group	0 Favours imir	5 pramine	10

13 Figure 591: Remission (ITT)



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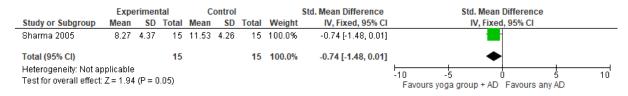
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2 More severe: Yoga group + any AD versus any AD

3 Figure 592: Depression symptomatology endpoint



5 Figure 593: Depression symptomatology change score

	E	xperimental			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Sharma 2005	-13	3.08304233	15	-7.94	2.92502991	15	100.0%	-1.64 [-2.48, -0.80]	-
Total (95% CI) Heterogeneity: Not ap Test for overall effect:	•		15			15	100.0%	-1.64 [-2.48, -0.80]	-10 -5 0 5 10 Favours yoga group+any AD Favours any AD

7 Figure 594: Remission (ITT)

	Experim	ental	Conti	rol		Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	ed, 95% CI	
Sharma 2005	7	15	2	15	100.0%	3.50 [0.86, 14.18]		-		
Total (95% CI)		15		15	100.0%	3.50 [0.86, 14.18]				
Total events	7		2							
Heterogeneity: Not as	pplicable						0.01	04	10	100
Test for overall effect	: Z = 1.76 (F	P = 0.08)				0.01	Favours any AD	Favours yoga gr	

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10 More severe: Traditional acupuncture versus waitlist

11 Figure 595: Remission (ITT)

	Experime	ental	Conti	rol		Risk Ratio		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	ed, 95% CI		
Allen 2006	8	53	4	52	100.0%	1.96 [0.63, 6.12]		_			
Total (95% CI)		53		52	100.0%	1.96 [0.63, 6.12]		-			
Total events	8		4								
Heterogeneity: Not ap Test for overall effect:		e = 0.25)				0.01	0.1 Favours waitlist	Favours ac	10 cupunct	100 ture

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13 Figure 596: Response (ITT)

	Experime	ental	Conti	rol		Risk Ratio		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% CI		
Allen 2006	11	53	9	52	100.0%	1.20 [0.54, 2.65]		_	_		
Total (95% CI)		53		52	100.0%	1.20 [0.54, 2.65]		~	>		
Total events	11		9								
Heterogeneity: Not ap Test for overall effect:	•	P = 0.65)				0.01	0.1 Favours waitlist	Favours a	10 cupunc	100 ture

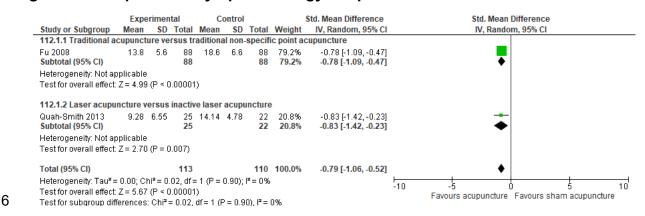
1 Figure 597: Discontinuation due to any reason

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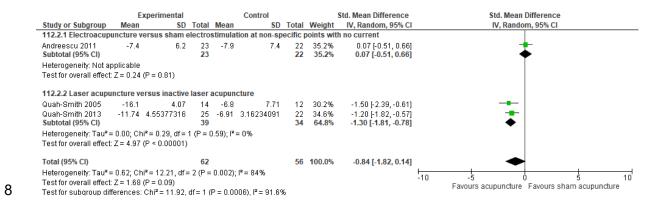


4 More severe: Acupuncture versus sham acupuncture

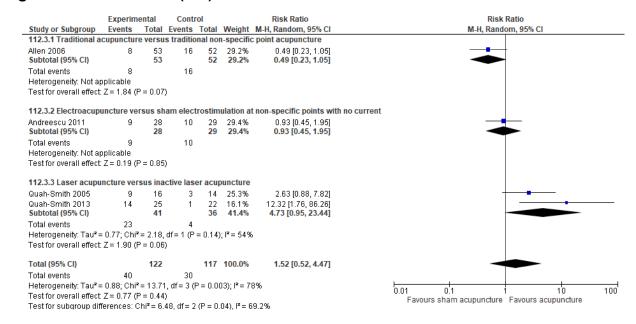
5 Figure 598: Depression symptomatology endpoint



7 Figure 599: Depression symptomatology change score

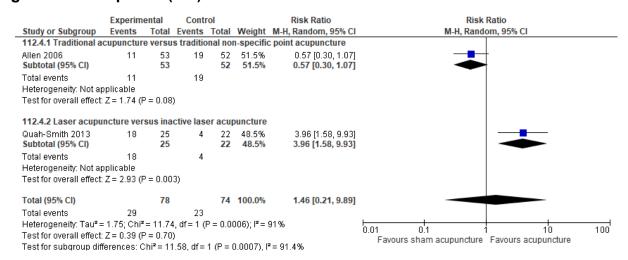


1 Figure 600: Remission (ITT)



3 Figure 601: Response (ITT)

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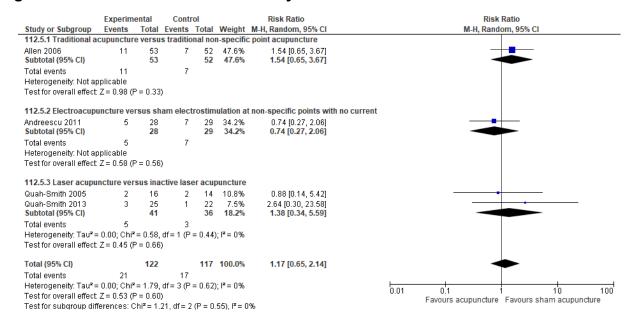
1 Figure 602: Discontinuation due to any reason

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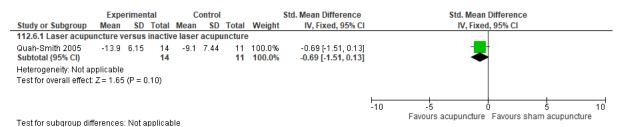
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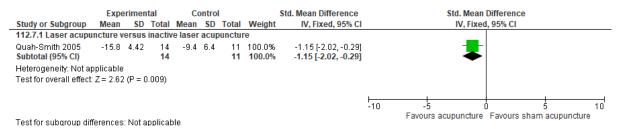
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3 Figure 603: Depression symptomatology change score at 1-month follow-up



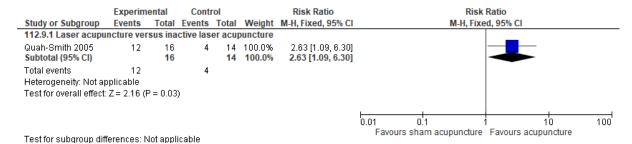
5 Figure 604: Depression symptomatology change score at 3-month follow-up



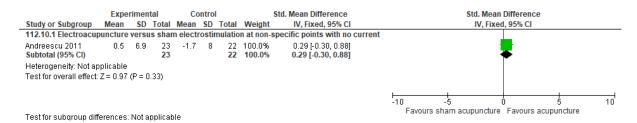
7 Figure 605: Remission at 1-month follow-up (ITT)



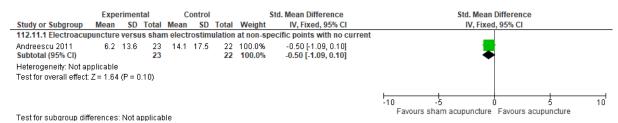
1 Figure 606: Remission at 3-month follow-up (ITT)



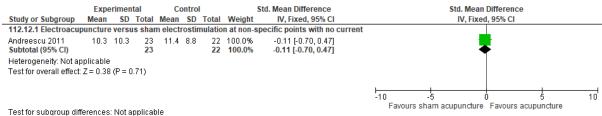
3 Figure 607: Quality of life (physical health component) change score



5 Figure 608: Quality of life (mental health component) change score



7 Figure 609: Global functioning change score



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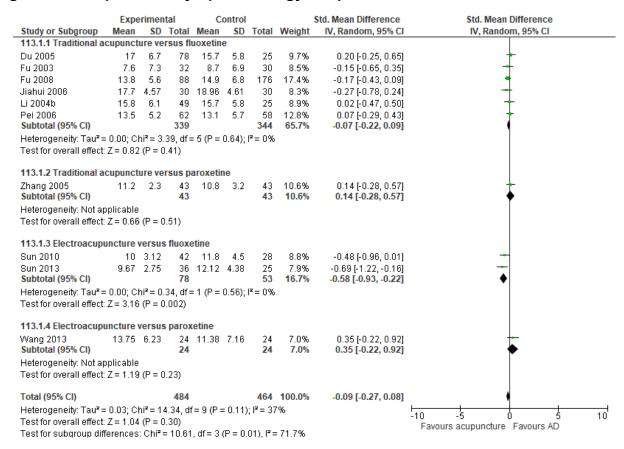
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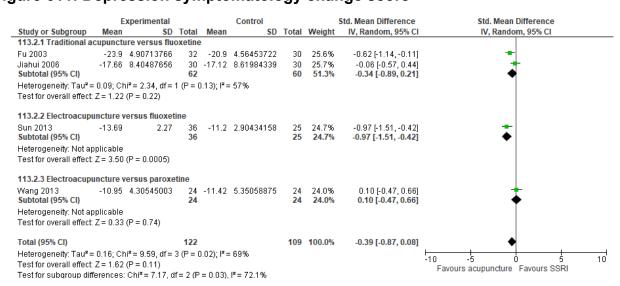
1 More severe: Acupuncture versus SSRI

2 Figure 610: Depression symptomatology endpoint

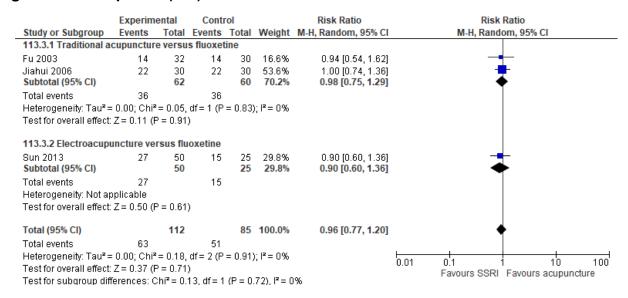


4 Figure 611: Depression symptomatology change score

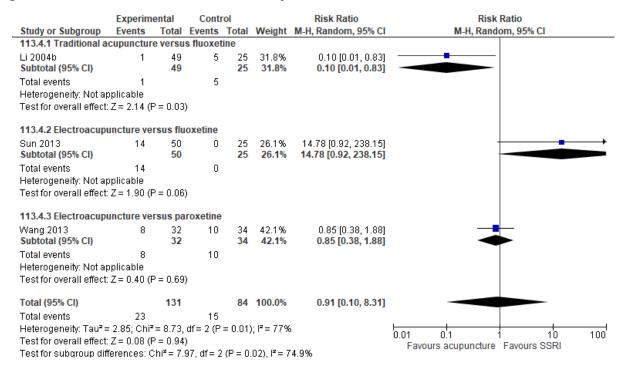
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1 Figure 612: Response (ITT)



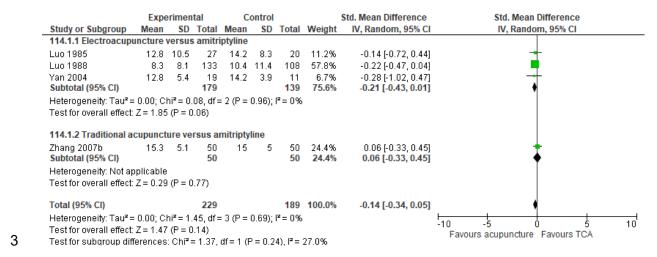
3 Figure 613: Discontinuation due to any reason



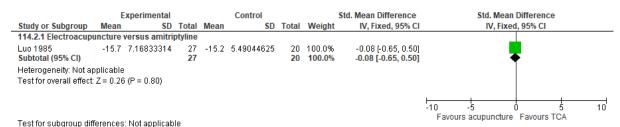
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1 More severe: Acupuncture versus TCA

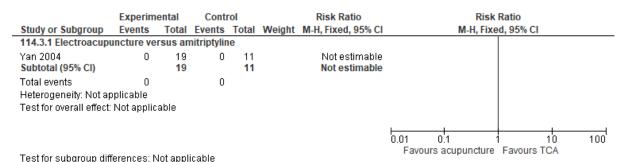
2 Figure 614: Depression symptomatology endpoint



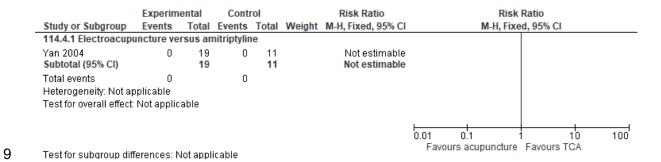
4 Figure 615: Depression symptomatology change score



6 Figure 616: Discontinuation due to SE



8 Figure 617: Discontinuation due to any reason including SE

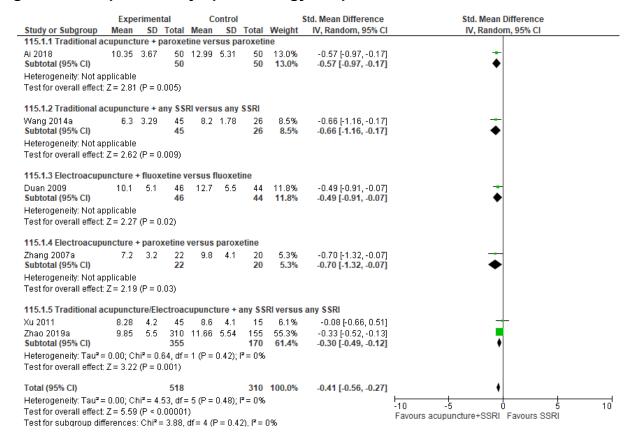


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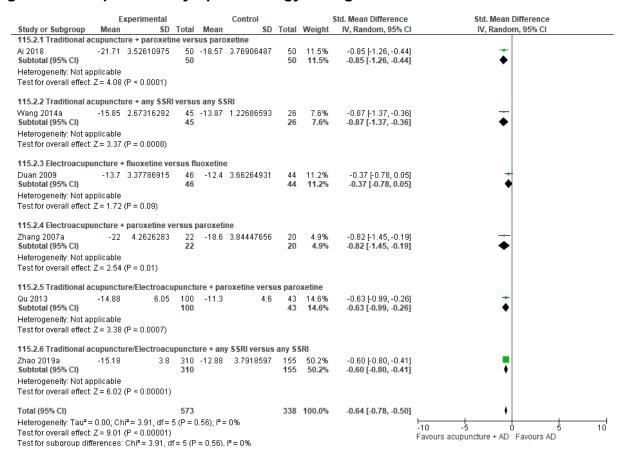
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1 More severe: Acupuncture + AD versus AD

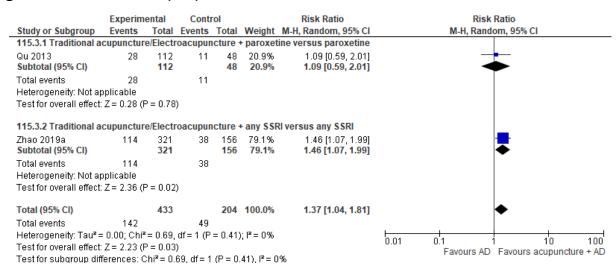
2 Figure 618: Depression symptomatology endpoint



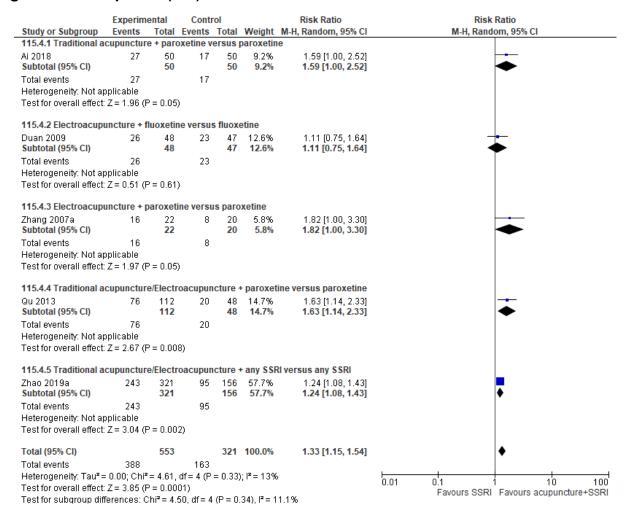
1 Figure 619: Depression symptomatology change score



3 Figure 620: Remission (ITT)

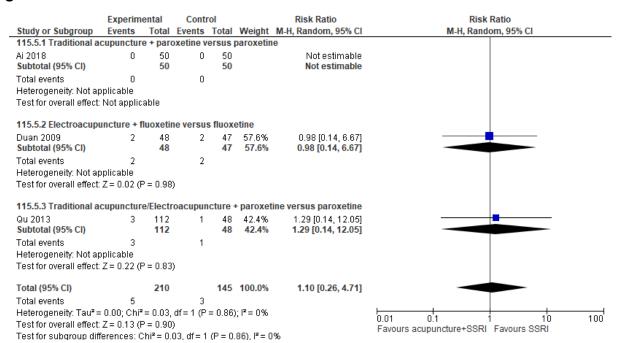


1 Figure 621: Response (ITT)

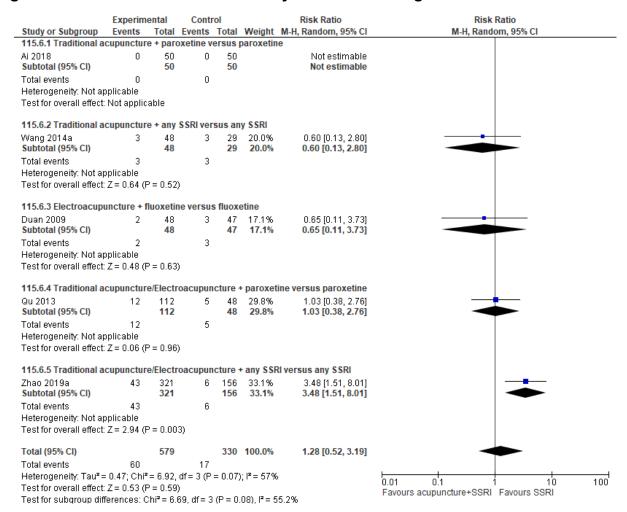


3 Figure 622: Discontinuation due to SE

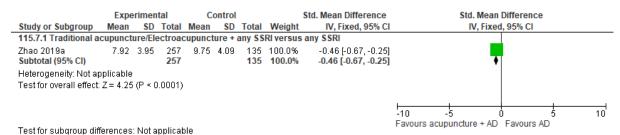
2



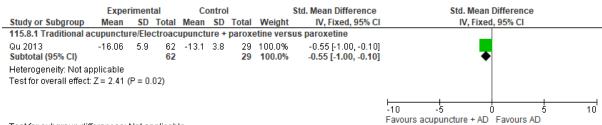
1 Figure 623: Discontinuation due to any reason including SE



3 Figure 624: Depression symptomatology at 1-month follow-up



5 Figure 625: Depression symptomatology change score at 1-month follow-up



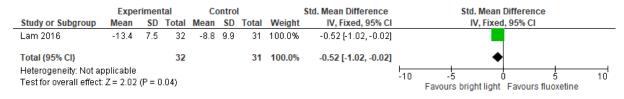
6 Test for subgroup differences: Not applicable

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1 More severe: Bright light therapy versus fluoxetine

2 Figure 626: Depression symptomatology change score



4 Figure 627: Remission (ITT)

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6 Figure 628: Response (ITT)

	Experime	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	I M-H, Fixed, 95% CI
Lam 2016	16	32	9	31	100.0%	1.72 [0.90, 3.30]	1
Total (95% CI)		32		31	100.0%	1.72 [0.90, 3.30]	ı
Total events	16		9				
Heterogeneity: Not ap Test for overall effect:		P = 0.10)				0.01 0.1 1 10 100 Favours fluoxetine Favours bright light

8 Figure 629: Discontinuation due to SE

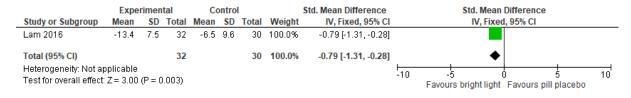


10 Figure 630: Discontinuation due to any reason including SE

	Experim	ental	Conti	rol		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% CI	
Lam 2016	4	32	4	31	100.0%	0.97 [0.27, 3.54]				
Total (95% CI)		32		31	100.0%	0.97 [0.27, 3.54]				
Total events	4		4							
Heterogeneity: Not ap Test for overall effect:		P = 0.96)				0.01	0.1 Favours bright light	10 Favours fluoxetine	100

1 More severe: Bright light therapy versus pill placebo

2 Figure 631: Depression symptomatology change score

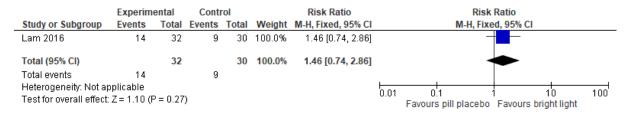


4 Figure 632: Remission (ITT)

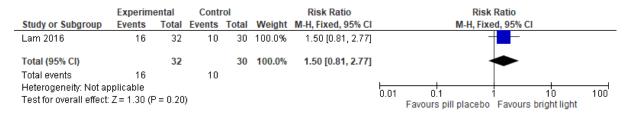
3

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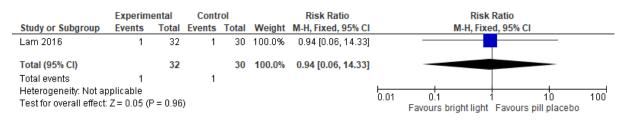
7



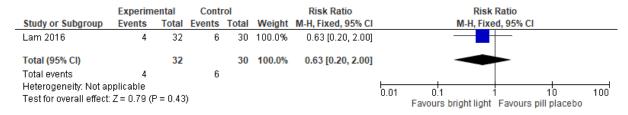
6 Figure 633: Response (ITT)



8 Figure 634: Discontinuation due to SE



10 Figure 635: Discontinuation due to any reason including SE



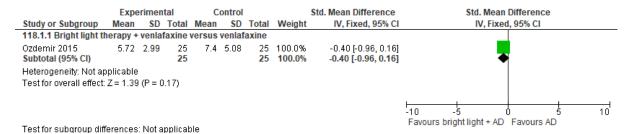
1 More severe: Bright light therapy + AD versus AD

2 Figure 636: Depression v endpoint

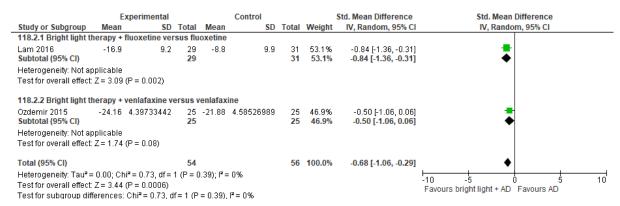
3

5

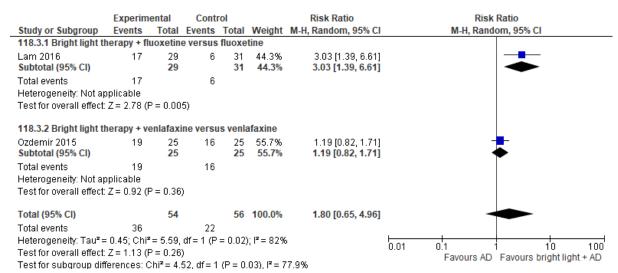
7



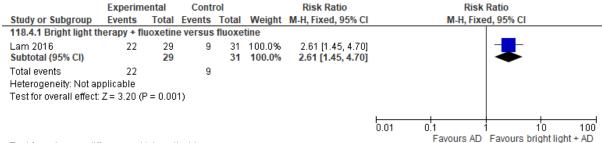
4 Figure 637: Depression symptomatology change score



6 Figure 638: Remission (ITT)

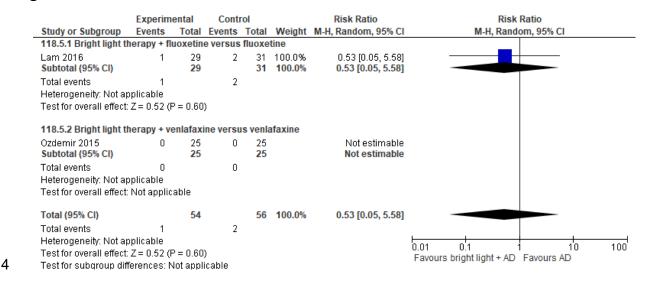


1 Figure 639: Response (ITT)

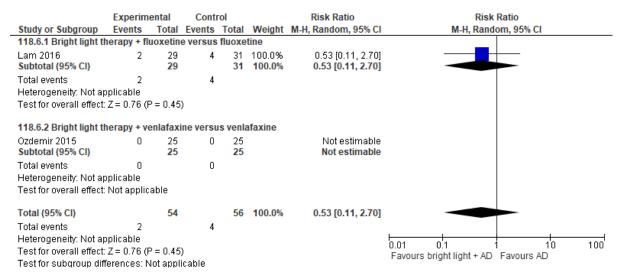


2 Test for subgroup differences: Not applicable

3 Figure 640: Discontinuation due to SE



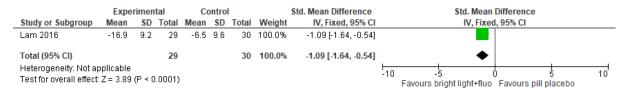
5 Figure 641: Discontinuation due to any reason including SE



1 More severe: Bright light therapy + fluoxetine versus pill

2 placebo

3 Figure 642: Depression symptomatology change score



5 Figure 643: Remission (ITT)

	Experimental		Control		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Lam 2016	17	29	9	30	100.0%	1.95 [1.04, 3.66]	-
Total (95% CI)		29		30	100.0%	1.95 [1.04, 3.66]	•
Total events	17		9				
Heterogeneity: Not ap Test for overall effect:	P = 0.04)				0.01 0.1 10 100 Favours pill placebo Favours bright light+fluo	

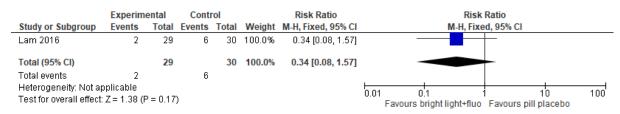
7 Figure 644: Response (ITT)

	Experimental		Control		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
Lam 2016	22	29	10	30	100.0%	2.28 [1.32, 3.93]	-	
Total (95% CI)		29		30	100.0%	2.28 [1.32, 3.93]	•	
Total events	22		10					
Heterogeneity: Not applicable Test for overall effect: Z = 2.95 (P = 0.003)							0.01 0.1 10 100 Favours pill placebo Favours bright light+fluo	

9 Figure 645: Discontinuation due to SE

	Experimental		Control		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Lam 2016	1	29	1	30	100.0%	1.03 [0.07, 15.77]	
Total (95% CI)		29		30	100.0%	1.03 [0.07, 15.77]	
Total events	1		1				
Heterogeneity: Not ap Test for overall effect:	•	P = 0.98)				0.01 0.1 10 100 Favours bright light+fluo Favours pill placebo

11 Figure 646: Discontinuation due to any reason including SE



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