Appendix 16b: Forest plots for clinical evidence reviews on pharmacological interventions

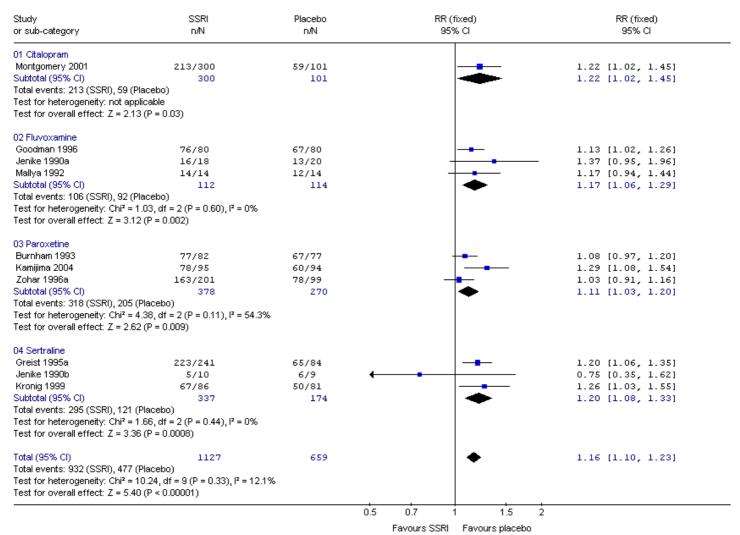
SSRIs (OCD, adults); Clomipramine (OCD, adults); TCAs (OCD); SNRIs (OCD); MAOIs (OCD); Anxiolytics (OCD); Other Pharmacological (OCD); Augmentation (OCD); SSRIs (OCD, children); Clomipramine (OCD, children); Pharmacological (BDD)

SSRIs (OCD, adults)

Review: OCD adults: SSRIs

Comparison: 01 SSRIs vs placebo (acute phase)

Outcome: 01 Adverse events



Review: OCD adults: SSRIs

Comparison: 01 SSRIs vs placebo (acute phase)

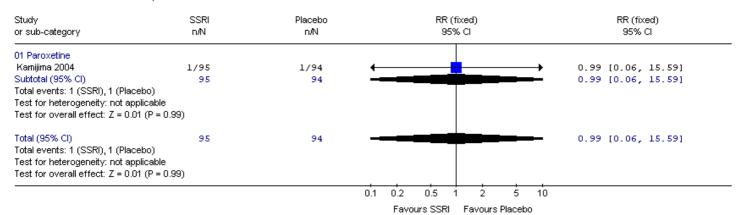
Outcome: 02 Serious adverse events

Study or sub-category	SSRI n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Paroxetine				
Kamijima 2004	3/95	3/94		0.99 [0.20, 4.78]
Subtotal (95% CI)	95	94		0.99 [0.20, 4.78]
Total events: 3 (SSRI), 3 (Placebo)			T	
Test for heterogeneity: not applicable				
Test for overall effect: Z = 0.01 (P = 0.9)	9)			
Total (95% CI) Total events: 3 (SSRI), 3 (Placebo)	95	94		0.99 [0.20, 4.78]
Test for heterogeneity: not applicable				
Test for overall effect: Z = 0.01 (P = 0.9	9)			
		0.	1 0.2 0.5 1 2 5 10	
			Favours SSRI Favours Placebo	

Review: OCD adults: SSRIs

Comparison: 01 SSRIs vs placebo (acute phase)

Outcome: 03 Suicide attempts



DRAFT FOR 1ST CONSULATION

OCD adults: SSRIs

Review:

Comparison: 01 SSRIs vs placebo (acute phase) Outcome: 04 Leaving study early SSRI Placebo RR (fixed) RR (fixed) Study or sub-category nNn/N 95% CI 95% CI 01 Citalopram Montgomery 2001 46/300 17/101 0.91 [0.55, 1.51] Subtotal (95% CI) 300 101 0.91 [0.55, 1.51] Total events: 46 (SSRI), 17 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.36 (P = 0.72) 02 Fluoxetine Jenike 1997 4/23 3/21 1.22 [0.31, 4.82] Montgomery 1993 41/160 15/57 0.97 [0.59, 1.62] 1.00 [0.62, 1.62] Subtotal (95% CI) 183 78 Total events: 45 (SSRI), 18 (Placebo) Test for heterogeneity: $Chi^2 = 0.09$, df = 1 (P = 0.76), $I^2 = 0\%$ Test for overall effect: Z = 0.02 (P = 0.99) 03 Fluvoxamine Goodman 1989 2/23 6/23 0.33 [0.07, 1.48] Goodman 1996 23/80 17/80 1.35 [0.78, 2.33] Hollander 2003b 43/127 31/126 1.38 [0.93, 2.03] Jenike 1990a 0/18 0/20 Not estimable Mallya 1992 5/19 6/20 0.88 [0.32, 2.40] Perse 1987 1/10 1/10 1.00 [0.07, 13.87] Subtotal (95% CI) 279 1.21 [0.91, 1.62] Total events: 74 (SSRI), 61 (Placebo) Test for heterogeneity: $Chi^2 = 3.85$, df = 4 (P = 0.43), $I^2 = 0\%$ Test for overall effect: Z = 1.30 (P = 0.19) 04 Paroxetine 20/77 1.31 [0.81, 2.13] Burnham 1993 28/82 1.21 [0.72, 2.04] Hollander 2003d 53/259 15/89 Zohar 1996a 49/201 39/99 0.62 [0.44, 0.87] Subtotal (95% CI) 542 265 0.91 [0.71, 1.16] Total events: 130 (SSRI), 74 (Placebo) Test for heterogeneity: $Chi^2 = 8.21$, df = 2 (P = 0.02), $I^2 = 75.6\%$ Test for overall effect: Z = 0.76 (P = 0.45) 05 Sertraline Chouinard 1990 0.44 [0.12, 1.59] 3/43 7/44 Greist 1995a 65/241 24/84 0.94 [0.63, 1.40] Jenike 1990b 0/10 0/9 Not estimable Kronig 1999 25/86 25/81 0.94 [0.59, 1.50] Subtotal (95% CI) 218 0.89 [0.67, 1.20] 380 Total events: 93 (SSRI), 56 (Placebo) Test for heterogeneity: $Chi^2 = 1.30$, df = 2 (P = 0.52), $I^2 = 0\%$ Test for overall effect: Z = 0.76 (P = 0.44) Total (95% CI) 941 0.98 [0.85, 1.13] Total events: 388 (SSRI), 226 (Placebo) Test for heterogeneity: Chi² = 16.94, df = 13 (P = 0.20), l² = 23.3% Test for overall effect: Z = 0.26 (P = 0.79)

0.1 0.2

0.5

Favours SSRI Favours placebo

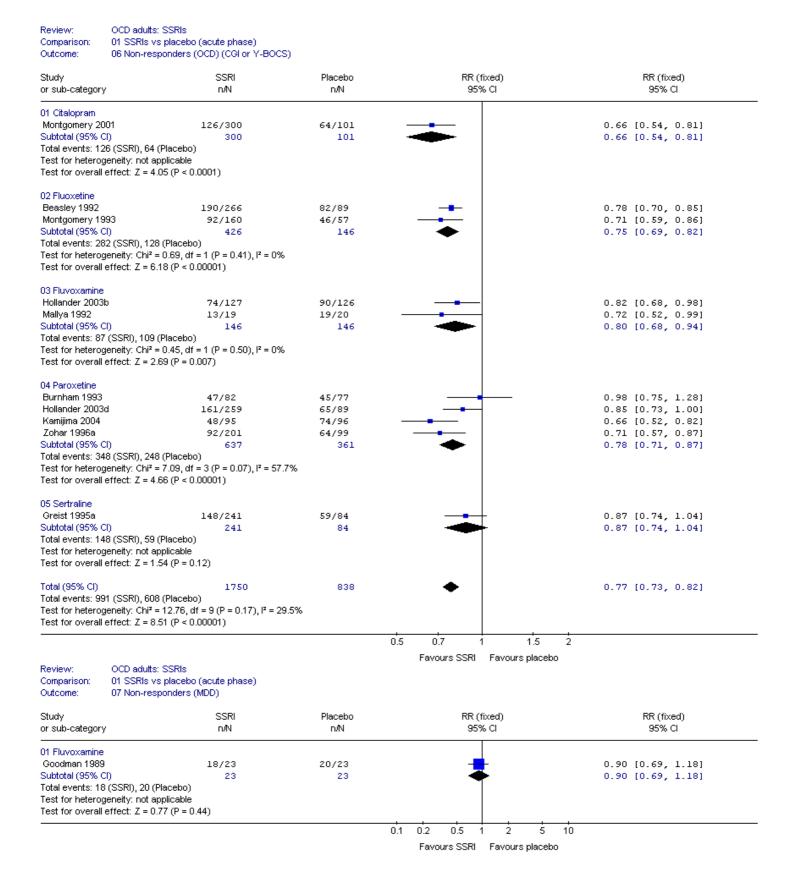
10

OCD adults: SSRIs

Review:

Comparison: 01 SSRIs vs placebo (acute phase) Outcome: 05 Leaving study early due to adverse events SSRI Placebo RR (fixed) RR (fixed) Study 95% CI or sub-category n/Ν n/N 95% CI 01 Citalopram Montgomery 2001 14/300 2/101 2.36 [0.54, 10.19] Subtotal (95% CI) 300 101 2.36 [0.54, 10.19] Total events: 14 (SSRI), 2 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.15 (P = 0.25) 02 Fluoxetine Beasley 1992 59/266 2/89 9.87 [2.46, 39.57] Montgomery 1993 2/57 1.25 [0.27, 5.83] 7/160 5.59 [2.06, 15.16] Subtotal (95% CI) 146 Total events: 66 (SSRI), 4 (Placebo) Test for heterogeneity: $Chi^2 = 4.28$, df = 1 (P = 0.04), $I^2 = 76.6\%$ Test for overall effect: Z = 3.38 (P = 0.0007)03 Fluvoxamine Goodman 1989 2/23 0/23 5.00 [0.25, 98.75] 2.50 [1.02, 6.12] Goodman 1996 15/80 6/80 Hollander 2003b 2.85 [1.33, 6.13] 23/127 8/126 Subtotal (95% CI) 230 229 2.78 [1.57, 4.92] Total events: 40 (SSRI), 14 (Placebo) Test for heterogeneity: $Chi^2 = 0.21$, df = 2 (P = 0.90), $I^2 = 0\%$ Test for overall effect: Z = 3.51 (P = 0.0004)

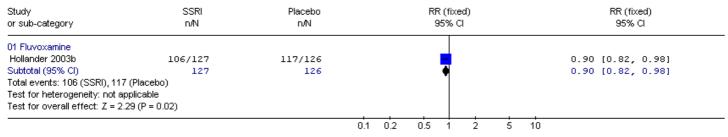
04 Paroxetine Burnham 1993 1.76 [0.79, 3.92] 15/82 8/77 Hollander 2003d 29/259 7/89 1.42 [0.65, 3.14] Kamijima 2004 9/95 9/96 1.01 [0.42, 2.43] Zohar 1996a 18/201 6/99 1.48 [0.61, 3.61] Subtotal (95% CI) 361 1.41 [0.93, 2.14] 637 Total events: 71 (SSRI), 30 (Placebo) Test for heterogeneity: $Chi^2 = 0.86$, df = 3 (P = 0.84), $I^2 = 0\%$ Test for overall effect: Z = 1.62 (P = 0.11) 05 Sertraline Chouinard 1990 1/43 3.07 [0.13, 73.30] 0/44 Greist 1995a 1.60 [0.63, 4.08] 23/241 5/84 2.12 [0.68, 6.61] Kronig 1999 9/86 4/81 Subtotal (95% CI) 370 209 1.84 [0.91, 3.71] Total events: 33 (SSRI), 9 (Placebo) Test for heterogeneity: Chi² = 0.24, df = 2 (P = 0.89), l² = 0% Test for overall effect: Z = 1.70 (P = 0.09)Total (95% CI) 1963 1046 2.15 [1.62, 2.86] Total events: 224 (SSRI), 59 (Placebo) Test for heterogeneity: $Chi^2 = 11.30$, df = 12 (P = 0.50), $I^2 = 0\%$ Test for overall effect: Z = 5.30 (P < 0.00001)0.01 10 100 Favours SSRI Favours placebo



Review: OCD adults: SSRIs

01 SSRIs vs placebo (acute phase) Comparison:

08 Non-remitters Outcome:



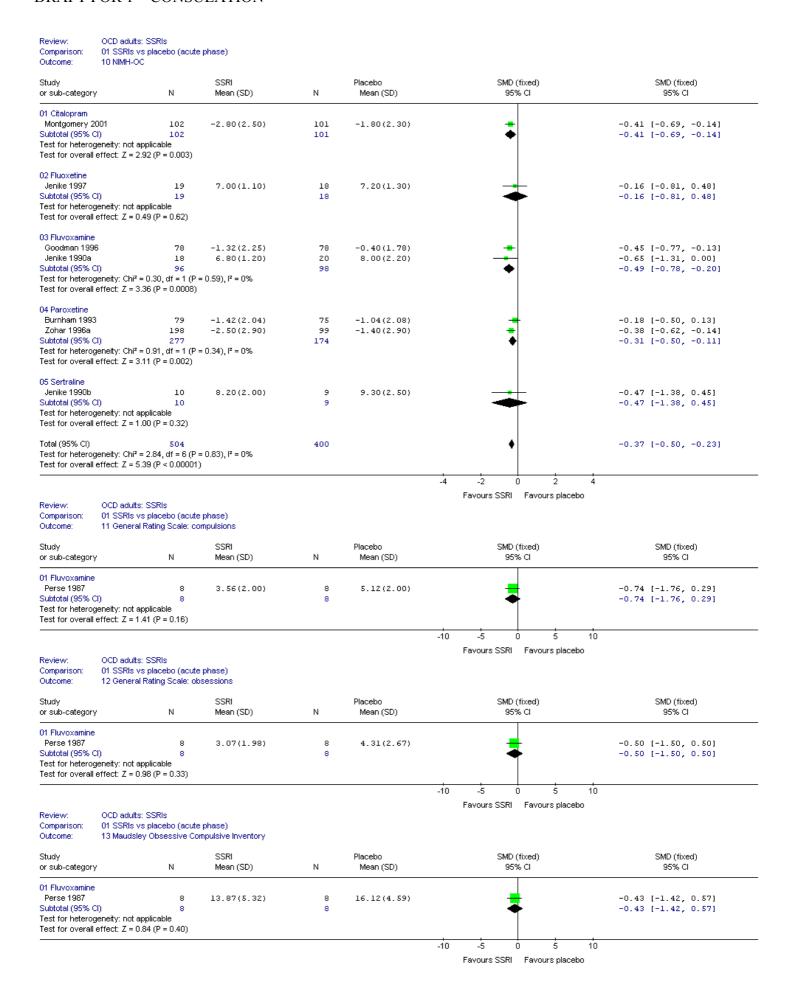
Favours SSRI Favours placebo

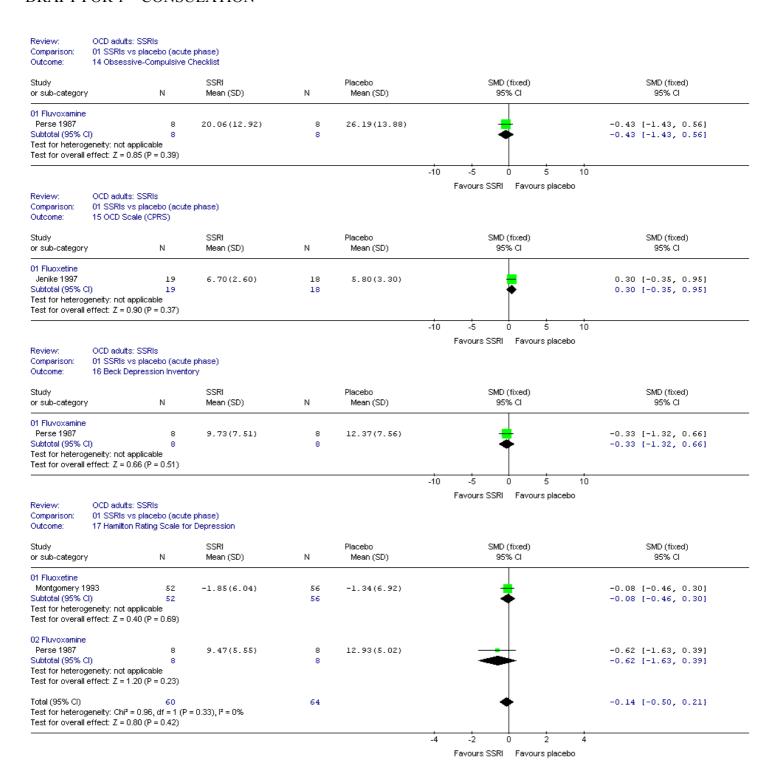
Review:

OCD adults: SSRIs 01 SSRIs vs placebo (acute phase) Comparison:

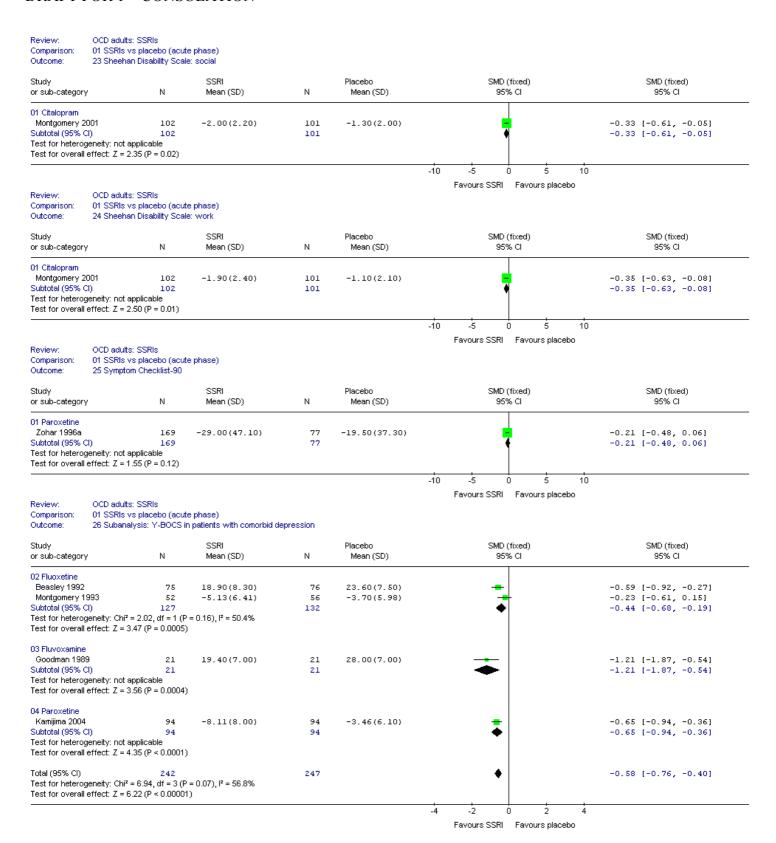
Outcome:

11 Citalopram Montgomery 2001 Subtotal (95% CI) Set for heterogeneity: not ap Set for overall effect: Z = 2.7	102 102	-8.40(7.30)				
Subtotal (95% CI) Test for heterogeneity: not ap	102	-8.40(7.30)				
est for heterogeneity: not ap			101	-5.60(6.90)	-	-0.39 [-0.67, -0.11]
	elia alda		101		•	-0.39 [-0.67, -0.11]
est for overall effect: $Z = 2.7$	plicable					
	77 (P = 0.006)					
2 Fluoxetine						
Beasley 1992	75	18.90(8.30)	76	23.60(7.50)		-0.59 [-0.92, -0.27]
Jenike 1997	19	16.20(6.30)	18	18.70(6.10)		-0.39 [-1.05, 0.26]
Montgomery 1993	52	-5.13(6.41)	56	-3.70(5.98)		-0.23 [-0.61, 0.15]
ubtotal (95% CI)	146		150		◆	-0.43 [-0.66, -0.20]
est for heterogeneity: Chi² =	2.03, df = 2 (P	= 0.36), I ² = 1.5%			.	
est for overall effect: Z = 3.6	66 (P = 0.0002)					
3 Fluvoxamine						
Goodman 1989	21	19.40(7.00)	21	28.00(7.00)		-1.21 [-1.87, -0.54]
Goodman 1996	78	-3.95(6.28)	78	-1.71(4.88)		-0.40 [-0.71, -0.08]
Hollander 2003b	117	-8.50(7.57)	120	-5.60(7.67)	-	-0.38 [-0.64, -0.12]
Jenike 1990a	18	18.80(4.00)	20	21.80(7.60)		-0.48 [-1.12, 0.17]
ubtotal (95% CI)	234		239		◆	-0.46 [-0.64, -0.27]
est for heterogeneity: Chi² =	5.39, df = 3 (P	= 0.15), I ² = 44.4%			·	
est for overall effect: Z = 4.8						
4 Paroxetine						
Burnham 1993	79	-5.61(7.47)	75	-4.60(7.53)	-	-0.13 [-0.45, 0.18]
Kamijima 2004	94	-8.11(8.00)	94	-3.46(6.10)	-	-0.65 [-0.94, -0.36]
Zohar 1996a	198	-8.00(8.00)	99	-5.00(7.90)	-	-0.38 [-0.62, -0.13]
ubtotal (95% CI)	371		268		•	-0.40 [-0.56, -0.23]
est for heterogeneity: Chi² = est for overall effect: Z = 4.8						
5 Sertraline						
Jenike 1990b	10	20.60(9.20)	8	22.30(7.80)		-0.19 [-1.12, 0.74]
ubtotal (95% CI)	10		8		-	-0.19 [-1.12, 0.74]
est for heterogeneity: not ap	plicable					
est for overall effect: $Z = 0.4$	10 (P = 0.69)					
otal (95% CI)	863		766		•	-0.42 [-0.52, -0.32]
est for heterogeneity: Chi² =	13.50, df = 11	(P = 0.26), I ² = 18.5%			.	
est for overall effect: $Z = 8.2$	23 (P < 0.00001)				
				-4	-2 0 2	4





Review: OCD adults: SSRIs Comparison: 01 SSRIs vs placebo (acute phase) Outcome 18 Montgomery-Asberg Depression Rating Scale SMD (fixed) SMD (fixed) Study Placebo or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI 01 Citalopram Montgomery 2001 102 -3.40(6.30) 101 -1.30(6.70) -0.32 [-0.60, -0.04] Subtotal (95% CI) 102 101 -0.32 [-0.60, -0.04] Test for heterogeneity: not applicable Test for overall effect: Z = 2.28 (P = 0.02) Montgomery 1993 52 -2.96(8.09) 56 -2.88(9.27) -0.01 [-0.39, 0.37] Subtotal (95% CI) 52 56 -0.01 [-0.39, 0.37] Test for heterogeneity: not applicable Test for overall effect: Z = 0.05 (P = 0.96) 03 Paroxetine -0.35 [-0.60, -0.11] -0.35 [-0.60, -0.11] Zohar 1996a 198 -3.40(7.90) 99 -0.60(7.90) Subtotal (95% CI) 198 Test for heterogeneity: not applicable Test for overall effect: Z = 2.85 (P = 0.004) -0.28 [-0.44, -0.11] Test for heterogeneity: Chi² = 2.42, df = 2 (P = 0.30), l² = 17.2% Test for overall effect: Z = 3.30 (P = 0.0010) Favours SSRI Favours placebo OCD adults: SSRIs Review: Comparison: 01 SSRIs vs placebo (acute phase) 19 Hamilton Anxiety Scale Outcome SSRI SMD (fixed) SMD (fixed) Study Placebo Mean (SD) N Mean (SD) 95% CI 95% CI or sub-category Ν 01 Fluvoxamine Perse 1987 7.69(3.60) 8 12.37(7.56) -0.75 [-1.77, 0.28] Subtotal (95% CI) -0.75 [-1.77, 0.28] Test for heterogeneity: not applicable Test for overall effect: Z = 1.43 (P = 0.15) -10 -5 10 0 Favours SSRI Favours placebo Review: OCD adults: SSRIs Comparison: 01 SSRIs vs placebo (acute phase) 20 Clinical Global Impression Outcome SSRI SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine 19 3.10(1.00) 18 3.20(1.00) -0.10 [-0.74, 0.55] Subtotal (95% CI) 19 18 -0.10 [-0.74, 0.55] Test for heterogeneity: not applicable Test for overall effect: Z = 0.30 (P = 0.77) -10 -5 Ó 5 10 Favours SSRI Favours placebo Review: OCD adults: SSRIs 01 SSRIs vs placebo (acute phase) Comparison: Outcome 21 Clinical Global Impressions: severity SMD (fixed) SMD (fixed) Study SSRI Placebo Mean (SD) N Mean (SD) or sub-category 01 Paroxetine -0.36 [-0.61, -0.12] -0.36 [-0.61, -0.12] Zohar 1996a -1.20(1.40) -0.70(1.30) 194 99 99 Subtotal (95% CI) 194 Test for heterogeneity: not applicable Test for overall effect: Z = 2.93 (P = 0.003) Ó Favours SSRI Favours placebo Review: OCD adults: SSRIs 01 SSRIs vs placebo (acute phase) Comparison: 22 Sheehan Disability Scale: family Outcome Study SSRI Placebo SMD (fixed) SMD (fixed) Mean (SD) or sub-category Ν Ν Mean (SD) 95% CI 95% CI 01 Citalopram Montgomery 2001 102 -1.80(2.40) 101 -1.00(2.40) -0.33 [-0.61, -0.06] -0.33 [-0.61, -0.06] Subtotal (95% Ch. 102 101 Test for heterogeneity; not applicable Test for overall effect: Z = 2.35 (P = 0.02) -10 10 -5 Ó Favours SSRI Favours placebo



Test for overall effect: Z = 0.20 (P = 0.84)

Review: OCD adults: SSRIs Comparison: 01 SSRIs vs placebo (acute phase) 27 Subanalysis: Non-responders (OCD) (CGI or Y-BOCS) in patients with comorbid depression Outcome: SSRI Placebo RR (fixed) Study 95% CI or sub-category n/N n/N 95% CI 02 Fluoxetine Beasley 1992 190/266 82/89 0.78 [0.70, 0.85] Montgomery 1993 92/160 46/57 0.71 [0.59, 0.86] Subtotal (95% CI) 146 0.75 [0.69, 0.82] Total events: 282 (SSRI), 128 (Placebo) Test for heterogeneity: $Chi^2 = 0.69$, df = 1 (P = 0.41), $I^2 = 0\%$ Test for overall effect: Z = 6.18 (P < 0.00001)04 Paroxetine Kamijima 2004 48/95 74/96 0.66 [0.52, 0.82] Subtotal (95% CI) 96 0.66 [0.52, 0.82] Total events: 48 (SSRI), 74 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 3.65 (P = 0.0003) Total (95% CI) 242 0.73 [0.66, 0.79] Total events: 330 (SSRI), 202 (Placebo) Test for heterogeneity: Chi² = 2.58, df = 2 (P = 0.28), l² = 22.4% Test for overall effect: Z = 7.03 (P < 0.00001)0.5 0.7 1.5 Favours SSRI Favours placebo Review: OCD adults: SSRIs 02 SSRIs at different doses (acute phase) Comparison: Outcome: 01 Adverse events RR (fixed) RR (fixed) Study Dose 1 Dose 2 or sub-category n/N n/N 95% CI 95% CI 01 Citalopram 40mg vs Citalopram 20mg 0.94 [0.79, 1.13] 0.94 [0.79, 1.13] Montgomery 2001 74/102 67/98 Subtotal (95% CD) 98 102 Total events: 67 (Dose 1), 74 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.65 (P = 0.52) 02 Citalopram 60mg vs Citalopram 20mg 72/100 0.99 [0.84, 1.18] Montgomery 2001 74/102 Subtotal (95% CI) 100 102 0.99 [0.84, 1.18] Total events: 72 (Dose 1), 74 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.09 (P = 0.93) 03 Citalopram 60mg vs Citalopram 40mg 1.05 [0.88, 1.26] Montgomery 2001 72/100 67/98 Subtotal (95% CI) 100 98 1.05 [0.88, 1.26] Total events: 72 (Dose 1), 67 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.56 (P = 0.58) 04 Sertraline rapid titration vs slow titration Bogetto 2002 13/17 11/15 1.04 [0.70, 1.56] Subtotal (95% CI) 15 1.04 [0.70, 1.56] Total events: 13 (Dose 1), 11 (Dose 2) Test for heterogeneity: not applicable

0.5

0.7

Favours Dose 1 Favours Dose 2

1.5

Review: Comparison: Outcome: OCD adults: SSRIs 02 SSRIs at different doses (acute phase) 02 Leaving study early

Study or sub-category	Dose 1 n/N	Dose 2 n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Citalopram 40mg vs Citalopram 20mg Montgomery 2001 Subtotal (95% CI) fotal events: 15 (Dose 1), 16 (Dose 2) Fest for heterogeneity: not applicable Fest for overall effect: Z = 0.07 (P = 0.94	15/98 98	16/102 102	+	0.98 [0.51, 1.86] 0.98 [0.51, 1.86]
2 Citalopram 60mg vs Citalopram 20mg Montgomery 2001 Jubtotal (95% Cl) otal events: 15 (Dose 1), 16 (Dose 2) est for heterogeneity: not applicable est for overall effect: Z = 0.14 (P = 0.89	15/100 100	16/102 102	*	0.96 [0.50, 1.83] 0.96 [0.50, 1.83]
3 Citalopram 60mg vs Citalopram 40mg fontgomery 2001 ubtotal (95% Cl) otal events: 15 (Dose 1), 15 (Dose 2) est for heterogeneity: not applicable est for overall effect: Z = 0.06 (P = 0.95	15/100 100	15/98 98	+	0.98 [0.51, 1.89] 0.98 [0.51, 1.89]
4 Fluoxetine 40mg vs Fluoxetine 20mg fontgomery 1993 ubtotal (95% C) otal events: 13 (Dose 1), 14 (Dose 2) ast for heterogeneity: not applicable est for overall effect: Z = 0.17 (P = 0.87	13/52 52	14/53 53	+	0.95 [0.49, 1.81] 0.95 [0.49, 1.81]
5 Fluoxetine 60mg vs Fluoxetine 20mg fontgomery 1993 ubtotal (95% Cl) otal events: 14 (Dose 1), 14 (Dose 2) est for heterogeneity: not applicable est for overall effect: Z = 0.11 (P = 0.91	14/55 55	14/53 53	+	0.96 [0.51, 1.82] 0.96 [0.51, 1.82]
6 Fluoxetine 60mg vs Fluoxetine 40mg fontgomery 1993 ubtotal (95% Cl) otal events: 14 (Dose 1), 13 (Dose 2) est for heterogeneity: not applicable est for overall effect: Z = 0.05 (P = 0.96	14/55 55	13/52 52	+	1.02 [0.53, 1.96] 1.02 [0.53, 1.96]
7 Paroxetine 40mg vs Paroxetine 20mg tollander 2003d ubtotal (95% Cl) otal events: 20 (Dose 1), 14 (Dose 2) est for heterogeneity: not applicable est for overall effect: Z = 1.21 (P = 0.23	20/86 86	14/88 88	-	1.46 [0.79, 2.70] 1.46 [0.79, 2.70]
B Paroxetine 60mg vs Paroxetine 20mg tollander 2003d ubtotal (95% Cl) otal events: 19 (Dose 1), 14 (Dose 2) est for heterogeneity: not applicable est for overall effect: Z = 1.07 (P = 0.28	19/85 85	14/88 88	-	1.41 [0.75, 2.62] 1.41 [0.75, 2.62]
9 Paroxetine 60mg vs Paroxetine 40mg Iollander 2003d Jototal (95% Cl) Iotal events: 19 (Dose 1), 20 (Dose 2) set for heterogeneity: not applicable set for overall effect: Z = 0.14 (P = 0.88	19/85 85	20/86 86	*	0.96 [0.55, 1.67] 0.96 [0.55, 1.67]
) O Sertraline 100mg vs Sertraline 50mg	27/81 81	17/80 80	-	1.57 [0.93, 2.64] 1.57 [0.93, 2.64]
1 Sertraline 200mg vs Sertraline 50mg	21/80 80	17/80 80	-	1.24 [0.71, 2.16] 1.24 [0.71, 2.16]
2 Sertraline 200mg vs Sertraline 100mg	21/80 80	27/81 81	-	0.79 [0.49, 1.27] 0.79 [0.49, 1.27]
3 Sertraline rapid titration vs slow titration of slow titration (195% CI) obtail events: 3 (Dose 1), 2 (Dose 2) est for heterogeneity: not applicable set for overall effect: Z = 0.33 (P = 0.74)	on 3/17 17	2/15 15		1.32 [0.25, 6.88] 1.32 [0.25, 6.88]

DRAFT FOR 1ST CONSULATION

Review: OCD adults: SSRIs Comparison: 02 SSRIs at different doses (acute phase) 03 Leaving study early due to adverse events RR (fixed) RR (fixed) or sub-category 95% CI 95% CI 01 Citalopram 40mg vs Citalopram 20mg 4/102 1.56 [0.45, 5.36] Montgomery 2001 Subtotal (95% CI) 102 1.56 [0.45, 5.36] Total events: 6 (Dose 1), 4 (Dose 2) Test for heterogeneity; not applicable Test for overall effect: Z = 0.71 (P = 0.48) 02 Citalopram 60mg vs Citalopram 20mg Montgomery 2001 4/100 4/102 1.02 [0.26, 3.97] Subtotal (95% CI)
Total events: 4 (Dose 1), 4 (Dose 2) Test for heterogeneity: not applicable
Test for overall effect: Z = 0.03 (P = 0.98) 03 Citalopram 60mg vs Citalopram 40mg Montgomery 2001 Subtotal (95% CI) 0.65 [0.19, 2.24] 0.65 [0.19, 2.24] 4/100 6/98 Total events: 4 (Dose 1), 6 (Dose 2) Test for heterogeneity; not applicable Test for overall effect: Z = 0.68 (P = 0.50) 04 Fluoxetine 40mg vs Fluoxetine 20mg Beasley 1992 30/87 0.39 [0.21, 0.71] Montgomery 1993 Subtotal (95% CI) 0.51 [0.10, 2.66] 0.40 [0.23, 0.71] 140 Total events: 14 (Dose 1), 34 (Dose 2)
Test for heterogeneity: Chi² = 0.09, df = 1 (P = 0.77), l² = 0% Test for overall effect: Z = 3.14 (P = 0.002) 05 Fluoxetine 60mg vs Fluoxetine 20mg Beasley 1992 0.55 [0.33, 0.92] 30/87 Montgomery 1993 Subtotal (95% CI) 0.24 [0.03, 2.09] 0.51 [0.31, 0.85] 1/55 4/53 140 145 Total events: 18 (Dose 1), 34 (Dose 2) Test for heterogeneity: Chi² = 0.53, df = 1 (P = 0.46), l² = 0% Test for overall effect: Z = 2.61 (P = 0.009) 06 Fluoxetine 60mg vs Fluoxetine 40mg Beasley 1992 1.40 [0.71, 2.76] Montgomery 1993 Subtotal (95% CI) 1/55 2/52 0.47 [0.04, 5.06] 1.27 [0.66, 2.41] Total events: 18 (Dose 1), 14 (Dose 2) Test for heterogeneity: $Chi^2 = 0.75$, df = 1 (P = 0.39), $I^2 = 0\%$ Test for overall effect: Z = 0.72 (P = 0.47) 07 Paroxetine 40mg vs Paroxetine 20mg Hollander 2003d 0.91 [0.37, 2.25] Subtotal (95% CI) 88 0.91 [0.37, 2.25] Total events: 8 (Dose 1), 9 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.21 (P = 0.84) 08 Paroxetine 60mg vs Paroxetine 20mg Hollander 2003d 12/85 9/88 1.38 [0.61, 3.11] 1.38 [0.61, 3.11] Subtotal (95% CI) Total events: 12 (Dose 1), 9 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.78 (P = 0.44) 09 Paroxetine 60mg vs Paroxetine 40mg Hollander 2003d 1.52 [0.65, 3.53] Subtotal (95% CI) 1.52 [0.65, 3.53] Total events: 12 (Dose 1), 8 (Dose 2) Test for heterogeneity; not applicable Test for overall effect: Z = 0.97 (P = 0.33) 10 Sertraline 100mg vs Sertraline 50mg Greist 1995a 6/80 1.81 [0.70, 4.66] Subtotal (95% CI) Total events: 11 (Dose 1), 6 (Dose 2) Test for heterogeneity: not applicable
Test for overall effect: Z = 1.23 (P = 0.22) 11 Sertraline 200mg vs Sertraline 50mg Greist 1995a 6/80 1.00 [0.34, 2.97] Subtotal (95% CI) 1.00 [0.34, 2.97] 80 Total events: 6 (Dose 1), 6 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.00 (P = 1.00) 12 Sertraline 200mg vs Sertraline 100mg 0.55 [0.21, 1.42] Greist 1995a 11/81 Subtotal (95% CI) 0.55 [0.21, 1.42] Total events: 6 (Dose 1), 11 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.23 (P = 0.22) 13 Sertraline rapid titration vs slow titration Bogetto 2002 Subtotal (95% CI) 2/15 0.88 [0.14, 5.52] 0.88 [0.14, 5.52] Total events: 2 (Dose 1), 2 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.13 (P = 0.89) 0.2 0.5 1 2 5

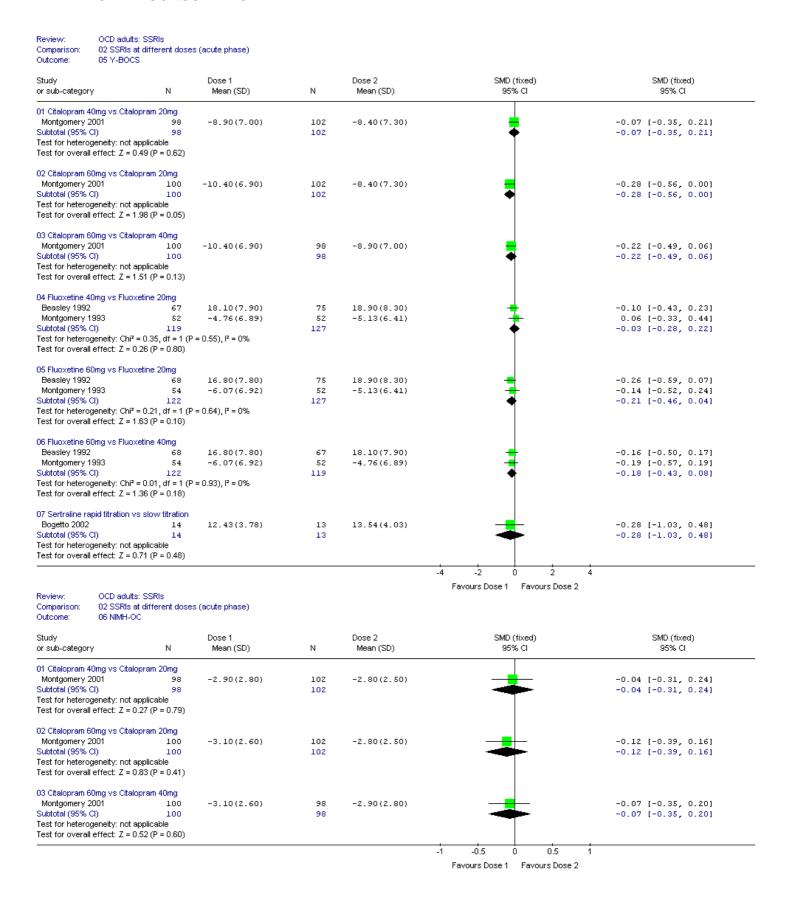
Favours Dose 1 Favours Dose 2

DRAFT FOR 1ST CONSULATION

OCD adults: SSRIs

Review:

02 SSRIs at different doses (acute phase) Comparison: Outcome: 04 Non-responders Dose 1 Dose 2 RR (fixed) RR (fixed) Study or sub-category n/Ν n/N 95% CI 95% CI 01 Citalopram 40mg vs Citalopram 20mg Montgomery 2001 47/98 44/102 1.11 [0.82, 1.51] Subtotal (95% CI) 102 1.11 [0.82, 1.51] Total events: 47 (Dose 1), 44 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.68 (P = 0.49) 02 Citalopram 60mg vs Citalopram 20mg Montgomery 2001 35/100 44/102 0.81 [0.57, 1.15] Subtotal (95% CI) 102 0.81 [0.57, 1.15] Total events: 35 (Dose 1), 44 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.18 (P = 0.24)03 Citalopram 60mg vs Citalopram 40mg Montgomery 2001 35/100 47/98 0.73 [0.52, 1.02] Subtotal (95% CI) 100 98 0.73 [0.52, 1.02] Total events: 35 (Dose 1), 47 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.83 (P = 0.07) 04 Fluoxetine 40mg vs Fluoxetine 20mg Beasley 1992 62/87 1.02 [0.85, 1.23] 0.86 [0.66, 1.12] Montgomery 1993 33/52 39/53 Subtotal (95% CI) 140 0.96 [0.83, 1.12] 141 Total events: 98 (Dose 1), 101 (Dose 2) Test for heterogeneity: Chi² = 1.12, df = 1 (P = 0.29), l² = 10.9% Test for overall effect: Z = 0.49 (P = 0.62) 05 Fluoxetine 60mg vs Fluoxetine 20mg Beasley 1992 0.98 [0.81, 1.19] 63/90 62/87 Montgomery 1993 0.84 [0.65, 1.09] 34/55 39/53 Subtotal (95% CI) 145 140 0.93 [0.79, 1.08] Total events: 97 (Dose 1), 101 (Dose 2) Test for heterogeneity: $Chi^2 = 0.89$, df = 1 (P = 0.34), $I^2 = 0\%$ Test for overall effect: Z = 0.96 (P = 0.34) 06 Fluoxetine 60mg vs Fluoxetine 40mg Beasley 1992 63/90 65/89 0.96 [0.80, 1.15] Montgomery 1993 34/55 33/52 0.97 [0.73, 1.31] Subtotal (95% CI) 141 0.96 [0.82, 1.13] Total events: 97 (Dose 1), 98 (Dose 2) Test for heterogeneity: $Chi^2 = 0.01$, df = 1 (P = 0.93), $I^2 = 0\%$ Test for overall effect: Z = 0.46 (P = 0.65) 07 Paroxetine 40mg vs Paroxetine 20mg Hollander 2003d 0.84 [0.67, 1.05] 62/88 Subtotal (95% CI) 88 0.84 [0.67, 1.05] Total events: 51 (Dose 1), 62 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.53 (P = 0.13) 08 Paroxetine 60mg vs Paroxetine 20mg Hollander 2003d 48/85 62/88 0.80 [0.64, 1.01] Subtotal (95% CI) 0.80 [0.64, 1.01] 85 88 Total events: 48 (Dose 1), 62 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.88 (P = 0.06) 09 Paroxetine 60mg vs Paroxetine 40mg 0.95 [0.74, 1.23] Hollander 2003d 48/85 51/86 0.95 [0.74, 1.23] Subtotal (95% CI) 85 86 Total events: 48 (Dose 1), 51 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.37 (P = 0.71) ż 0.7 1.5 Favours Dose 1 Favours Dose 2



Review: OCD adults: SSRIs

02 SSRIs at different doses (acute phase) 07 Hamilton Rating Scale for Depression Comparison: Outcome:

Study or sub-category	N	Dose 1 Mean (SD)	N	Dose 2 Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Fluoxetine 40mg vs Fluoxe	etine 20mg					
Montgomery 1993	52	-2.55(6.77)	52	-1.85(6.04)		-0.11 [-0.49, 0.28]
Subtotal (95% CI)	52		52			-0.11 [-0.49, 0.28]
Test for heterogeneity: not ap	oplicable					
Test for overall effect: $Z = 0$.	55 (P = 0.58)					
02 Fluoxetine 60mg vs Fluoxe	etine 20mg					
Montgomery 1993	54	-3.41(6.23)	52	-1.85(6.04)		-0.25 [-0.63, 0.13]
Subtotal (95% CI)	54		52			-0.25 [-0.63, 0.13]
Fest for heterogeneity: not ap	oplicable					
est for overall effect: $Z = 1$.	29 (P = 0.20)					
03 Fluoxetine 60mg vs Fluoxe	etine 40mg					
Montgomery 1993	54	-3.41(6.23)	52	-2.55(6.77)		-0.13 [-0.51, 0.25]
Subtotal (95% CI)	54		52			-0.13 [-0.51, 0.25]
Fest for heterogeneity: not ap	oplicable					·
Test for overall effect: $Z = 0$.	68 (P = 0.50)					

Favours Dose 1 Favours Dose 2

Favours Dose 1 Favours Dose 2

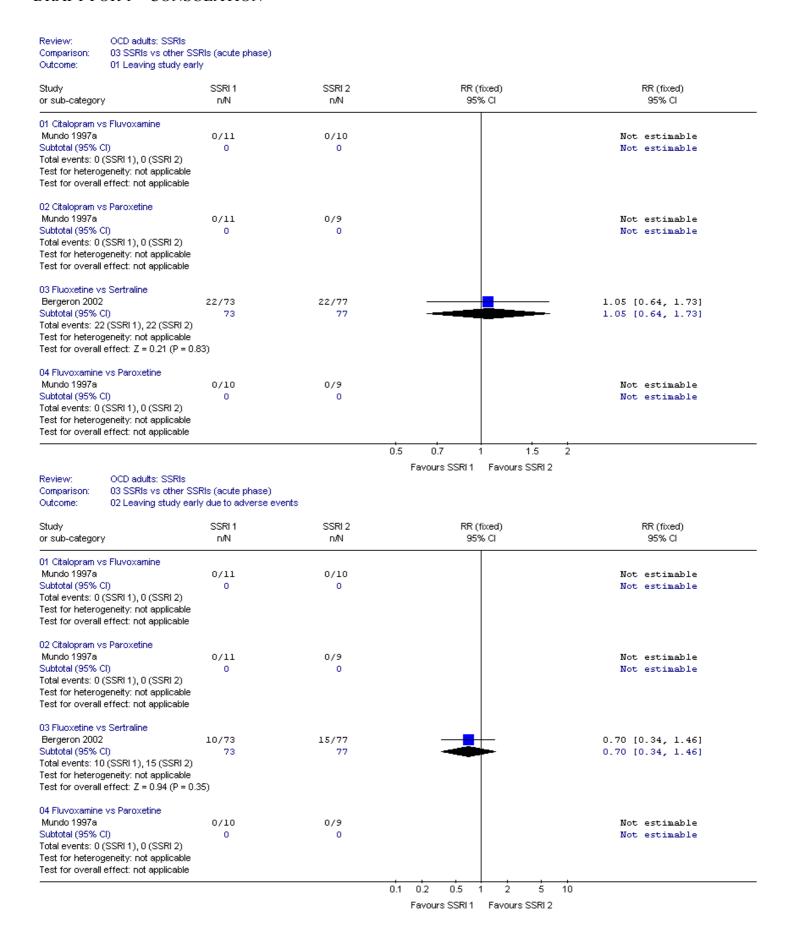
Review:

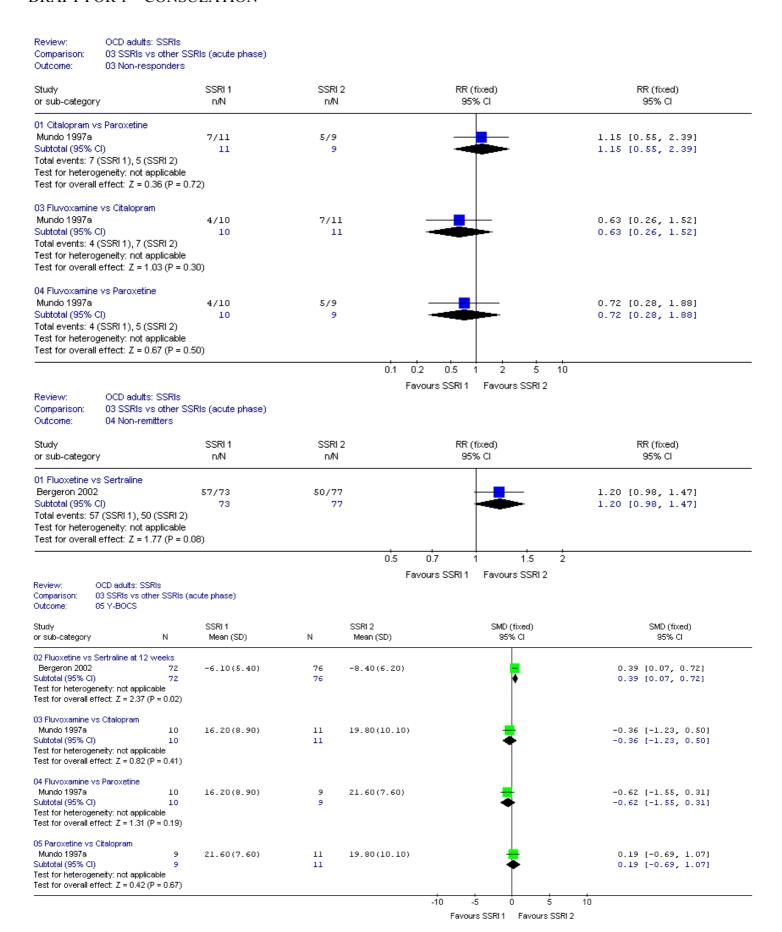
Review: OCD adults: SSRIs
Comparison: 02 SSRIs at different doses (acute phase)
Outcome: 08 Montgomery-Asberg Depression Rating Scale

Study or sub-category 1º	1	Dose 1 Mean (SD)	N	Dose 2 Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
D1 Citalopram 40mg vs Citalopram 20i	mg					
Montgomery 2001	98	-3.90(5.20)	102	-3.40(6.30)		-0.09 [-0.36, 0.19]
Subtotal (95% CI)	98		102			-0.09 [-0.36, 0.19]
Test for heterogeneity: not applicable					-	
est for overall effect: Z = 0.61 (P = 0	0.54)					
02 Citalopram 60mg vs Citalopram 20i	mg					
	100	-4.00(6.50)	102	-3.40(6.30)		-0.09 [-0.37, 0.18]
Subtotal (95% CI)	100		102			-0.09 [-0.37, 0.18]
Test for heterogeneity: not applicable					-	
Test for overall effect: Z = 0.66 (P = 0	0.51)					
03 Citalopram 60mg vs Citalopram 40i	mg					
Montgomery 2001	100	-4.00(6.50)	98	-3.90(5.20)	- 	-0.02 [-0.30, 0.26]
	100		98			-0.02 [-0.30, 0.26]
Test for heterogeneity: not applicable						
Test for overall effect: Z = 0.12 (P = 0	0.91)					
04 Fluoxetine 40mg vs Fluoxetine 20m	ng					
Montgomery 1993	52	-5.20(8.19)	52	-2.96(8.09)		-0.27 [-0.66, 0.11]
Subtotal (95% CI)	52		52			-0.27 [-0.66, 0.11]
est for heterogeneity: not applicable						
est for overall effect: Z = 1.39 (P = 0	0.17)					
05 Fluoxetine 60mg vs Fluoxetine 20m	ng					
Montgomery 1993	54	-5.20(8.73)	52	-2.96(8.09)		-0.26 [-0.65, 0.12]
Subtotal (95% CI)	54		52			-0.26 [-0.65, 0.12]
Test for heterogeneity: not applicable						
Fest for overall effect: Z = 1.35 (P = 0	0.18)					
06 Fluoxetine 60mg vs Fluoxetine 40m	ng					
Montgomery 1993	54	-5.20(8.73)	52	-5.20(8.19)	- •	0.00 [-0.38, 0.38]
Subtotal (95% CI)	54		52			0.00 [-0.38, 0.38]
Fest for heterogeneity: not applicable						
Test for overall effect: Z = 0.00 (P = 1	1.00)					

OCD adults: SSRIs Review: Comparison: 02 SSRIs at different doses (acute phase) Outcome: 09 Sheehan Disability Score: family SMD (fixed) SMD (fixed) Study Dose 2 or sub-category Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Citalopram 40mg vs Citalopram 20mg Montgomery 2001 -2.10(2.30) 102 -1.80(2.40) -0.13 [-0.40, 0.15] 98 Subtotal (95% CI) 102 -0.13 [-0.40, 0.15] Test for heterogeneity: not applicable Test for overall effect: Z = 0.90 (P = 0.37)02 Citalopram 60mg vs Citalopram 20mg Montgomery 2001 100 -2.30(2.40) 102 -1.80(2.40) -0.21 [-0.48, 0.07] Subtotal (95% CI) -0.21 [-0.48, 0.07] 100 102 Test for heterogeneity: not applicable Test for overall effect: Z = 1.47 (P = 0.14) 03 Citalopram 60mg vs Citalopram 40mg Montgomery 2001 -2.30(2.40) -0.08 [-0.36, 0.19] 100 98 -2.10(2.30) Subtotal (95% CI) -0.08 [-0.36, 0.19] Test for heterogeneity: not applicable Test for overall effect: Z = 0.60 (P = 0.55) 0.5 Favours Dose 1 Favours Dose 2 OCD adults: SSRIs Review: 02 SSRIs at different doses (acute phase) Comparison: 10 Sheehan Disability Score: social Outcome: SMD (fixed) SMD (fixed) Study Dose 1 Dose 2 Mean (SD) Mean (SD) 95% CI or sub-category Ν 95% CI 01 Citalopram 40mg vs Citalopram 20mg Montgomery 2001 -1.90(2.30) 102 -2.00(2.20) 0.04 [-0.23, 0.32] Subtotal (95% CI) 98 102 0.04 [-0.23, 0.32] Test for heterogeneity: not applicable Test for overall effect: Z = 0.31 (P = 0.75) 02 Citalopram 60mg vs Citalopram 20mg Montgomery 2001 100 -2.40(2.50) 102 -2.00(2.20) -0.17 [-0.45, 0.11] Subtotal (95% CI) 102 -0.17 [-0.45, 0.11] Test for heterogeneity: not applicable Test for overall effect: Z = 1.20 (P = 0.23)03 Citalopram 60mg vs Citalopram 40mg -0.21 [-0.49, 0.07] -0.21 [-0.49, 0.07] Montgomery 2001 -2.40(2.50) 98 -1.90(2.30) Subtotal (95% CI) 100 98 Test for heterogeneity: not applicable Test for overall effect: Z = 1.45 (P = 0.15) -0.5 0.5 Ó Favours Dose 1 Favours Dose 2 OCD adults: SSRIs Comparison: 02 SSRIs at different doses (acute phase) 11 Sheehan Disability Score: work Outcome: Dose 2 SMD (fixed) SMD (fixed) or sub-category Mean (SD) Mean (SD) 95% CI 95% CI

-2.10(2.30)	102	-1.90(2.40)		_		-0.0	8 [-0.36, 0	.19]
	102			-		-0.0	8 [-0.36, 0	.19]
				-				
-2.00(2.50)	102	-1.90(2.40)		_		-0.0	4 [-0.32, 0	.24]
	102					-0.0	4 [-0.32, 0	.24]
				T				
-2.00(2.50)	98	-2.10(2.30)		_	_	0.0	4 [-0.24, 0	.32]
	98			-	-	0.0	4 [-0.24, 0	.32]
							•	
			-1 -0.5	ó	0.5	1		
			Favours D	ose 1 Fa	ours Dose 2			
	-2.00(2.50)	-2.00(2.50) 102 102	-2.00(2.50) 102 -1.90(2.40) 102 -2.00(2.50) 98 -2.10(2.30)	-2.00(2.50) 102 -1.90(2.40) 102 -2.00(2.50) 98 -2.10(2.30) 98	-2.00(2.50) 102 -1.90(2.40) 102 -2.00(2.50) 98 -2.10(2.30) 98 -4 -0.5 0	-2.00(2.50) 102 -1.90(2.40) 102 -2.00(2.50) 98 -2.10(2.30) 98 -2.10(2.30)	-2.00(2.50)	-2.00(2.50)





DRAFT FOR 1ST CONSULATION

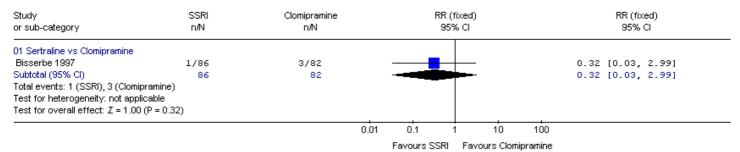
Review: OCD adults: SSRIs Comparison: 03 SSRIs vs other SSRIs (acute phase) Outcome: 06 NIMH-OC SSRI 2 Study SMD (fixed) SMD (fixed) or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI 01 Fluoxetine vs Sertraline Bergeron 2002 72 5.70(2.60) 76 5.50(2.80) 0.07 [-0.25, 0.40] Subtotal (95% CI) 72 0.07 [-0.25, 0.40] Test for heterogeneity: not applicable Test for overall effect: Z = 0.45 (P = 0.65) Mundo 1997a 10 6.23(1.81) 11 8.58(1.88) -1.22 [-2.17, -0.27] Subtotal (95% CI) 10 11 -1.22 [-2.17, -0.27] Test for heterogeneity; not applicable Test for overall effect: Z = 2.52 (P = 0.01) 03 Fluvoxamine vs Paroxetine Mundo 1997a 10 6.23(1.81) 9 7.77(2.02) -0.77 [-1.71, 0.17] Subtotal (95% CI) 10 -0.77 [-1.71, 0.17] Test for heterogeneity: not applicable Test for overall effect: Z = 1.60 (P = 0.11)04 Paroxetine vs Citalopram Mundo 1997a 7.77(2.02) 8.58(1.88) -0.40 [-1.29, 0.49] 11 Subtotal (95% CI) 1.1 -0.40 [-1.29, 0.49] Test for heterogeneity; not applicable Test for overall effect: Z = 0.88 (P = 0.38) Favours SSRI1 Favours SSRI2 Review: OCD adults: SSRIs Comparison: 03 SSRIs vs other SSRIs (acute phase) Outcome 07 Hamilton Rating Scale for Depression SMD (fixed) Study SSRI1 SSRI 2 SMD (fixed) or sub-category Ν Mean (SD) M Mean (SD) 95% CI 95% CI 01 Fluoxetine vs Sertraline Bergeron 2002 6.20(4.60) 72 7.10(5.40) 76 0.18 [-0.14, 0.50] Subtotal (95% CI) 0.18 [-0.14, 0.50] 72 Test for heterogeneity: not applicable Test for overall effect: Z = 1.09 (P = 0.28)-0.5 0.5 Ó Favours SSRI1 Favours SSRI2 Review: OCD adults: SSRIs. Comparison: 04 SSRIs vs Clomipramine (acute phase) Outcome: 01 Adverse events SSRI RR (fixed) RR (fixed) Study Clomipramine or sub-category n/Ν n/N 95% CI 95% CI 01 Fluvoxamine vs Clomipramine Freeman 1994 30/34 24/30 1.10 [0.89, 1.37] Koran 1996a 35/37 39/41 0.99 [0.90, 1.10] 0.94 [0.80, 1.10] Mundo 2001 81/115 84/112 Subtotal (95% CI) 186 183 0.98 [0.89, 1.09] Total events: 146 (SSRI), 147 (Clomipramine) Test for heterogeneity: $Chi^2 = 1.47$, df = 2 (P = 0.48), $I^2 = 0\%$ Test for overall effect: Z = 0.36 (P = 0.72) 02 Paroxetine vs Clomipramine 0.96 [0.90, 1.03] Burnham 1993 77/82 80/82 0.94 [0.85, 1.05] Zohar 1996a 163/201 85/99 Subtotal (95% CI) 283 181 0.95 [0.89, 1.02] Total events: 240 (SSRI), 165 (Clomipramine) Test for heterogeneity: $Chi^2 = 0.13$, df = 1 (P = 0.72), $I^2 = 0\%$ Test for overall effect: Z = 1.45 (P = 0.15) 03 Sertraline vs Clomipramine Askin 1999 7/18 13/18 0.54 [0.28, 1.03] Bisserbe 1997 56/86 57/82 0.94 [0.76, 1.16] Subtotal (95% CI) 0.86 [0.71, 1.06] Total events: 63 (SSRI), 70 (Clomipramine) Test for heterogeneity: Chi² = 2.62, df = 1 (P = 0.11), l² = 61.8% Test for overall effect: Z = 1.41 (P = 0.16) Total (95% CI) 464 0.95 [0.89, 1.00] Total events: 449 (SSRI), 382 (Clomipramine) Test for heterogeneity: Chi² = 5.93, df = 6 (P = 0.43), l² = 0% Test for overall effect: Z = 1.80 (P = 0.07)0.5 0.7 1.5 ż

Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

Outcome: 02 Attempted suicide



Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

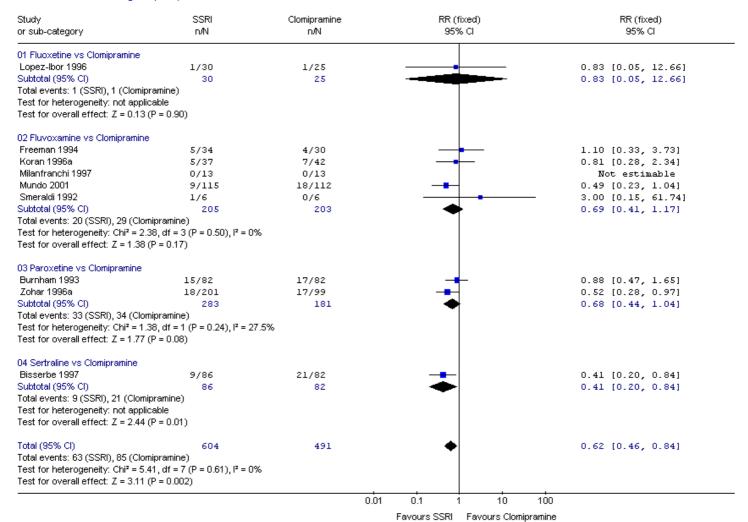
Outcome: 03 Leaving study early

Study	SSRI	Clomipramine	RR (fixed)	RR (fixed)
or sub-category	n/N	n/N	95% CI	95% CI
01 Fluoxetine vs Clomipramine				
Lopez-lbor 1996	5/30	4/25		1.04 [0.31, 3.47]
Subtotal (95% CI)	5/30	4/25		1.04 [0.31, 3.47]
Test for heterogeneity: not app	plicable			
Test for overall effect: $Z = 0.0$	7 (P = 0.95)			
02 Fluvoxamine vs Clomipramii	ne			
Freeman 1994	6/34	11/32		0.51 [0.22, 1.23]
Koran 1996a	8/37	15/42		0.61 [0.29, 1.26]
Milanfranchi 1997	0/13	1/13	-	- 0.33 [0.01, 7.50]
Mundo 2001	19/115	26/112		0.71 [0.42, 1.21]
Smeraldi 1992	1/6	1/6 ←		→ 1.00 [0.08, 12.56]
Subtotal (95% CI)	34/205	54/205	-	0.64 [0.44, 0.93]
Γest for heterogeneity: Chi² = ι	0.71 , df = 4 (P = 0.95), $I^2 = 0$	%	-	
Test for overall effect: Z = 2.3				
03 Paroxetine vs Clomipramine	•			
Burnham 1993	28/82	28/82	-	1.00 [0.65, 1.53]
Zohar 1996a	49/201	34/99		0.71 [0.49, 1.02]
Subtotal (95% Cl)	77/283	62/181	•	0.82 [0.62, 1.08]
Test for heterogeneity: Chi² = 1	1.44 , df = 1 (P = 0.23), $I^2 = 3$	0.4%	7	,
Test for overall effect: Z = 1.4				
04 Sertraline vs Clomipramine				
Askin 1999	2/20	4/22 -	<u> </u>	0.55 [0.11, 2.69]
Bisserbe 1997	23/86	35/82		0.63 [0.41, 0.96]
Subtotal (95% CI)	25/106	39/104	-	0.62 [0.41, 0.94]
Test for heterogeneity: Chi² = I	0.02, df = 1 (P = 0.88), l ² = 0		-	•
「est for overall effect: Z = 2.2				
Total (95% CI)	141/624	159/515	•	0.72 [0.59, 0.88]
Test for heterogeneity: Chi² = 4	4.26 , $df = 9 (P = 0.89)$, $I^2 = 0$	%	7	•
Test for overall effect: Z = 3.2				
		0.1	0.2 0.5 1 2 5	10

Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)
Outcome: 04 Leaving study early due to adverse events



Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)
Outcome: 05 Non-responders

Study	SSRI	Clomipramine	RR (fixed)	RR (fixed)
r sub-category	n/N	n/N	95% Cl	95% CI
1 Fluoxetine vs Clomipramine				
Lopez-lbor 1996	22/30	11/25	-	1.67 [1.02, 2.73]
Subtotal (95% CI)	30	25	-	1.67 [1.02, 2.73]
otal events: 22 (SSRI), 11 (Clom				
est for heterogeneity: not applic	cable			
est for overall effect: Z = 2.03 ((P = 0.04)			
2 Fluvoxamine vs Clomipramine				
(oran 1996a	18/37	21/42		0.97 [0.62, 1.52]
Milanfranchi 1997	2/13	3/13 -		0.67 [0.13, 3.35]
Mundo 2001	46/115	44/112		1.02 [0.74, 1.40]
ubtotal (95% CI)	165	167	•	0.99 [0.76, 1.28]
otal events: 66 (SSRI), 68 (Clori			T	,
est for heterogeneity: Chi ² = 0.2	, ,	0%		
est for overall effect: Z = 0.08 (
3 Paroxetine vs Clomipramine				
Burnham 1993	47/82	42/82	- 	1.12 [0.84, 1.48]
Zohar 1996a	92/201	47/99	-	0.96 [0.75, 1.25]
ubtotal (95% CI)	283	181	•	1.03 [0.85, 1.24]
otal events: 139 (SSRI), 89 (Clo	mipramine)		ſ	
est for heterogeneity: $Chi^2 = 0.5$ est for overall effect: $Z = 0.27$ (, , , , ,	0%		
est for overall effect. Z = 0.27 (,r = 0.79)			
4 Sertraline vs Clomipramine Bisserbe 1997	24 (05	20 (02	_	0.70 (0.50 1.24)
ubtotal (95% CI)	24/86 86	29/82		0.79 [0.50, 1.24] 0.79 [0.50, 1.24]
		82		0.79 [0.80, 1.24]
otal events: 24 (SSRI), 29 (Clom est for heterogeneity: not applic				
- ,				
est for overall effect: Z = 1.04 ((P = 0.30)			
otal (95% CI)	564	455	•	1.02 [0.89, 1.17]
otal events: 251 (SSRI), 197 (CI	lomipramine)		ſ	• •
est for heterogeneity: Chi² = 6.0	01 , df = 6 (P = 0.42), l ² = 0	0.1%		
est for overall effect: Z = 0.24 (
		0.1	0.2 0.5 1 2 5	10
			Favours SSRI Favours Clomip	ramine
eview: OCD adults: SSRIs				

Review: OCD adults: SSRIs
Comparison: 04 SSRIs vs Clomipramine (acute phase)
Outcome: 06 Y-BOCS

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)		(fixed) % Cl	SMD (fixed) 95% Cl
	ne						
Lopez-lbor 1996	30	-7.50(9.29)	24	-8.90(7.13)		-	0.16 [-0.37, 0.70]
Subtotal (95% CI)	30		24				0.16 [-0.37, 0.70]
Test for heterogeneity: not a	applicable						·
Test for overall effect: $Z = 0$).60 (P = 0.55)						
02 Fluvoxamine vs Clomipra	mine						
Koran 1996a	34	17.80(7.70)	39	17.00(8.55)		 -	0.10 [-0.36, 0.56]
Milanfranchi 1997	13	18.40(9.20)	12	16.50(11.00)		+-	0.18 [-0.60, 0.97]
Mundo 2001	67	14.70(10.10)	61	12.50(8.00)	-		0.24 [-0.11, 0.59]
Smeraldi 1992	5	18.20(2.50)	5	15.20(12.40)		 	0.30 [-0.95, 1.55]
Subtotal (95% CI)	119		117			-	0.19 [-0.06, 0.45]
Test for heterogeneity: Chi ²		= 0.97), I ² = 0%					
Test for overall effect: Z = 1	.46 (P = 0.14)						
03 Paroxetine vs Clomiprami	ine						
Burnham 1993	79	-5.61(7.47)	78	-7.73(7.42)			0.28 [-0.03, 0.60]
Zohar 1996a	198	-8.00(8.00)	94	-8.00(8.20)		+	0.00 [-0.25, 0.25]
Subtotal (95% CI)	277		172			-	0.11 [-0.09, 0.30]
Test for heterogeneity: Chi²		= 0.16), I ² = 48.4%					
Test for overall effect: Z = 1	.09 (P = 0.28)						
Total (95% CI)	426		313			•	0.14 [-0.01, 0.29]
Test for heterogeneity: Chi²	= 2.47, df = 6 (P	= 0.87), I ² = 0%					
Test for overall effect: $Z = 1$.85 (P = 0.06)						
					I -0.5	0 0.5 1	
					Favours SSRI	Favours Clomipramin	e

Review: OCD adults: SSRIs

04 SSRIs vs Clomipramine (acute phase) 07 NIMH-OC Comparison:

Outcome:

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Fluvoxamine vs Clomipr	ramine					
Mundo 2001	112	5.90(3.10)	105	5.90(2.80)		0.00 [-0.27, 0.27]
Subtotal (95% CI)	112		105			0.00 [-0.27, 0.27]
Test for heterogeneity: not	: applicable				T	·
Test for overall effect: Z =	0.00 (P = 1.00)					
02 Paroxetine vs Clomiprar	mine					
Burnham 1993	79	-1.42(2.04)	78	-2.06(2.03)		0.31 [0.00, 0.63]
Zohar 1996a	198	-2.50(2.90)	94	-2.50(2.60)		0.00 [-0.25, 0.25]
Subtotal (95% CI)	277		172		-	0.12 [-0.08, 0.31]
Test for heterogeneity: Chi	i ² = 2.36, df = 1 (P	= 0.12), I ² = 57.6%				
Test for overall effect: Z =	1.20 (P = 0.23)					
Total (95% CI)	389		277		•	0.08 [-0.08, 0.23]
Fest for heterogeneity: Chi	i ² = 2.86, df = 2 (P	= 0.24), I ² = 30.0%			_	
Test for overall effect: Z =	0.97 (P = 0.33)					
				-1	-0.5 0 0.5	1

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

08 Comprehensive Psychopathological Rating Scale: obsessive-compulsive

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)		SMD (fixed) 95% Cl)	SMD (fixed) 95% CI
01 Fluoxetine vs Clomiprar	nine							
Lopez-lbor 1996	30	-8.10(7.64)	24	-10.90(7.33)		_	-	0.37 [-0.17, 0.91]
Subtotal (95% CI)	30		24					0.37 [-0.17, 0.91]
Test for heterogeneity: no	t applicable						_	
Test for overall effect: Z =	: 1.33 (P = 0.18)							
					-1 -0	15 0	0.5 1	

Favours SSRI Favours Clomipramine

Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs 04 SSRIs vs Clomipramine (acute phase) 09 Hamilton Rating Scale for Depression Comparison: Outcome:

tudy		SSRI N Mean (SD)		Clomipramine	SMD (fixed)	SMD (fixed)
r sub-category	N			Mean (SD)	95% CI	95% CI
1 Fluoxetine vs Clomipramina	e					
Lopez-lbor 1996	30	-7.50(5.93)	24	-9.40(7.71)		0.28 [-0.26, 0.82]
ubtotal (95% CI)	30		24			- 0.28 [-0.26, 0.82]
est for heterogeneity: not ap	pplicable					
est for overall effect: $Z = 1.0$	00 (P = 0.32)					
2 Fluvoxamine vs Clomipram	nine					
Koran 1996a	34	6.10(3.30)	39	5.80(4.70)		0.07 [-0.39, 0.53]
Mundo 2001	112	7.70(6.00)	105	7.00(4.50)	 	0.13 [-0.14, 0.40]
ubtotal (95% CI)	146		144			0.12 [-0.11, 0.35]
est for heterogeneity: Chi² =	0.05, df = 1 (P	= 0.83), I ² = 0%				
est for overall effect: $Z = 0.9$	99 (P = 0.32)					
otal (95% CI)	176		168		-	0.14 [-0.07, 0.35]
est for heterogeneity: Chi² =	0.33, df = 2 (P	= 0.85), I ² = 0%				
est for overall effect: $Z = 1.3$	30 (P = 0.19)					
est for heterogeneity: Chi² =	0.33, df = 2 (P	= 0.85), I ² = 0%		.1	-05 0	0.5

Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs Comparison: 04 SSRIs vs Clomipramine (acute phase) Outcome 10 Montgomery-Asberg Depression Rating Scale SMD (fixed) SMD (fixed) Study Clomipramine or sub-category Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine vs Clomipramine Lopez-lbor 1996 30 -10.10(8.20) 24 -13.80(9.09) 0.42 [-0.12, 0.97] Subtotal (95% CI) 30 24 0.42 [-0.12, 0.97] Test for heterogeneity: not applicable Test for overall effect: Z = 1.53 (P = 0.13) Smeraldi 1992 5 11.80(6.80) 5 9.60(10.30) 0.23 [-1.02, 1.47] Subtotal (95% CI) 0.23 [-1.02, 1.47] 5 Test for heterogeneity: not applicable Test for overall effect: Z = 0.36 (P = 0.72) 03 Paroxetine vs Clomipramine Zohar 1996a 198 -3.40(7.90) 94 -2.40(7.30) -0.13 [-0.38, 0.12] Subtotal (95% CI) -0.13 [-0.38, 0.12] 198 Test for heterogeneity: not applicable Test for overall effect: Z = 1.03 (P = 0.30) -0.03 [-0.25, 0.19] Test for heterogeneity: Chi² = 3.47, df = 2 (P = 0.18), l² = 42.4% Test for overall effect: Z = 0.24 (P = 0.81) Favours SSRI Favours Clomipramine OCD adults: SSRIs Review: Comparison: 04 SSRIs vs Clomipramine (acute phase) 11 Depression (HRSD; MADRS) Outcome SMD (fixed) SMD (fixed) Study SSRI Clomipramine Mean (SD) Ν Mean (SD) 95% CI 95% CI or sub-category Ν 01 Fluvoxamine vs Clomipramine Koran 1996a 34 6.10(3.30) 39 5.80(4.70) 0.07 [-0.39, 0.53] Mundo 2001 0.13 [-0.14, 0.40] 112 7.70(6.00) 105 7.00(4.50) Smeraldi 1992 5 11.80(6.80) 9.60(10.30) 0.23 [-1.02, 1.47] Subtotal (95% CI) 151 149 0.12 [-0.11, 0.35] Test for heterogeneity: $Chi^2 = 0.08$, df = 2 (P = 0.96), $I^2 = 0\%$ Test for overall effect: Z = 1.04 (P = 0.30)02 Paroxetine vs Clomipramine 198 Zohar 1996a -3.40(7.90) 94 -2.40(7.30) -0.13 [-0.38, 0.12] Subtotal (95% CI) -0.13 [-0.38, 0.12] 198 94 Test for heterogeneity: not applicable Test for overall effect: Z = 1.03 (P = 0.30) Total (95% CI) 243 0.01 [-0.16, 0.17] Test for heterogeneity: Chi² = 2.21, df = 3 (P = 0.53), l² = 0% Test for overall effect: Z = 0.06 (P = 0.95) -4 -2 Ò Favours SSRI Favours Clomipramine OCD adults: SSRIs Review: Comparison: 04 SSRIs vs Clomipramine (acute phase) Outcome 12 Clinical Anxiety Scale SMD (fixed) SMD (fixed) Study or sub-category Mean (SD) N Mean (SD) 95% CI 95% CI 01 Fluvoxamine vs Clomipramine Mundo 2001 7.00(4.60) 105 6.70(4.30) 0.07 [-0.20, 0.33] Subtotal (95% CI) 0.07 [-0.20, 0.33] Test for heterogeneity: not applicable Test for overall effect: Z = 0.49 (P = 0.62)-0.5 0.5 Ó Favours SSRI Favours Clomipramine Review: OCD adults: SSRIs 04 SSRIs vs Clomipramine (acute phase) Comparison: Outcome 13 Covi Anxiety Scale SMD (fixed) SMD (fixed) Study SSRI Clomipramine or sub-category Mean (SD) Mean (SD) 95% CI 95% CI 01 Fluoxetine vs Clomipramine Lopez-Ibor 1996 30 -2.40(3.10) 24 -2.40(3.09) 0.00 [-0.54, 0.54] 0.00 [-0.54, 0.54] Subtotal (95% CI) 30 24 Test for heterogeneity: not applicable Test for overall effect: Z = 0.00 (P = 1.00) -0.5 0.5 Ó Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

Outcome: 14 Anxiety (Clinical Anxiety Scale; Covi Anxiety Scale)

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Fluoxetine vs Clomiprar	mine					
Lopez-lbor 1996	30	-2.40(3.10)	24	-2.40(3.09)		0.00 [-0.54, 0.54]
Subtotal (95% CI)	30		24			0.00 [-0.54, 0.54]
Test for heterogeneity: not	t applicable				_T_	
Test for overall effect: Z =	0.00 (P = 1.00)					
02 Fluvoxamine vs Clomipi	ramine					
Mundo 2001	112	7.00(4.60)	105	6.70(4.30)		0.07 [-0.20, 0.33]
Subtotal (95% CI)	112		105			0.07 [-0.20, 0.33]
Test for heterogeneity: not	t applicable				_	
Test for overall effect: Z =	0.49 (P = 0.62)					
Total (95% CI)	142		129			0.05 [-0.18, 0.29]
Test for heterogeneity: Ch	$i^2 = 0.05$, $df = 1$ (P	= 0.83), I ² = 0%			-	
Test for overall effect: Z =		••				
					-1 -0.5 0 0.5	1

OCD adults: SSRIs

Review:

Comparison: 04 SSRIs vs Clomipramine (acute phase) 15 Clinical Global Impressions: global improvement Outcome:

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
	iine					
Lopez-lbor 1996	30	-2.60(1.13)	24	-2.60(1.19)		0.00 [-0.54, 0.54]
Subtotal (95% CI)	30		24			0.00 [-0.54, 0.54]
Test for heterogeneity: not	applicable				T	
Test for overall effect: Z =	0.00 (P = 1.00)					
02 Fluvoxamine vs Clomipra	amine					
Mundo 2001	112	2.30(1.00)	105	2.30(1.00)		0.00 [-0.27, 0.27]
Subtotal (95% CI)	112		105			0.00 [-0.27, 0.27]
Test for heterogeneity: not	applicable				Ī	
Test for overall effect: Z =	0.00 (P = 1.00)					
Total (95% CI)	142		129			0.00 [-0.24, 0.24]
Test for heterogeneity: Chi-	$^{2} = 0.00$, df = 1 (P	= 1.00), I ² = 0%			T	
Test for overall effect: Z =	0.00 (P = 1.00)					

Favours SSRI Favours Clomipramine

Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs Comparison:

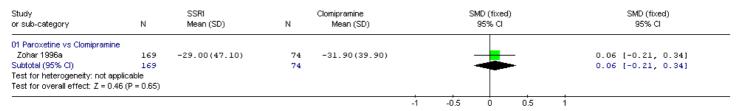
04 SSRIs vs Clomipramine (acute phase) 16 Clinical Global Impressions: severity of illness Outcome:

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)			(fixed) 5% Cl			SMD (fixed) 95% Cl
01 Fluoxetine vs Clomipramine	•									
Lopez-lbor 1996	30	-0.90(1.23)	24	-1.90(1.14)			-	-		0.83 [0.27, 1.39]
Subtotal (95% CI)	30		24				•	•		0.83 [0.27, 1.39]
Test for heterogeneity: not ap	plicable						-			
Test for overall effect: $Z = 2.8$	39 (P = 0.004)									
02 Fluvoxamine vs Clomiprami	ine									
Mundo 2001	112	3.40(1.30)	105	3.20(1.20)			=			0.16 [-0.11, 0.43]
Subtotal (95% CI)	112		105				•			0.16 [-0.11, 0.43]
Test for heterogeneity: not ap	plicable						1			
Test for overall effect: $Z = 1.1$	17 (P = 0.24)									
03 Paroxetine vs Clomipramine	e									
Zohar 1996a	194	-1.20(1.40)	94	-1.10(1.20)			-			-0.07 [-0.32, 0.17]
Subtotal (95% CI)	194		94				•			-0.07 [-0.32, 0.17]
Test for heterogeneity: not ap	plicable						1			
Test for overall effect: $Z = 0.5$	59 (P = 0.55)									
Total (95% CI)	336		223				•			0.11 [-0.06, 0.28]
Test for heterogeneity: Chi² =	8.57, df = 2 (P	= 0.01), I ² = 76.7%					ľ			
Test for overall effect: $Z = 1.2$	23 (P = 0.22)									
					-4	-2	 	2	4	
					F	avours SSRI	Favo	urs Clomi	oramine	
					1.0	avours ssivi	, avc	iai a Cibilii	or annillie	

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

17 Symptom Checklist-90 Outcome:



Favours SSRI Favours Clomipramine

Favours SSRI Favours Clomipramine

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

Outcome: 18 Subanalysis: Non-responders in patients with comorbid depression

Study or sub-category	SSRI n/N	Clomipramine n <i>i</i> N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Fluoxetine vs Clomipramine				
Lopez-lbor 1996	22/30	11/25		1.67 [1.02, 2.73]
Subtotal (95% CI)	30	25	-	1.67 [1.02, 2.73]
Total events: 22 (SSRI), 11 (Clomiprai	mine)			
Test for heterogeneity: not applicable				
Test for overall effect: Z = 2.03 (P = 0	0.04)			
02 Fluvoxamine vs Clomipramine				
Mundo 2001	46/115	44/112	-	1.02 [0.74, 1.40]
Subtotal (95% CI)	115	112	•	1.02 [0.74, 1.40]
Total events: 46 (SSRI), 44 (Clomiprai	mine)		Ī	
Test for heterogeneity: not applicable	1			
Test for overall effect: Z = 0.11 (P = 0	0.91)			
Total (95% CI)	145	137		1.16 [0.88, 1.51]
Total events: 68 (SSRI), 55 (Clomiprai	mine)		*	, ,
Test for heterogeneity: Chi ² = 2.72, di		:.3%		
Test for overall effect: Z = 1.06 (P = 0				
		0.1	0.2 0.5 1 2 5	10

Review: OCD adults: SSRIs

Comparison:

04 SSRts vs Clomipramine (acute phase) 19 Subanalysis: Y-BOCS in patients with comorbid depression Outcome:

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)			D (fixed) 95% Cl			SMD (fixed) 95% CI
01 Fluoxetine vs Clomiprami	ine									
Lopez-lbor 1996	30	-7.50(9.29)	24	-8.90(7.13)			-			0.16 [-0.37, 0.70]
Subtotal (95% CI)	30		24							0.16 [-0.37, 0.70]
Test for heterogeneity: not a	applicable									
Test for overall effect: $Z = 0$	0.60 (P = 0.55)									
02 Fluvoxamine vs Clomipra	mine									
Mundo 2001	67	14.70(10.10)	61	12.50(8.00)			+=			0.24 [-0.11, 0.59]
Smeraldi 1992	5	18.20(2.50)	5	15.20(12.40)	_		-		\rightarrow	0.30 [-0.95, 1.55]
Subtotal (95% CI)	72		66				-			0.24 [-0.09, 0.58]
Test for heterogeneity: Chi ²	= 0.01, df = 1 (P	= 0.92), I ² = 0%								
Test for overall effect: $Z = 1$	1.42 (P = 0.16)									
Total (95% CI)	102		90					-		0.22 [-0.06, 0.51]
Test for heterogeneity: Chi ²	= 0.07, df $= 2$ (P	= 0.97), I ² = 0%								
Test for overall effect: $Z = 1$	1.52 (P = 0.13)									
					-1	-0.5	ó	0.5	i	
						Favours SSF	RI Favou	ırs Clomi	pramine	

Review: OCD adults: SSRIs

Comparison: 04 SSRIs vs Clomipramine (acute phase)

Outcome: 20 Subanalysis: Hamilton Rating Scale for Depression in patients with comorbid depression

Study or sub-category	N	SSRI Mean (SD)	N	Clomipramine Mean (SD)			MD (fixed) 95% Cl			SMD (fixed) 95% Cl
01 Fluoxetine vs Clomipra	mine									
Lopez-lbor 1996	30	-7.50(5.93)	24	-9.40(7.71)		_	-			0.28 [-0.26, 0.82]
Subtotal (95% CI)	30		24			-				0.28 [-0.26, 0.82]
Test for heterogeneity: no	t applicable						-			
Test for overall effect: Z =	= 1.00 (P = 0.32)									
02 Fluvoxamine vs Clomip	ramine									
Mundo 2001	112	7.70(6.00)	105	7.00(4.50)			_	_		0.13 [-0.14, 0.40]
Subtotal (95% CI)	112		105				-	-		0.13 [-0.14, 0.40]
Test for heterogeneity: no	nt applicable						-			
Test for overall effect: Z =	= 0.96 (P = 0.34)									
Total (95% CI)	142		129					-		0.16 [-0.08, 0.40]
Test for heterogeneity: Ch	$hi^2 = 0.22$, $df = 1$ (P	= 0.64), I ² = 0%					-			
Test for overall effect: Z =	= 1.31 (P = 0.19)	••								
					-1	-0.5	ó	0.5	1	
					F	avours SS	RI Favo	ours Clomip	amine	

Review: OCD adults: SSRIs

05 SSRIs/Clomipramine vs Non-SRIs (acute phase) 01 Y-BOCS Comparison:

Outcome:

Study or sub-category	N	SSRI Mean (SD)	N	Other drug Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Fluoxetine vs Phenelzine						
Jenike 1997	19	16.20(6.30)	17	16.30(7.00)		-0.01 [-0.67, 0.64]
Subtotal (95% CI)	19		17		•	-0.01 [-0.67, 0.64]
Test for heterogeneity: not app	licable				Ţ	
Test for overall effect: Z = 0.04	4 (P = 0.96)					
02 Fluvoxamine vs Desipramin	9					
Goodman 1990a	21	19.50(9.00)	19	25.80(6.00)	 -	-0.80 [-1.45, -0.15]
Subtotal (95% CI)	21		19		•	-0.80 [-1.45, -0.15]
Test for heterogeneity: not app	licable				-	
Test for overall effect: $Z = 2.42$	2 (P = 0.02)					
03 Clomipramine vs Buspirone						
Pato 1991	9	17.67(4.97)	9	16.78(6.46)		0.15 [-0.78, 1.07]
Subtotal (95% CI)	9		9			0.15 [-0.78, 1.07]
Test for heterogeneity: not app	licable					
Test for overall effect: $Z = 0.3^{\circ}$	I (P = 0.76)					
04 Sertraline vs Desipramine						
Hoehn-Saric 2000	79	-8.40(8.00)	85	-6.00(8.30)		-0.29 [-0.60, 0.02]
Subtotal (95% CI)	79		85		◆	-0.29 [-0.60, 0.02]
Test for heterogeneity: not app	licable					
Test for overall effect: Z = 1.86	S (P = 0.06)					
Total (95% CI)	128		130		•	-0.30 [-0.54, -0.05]
Test for heterogeneity: Chi ² = 3	3.91, df = 3 (P	= 0.27), I ² = 23.3%			•	
Test for overall effect: $Z = 2.35$	5(P = 0.02)					

Review: OCD adults: SSRIs

Comparison: Outcome: 05 SSRIs/Clomipramine vs Non-SRIs (acute phase) 02 NIMH-OC

Study or sub-category	N	SSRI Mean (SD)	N	Other drug Mean (SD)	SMD (fixed) 95% CI	SMD (fixed) 95% Cl
01 Fluoxetine vs Phenelzine						
Jenike 1997	19	7.00(1.10)	17	6.80(1.40)		0.16 [-0.50, 0.81]
Subtotal (95% CI)	19		17			0.16 [-0.50, 0.81]
Fest for heterogeneity: not ap	pplicable					
Test for overall effect: $Z = 0$.	.47 (P = 0.64)					
02 Sertraline vs Desipramine	!					
Hoehn-Saric 2000	79	-2.70(2.67)	85	-1.70(2.77)		-0.37 [-0.67, -0.06]
Subtotal (95% CI)	79		85		-	-0.37 [-0.67, -0.06]
Test for heterogeneity: not ap	pplicable					
Test for overall effect: $Z = 2$.	.32 (P = 0.02)					
03 Clomipramine vs Buspiron	ne					
Pato 1991	9	21.22(5.49)	9	19.22(5.97)	-	→ 0.33 [-0.60, 1.26]
Subtotal (95% CI)	9		9			0.33 [-0.60, 1.26]
Test for heterogeneity: not a	pplicable					
Test for overall effect: $Z = 0$.	.70 (P = 0.48)					
Total (95% CI)	107		111		-	-0.22 [-0.49, 0.05]
Test for heterogeneity: Chi ² =	= 3.47, df = 2 (P	= 0.18), I ² = 42.3%			-	
Test for overall effect: $Z = 1$.	.62 (P = 0.11)					

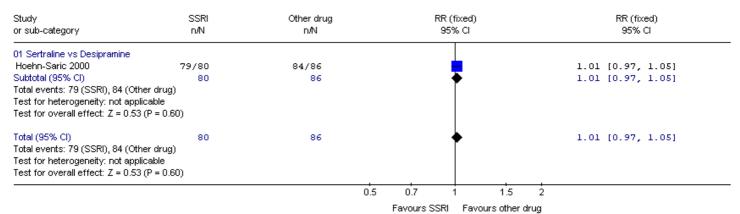
Favours SSRI Favours other drug

Favours SSRI Favours other drug

Review: OCD adults: SSRIs

Comparison: 05 SSRIs/Clomipramine vs Non-SRIs (acute phase)

Outcome: 03 Adverse events



Review: OCD adults: SSRIs

Comparison: 05 SSRIs/Clomipramine vs Non-SRIs (acute phase)
Outcome: 04 Leaving study early due to adverse events

Study or sub-category	SSRI n/N	Other drug n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Sertraline vs Desipramine				
Hoehn-Saric 2000	8/80	22/86	-	0.39 [0.18, 0.83]
Subtotal (95% CI)	80	86	<u>-</u>	0.39 [0.18, 0.83]
Total events: 8 (SSRI), 22 (Other	drug)		Ť	•
Test for heterogeneity: not applic	able			
Fest for overall effect: Z = 2.46 ((P = 0.01)			
02 Clomipramine vs Imipramine				
Volavka 1985	2/11	2/12		1.09 [0.18, 6.48]
Subtotal (95% CI)	11	12		1.09 [0.18, 6.48]
Total events: 2 (ŚSRI), 2 (Other o	drug)		T	
Test for heterogeneity: not applic				
Test for overall effect: Z = 0.10 (P = 0.92)			
03 Fluvoxamine vs Desipramine				
Goodman 1990a	0/21	2/19		0.18 [0.01, 3.56]
Subtotal (95% CI)	21	19		0.18 [0.01, 3.56]
Total events: 0 (SSRI), 2 (Other o	drug)		-	
Test for heterogeneity: not applic	able			
Test for overall effect: Z = 1.12 (P = 0.26)			
04 Clomipramine vs Buspirone				
Pato 1991	1/10	0/10		3.00 [0.14, 65.90]
Subtotal (95% CI)	10	10		3.00 [0.14, 65.90]
Fotal events: 1 (SSRI), 0 (Other o				
Test for heterogeneity: not applic				
Test for overall effect: Z = 0.70 (P = 0.49)			
05 Clomipramine vs Phenelzine				
Vallejo 1992	1/16	0/14	- •	2.65 [0.12, 60.21]
Subtotal (95% CI)	16	14		2.65 [0.12, 60.21]
Total events: 1 (SSRI), 0 (Other o				
Test for heterogeneity: not applic				
Test for overall effect: Z = 0.61 (P = 0.54)			
Total (95% CI)	138	141	•	0.51 [0.28, 0.95]
Total events: 12 (SSRI), 26 (Othe				
Test for heterogeneity: Chi² = 3.9		%		
Test for overall effect: Z = 2.14 (P = 0.03)			
		0.001	0.01 0.1 1 10 100	1000
			Favours SSRI Favours other o	drug

Review: OCD adults: SSRIs 05 SSRIs/Clomipramine vs Non-SRIs (acute phase) Comparison: Outcome: 05 Non-responders (OCD) SSRI RR (fixed) RR (fixed) Study Other drug or sub-category n/Ν n/N 95% CI 95% CI 02 Sertraline vs Desipramine Hoehn-Saric 2000 42/80 40/86 1.13 [0.83, 1.54] Subtotal (95% CI) 80 86 1.13 [0.83, 1.54] Total events: 42 (SSRI), 40 (Other drug) Test for heterogeneity: not applicable Test for overall effect: Z = 0.77 (P = 0.44) Total (95% CI) 80 86 1.13 [0.83, 1.54] Total events: 42 (SSRI), 40 (Other drug) Test for heterogeneity: not applicable Test for overall effect: Z = 0.77 (P = 0.44) 0.5 0.7 1.5 Favours SSRI Favours other drug Review: OCD adults: SSRIs Comparison: 06 SSRIs vs placebo (continuation phase) Outcome: 01 Leaving study early SSRI RR (fixed) RR (fixed) Study Placebo or sub-category 95% CI 95% CI π/N n/N 01 Fluoxetine 0.39 [0.08, 1.84] Beasley 1992 3/23 2/6 Montgomery 1993 16/61 2/12 1.57 [0.41, 5.97] Romano 2001 23/35 16/36 0.68 [0.44, 1.05] Subtotal (95% CI) 0.75 [0.50, 1.12] 120 53 Total events: 35 (SSRI), 27 (Placebo) Test for heterogeneity: $Chi^2 = 2.07$, df = 2 (P = 0.36), $I^2 = 3.3\%$ Test for overall effect: Z = 1.40 (P = 0.16) 02 Paroxetine Hollander 2003d 0.50 [0.34, 0.75] 19/53 37/52 Subtotal (95% CI) 53 52 0.50 [0.34, 0.75] Total events: 19 (SSRI), 37 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 3.36 (P = 0.0008) Total (95% CI) 105 0.61 [0.46, 0.81] Total events: 54 (SSRI), 64 (Placebo) Test for heterogeneity: $Chi^2 = 3.36$, df = 3 (P = 0.34), $I^2 = 10.7\%$ Test for overall effect: Z = 3.39 (P = 0.0007) 0.01 0.1 100 10 Favours SSRI Favours placebo Review: OCD adults: SSRIs Comparison 06 SSRIs vs placebo (continuation phase) Outcome: 02 Leaving study early due to adverse events Study SSRI Placebo RR (fixed) RR (fixed) or sub-category n/Ν n/N 95% CI 95% CI 01 Fluoxetine Montgomery 1993 2/61 0/12 1.05 [0.05, 20.58] Romano 2001 2/36 1/35 1.94 [0.18, 20.49] Subtotal (95% CI) 47 1.54 [0.25, 9.58] Total events: 4 (SSRI), 1 (Placebo) Test for heterogeneity: $Chi^2 = 0.10^{\circ}$, df = 1 (P = 0.75), $I^2 = 0\%$ Test for overall effect: Z = 0.46 (P = 0.64) 02 Paroxetine Hollander 2003d 3/53 20/52 0.15 [0.05, 0.47] Subtotal (95% CI) 0.15 [0.05, 0.47] 53 52 Total events: 3 (SSRI), 20 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 3.26 (P = 0.001) Total (95% CI) 99 0.26 [0.11, 0.63] Total events: 7 (SSRI), 21 (Placebo) Test for heterogeneity: Chi² = 4.58, df = 2 (P = 0.10), l² = 56.3% Test for overall effect: Z = 3.00 (P = 0.003)0.01 0.1 10 100

Favours SSRI Favours placebo

Test for overall effect: Z = 0.65 (P = 0.52)

Review: OCD adults: SSRIs Comparison: 06 SSRIs vs placebo (continuation phase) Outcome: 03 Non-responders SSRI Placebo RR (fixed) RR (fixed) Study 95% CI or sub-category nNn/N 95% CI 01 Fluoxetine Beasley 1992 14/23 3/6 1.22 [0.51, 2.89] Subtotal (95% CI) 1.22 [0.51, 2.89] Total events: 14 (SSRI), 3 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.45 (P = 0.66) 0.2 0.5 5 Favours SSRI Favours placebo OCD adults: SSRIs Review 06 SSRIs vs placebo (continuation phase) Comparison: 04 Y-BOCS Outcome: Study SSRI Placebo SMD (fixed) SMD (fixed) or sub-category Mean (SD) Ν Mean (SD) Ν 95% CI 95% CI 01 Fluoxetine Beasley 1992 23 9.80(7.30) 8.50(6.70) 0.18 [-0.72, 1.08] Romano 2001 35 1.46(7.08) 34 2.50(6.16) -0.15 [-0.63, 0.32] -0.08 [-0.50, 0.34] Subtotal (95% CI) 58 40 Test for heterogeneity: Chi² = 0.41, df = 1 (P = 0.52), l² = 0% Test for overall effect: Z = 0.39 (P = 0.70) 0 Favours SSRI Favours placebo Review: OCD adults: SSRIs 06 SSRIs vs placebo (continuation phase) Comparison: Outcome: 05 Hamilton Rating Scale for Depression Study SSRI Placebo SMD (fixed) SMD (fixed) Ν Mean (SD) Ν or sub-category Mean (SD) 95% CI 95% CI 01 Fluoxetine Romano 2001 35 1.20(5.37) 1.79(5.06) -0.11 [-0.58, 0.36] Subtotal (95% CI) 35 34 -0.11 [-0.58, 0.36] Test for heterogeneity; not applicable Test for overall effect: Z = 0.46 (P = 0.64) -0.5 Ó 0.5 Favours SSRI Favours placebo OCD adults: SSRIs Review: Comparison: 06 SSRIs vs placebo (continuation phase) Outcome 06 SF-36; social functioning SMD (fixed) Study SSRI Placebo SMD (fixed) or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine Romano 2001 0.15 [-0.32, 0.63] 34 9.56(19.23) 34 5.88(27.22) Subtotal (95% CI) 34 0.15 [-0.32, 0.63] Test for heterogeneity: not applicable Test for overall effect: Z = 0.64 (P = 0.53) Ó 0.5 Favours SSRI Favours placebo Review: OCD adults: SSRIs Comparison: 07 SSRIs vs placebo (discontinuation phase) Outcome: SSRI RR (fixed) RR (fixed) Study Placebo or sub-category n/N 95% CI 95% CI n/N 01 Sertraline Koran 2002 0/109 0.35 [0.01, 8.46] 1/114 Subtotal (95% CI) 0.35 [0.01, 8.46] 109 114 Total events: 0 (SSRI), 1 (Placebo) Test for heterogeneity: not applicable

0.01

0.1

Favours SSRI

10

Favours placebo

100

Test for overall effect: Z = 2.50 (P = 0.01)

Review: OCD adults: SSRIs 07 SSRIs vs placebo (discontinuation phase) Comparison: Outcome: 02 Leaving study early SSRI Placebo RR (fixed) RR (fixed) Study or sub-category n/N n/N 95% CI 95% CI 01 Sertraline Koran 2002 33/109 59/114 0.58 [0.42, 0.82] Subtotal (95% CI) 109 114 0.58 [0.42, 0.82] Total events: 33 (SSRI), 59 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 3.13 (P = 0.002) 0.2 0.5 2 Favours SSRI Favours placebo Review: OCD adults: SSRIs 07 SSRIs vs placebo (discontinuation phase) Comparison: 03 Leaving study early due to adverse effects Outcome: Study SSRI RR (fixed) Placebo RR (fixed) or sub-category n/N n/N 95% CI 95% CI 01 Sertraline Koran 2002 5/109 0.44 [0.16, 1.20] 12/114 Subtotal (95% CI) 109 114 0.44 [0.16, 1.20] Total events: 5 (SSRI), 12 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.61 (P = 0.11) 0.2 0.5 5 10 Favours SSRI Favours placebo OCD adults: SSRIs Review: Comparison: 07 SSRIs vs placebo (discontinuation phase) Outcome: 04 Relapse Study SSRI Placebo RR (fixed) RR (fixed) n/N 95% CI 95% CI or sub-category n/N 01 Sertraline Koran 2002 4/109 6/114 0.70 [0.20, 2.40] 0.70 [0.20, 2.40] Subtotal (95% CI) 109 114 Total events: 4 (SSRI), 6 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.57 (P = 0.57) Ś 0.2 0.5 2 Favours SSRI Favours placebo Review: OCD adults: SSRIs Comparison: 07 SSRIs vs placebo (discontinuation phase) 05 Y-BOCS Outcome SSRI Placebo SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Sertraline Koran 2002 108 11.40(7.50) 113 14.20(7.70) -0.37 [-0.63, -0.10] Subtotal (95% CI) 108 113 -0.37 [-0.63, -0.10] Test for heterogeneity: not applicable Test for overall effect: Z = 2.70 (P = 0.007) -0.5 Ò 0.5 Favours SSRI Favours placebo Review: OCD adults: SSRIs Comparison: 07 SSRIs vs placebo (discontinuation phase) Outcome 06 NIMH-OC Study SSRI SMD (fixed) SMD (fixed) Placebo Mean (SD) Ν Mean (SD) 95% CI or sub-category 01 Sertraline -0.34 [-0.60, -0.07] -0.34 [-0.60, -0.07] Koran 2002 108 4.80(2.60) 113 5.70(2.70) Subtotal (95% CI) 108 Test for heterogeneity: not applicable

-0.5 0 0.5
Favours SSRI Favours placebo

DRAFT FOR 1ST CONSULATION

Test for heterogeneity: not applicable Test for overall effect: Z = 0.10 (P = 0.92)

Review: OCD adults: SSRIs Comparison: 07 SSRIs vs placebo (discontinuation phase) Outcome 07 QoL Enjoyment and Satisfaction SMD (fixed) Study Placebo SMD (fixed) or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI 01 Sertraline Koran 2002 -77.30(16.10) 109 -67.50(20.30) -0.53 [-0.80, -0.26] 106 Subtotal (95% CI) 106 -0.53 [-0.80, -0.26] Test for heterogeneity: not applicable Test for overall effect: Z = 3.83 (P = 0.0001) -0.5 Ó 0.5 Favours SSRI Favours placebo Review: OCD adults: SSRIs Comparison: 08 SSRIs at different doses (continuation phase) 01 Leaving study early Outcome: Study Dose 1 Dose 2 RR (fixed) RR (fixed) or sub-category 95% CI 95% CI n/N n/N 01 40mg Fluoxetine v 20mg Fluoxetine 6/21 3/23 2.19 [0.63, 7.67] Beasley 1992 Montgomery 1993 6/20 5/18 1.08 [0.40, 2.94] Subtotal (95% CI) 1.47 [0.68, 3.19] 41 41 Total events: 12 (Dose 1), 8 (Dose 2) Test for heterogeneity: $Chi^2 = 0.75$, df = 1 (P = 0.39), $I^2 = 0\%$ Test for overall effect: Z = 0.98 (P = 0.33) 02 60mg Fluoxetine v 20mg Fluoxetine Beasley 1992 3/26 3/23 0.88 [0.20, 3.96] Montgomery 1993 5/23 5/18 0.78 [0.27, 2.29] Subtotal (95% CI) 49 41 0.82 [0.34, 1.97] Total events: 8 (Dose 1), 8 (Dose 2) Test for heterogeneity: $Chi^2 = 0.02$, df = 1 (P = 0.90), $I^2 = 0\%$ Test for overall effect: Z = 0.45 (P = 0.66) 03 60mg Fluoxetine v 40mg Fluoxetine Beasley 1992 3/26 6/21 0.40 [0.11, 1.43] Montgomery 1993 5/23 6/20 0.72 [0.26, 2.02] Subtotal (95% CI) 49 41 0.56 [0.26, 1.24] Total events: 8 (Dose 1), 12 (Dose 2) Test for heterogeneity: $Chi^2 = 0.50$, df = 1 (P = 0.48), $I^2 = 0\%$ Test for overall effect: Z = 1.43 (P = 0.15) 0.1 0.2 0.5 ż 10 Favours Dose 1 Favours Dose 2 Review: OCD adults: SSRIs Comparison: 08 SSRIs at different doses (continuation phase) Outcome: 02 Leaving study early due to adverse events RR (fixed) RR (fixed) Study Dose 1 Dose 2 n/N or sub-category n/N 95% CI 95% CI 01 40mg Fluoxetine v 20mg Fluoxetine 2.71 [0.12, 62.70] 2.71 [0.12, 62.70] Montgomery 1993 1/20 0/18 Subtotal (95% CI) 20 18 Total events: 1 (Dose 1), 0 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.62 (P = 0.53) 02 60mg Fluoxetine v 20mg Fluoxetine Montgomery 1993 2.38 [0.10, 55.06] 1/23 0/18 Subtotal (95% CI) 23 18 2.38 [0.10, 55.06] Total events: 1 (Dose 1), 0 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.54 (P = 0.59) 03 60mg Fluoxetine v 40mg Fluoxetine 0.87 [0.06, 13.02] Montgomery 1993 1/23 1/20 Subtotal (95% CI) 23 20 0.87 [0.06, 13.02] Total events: 1 (Dose 1), 1 (Dose 2)

0.01

0.1

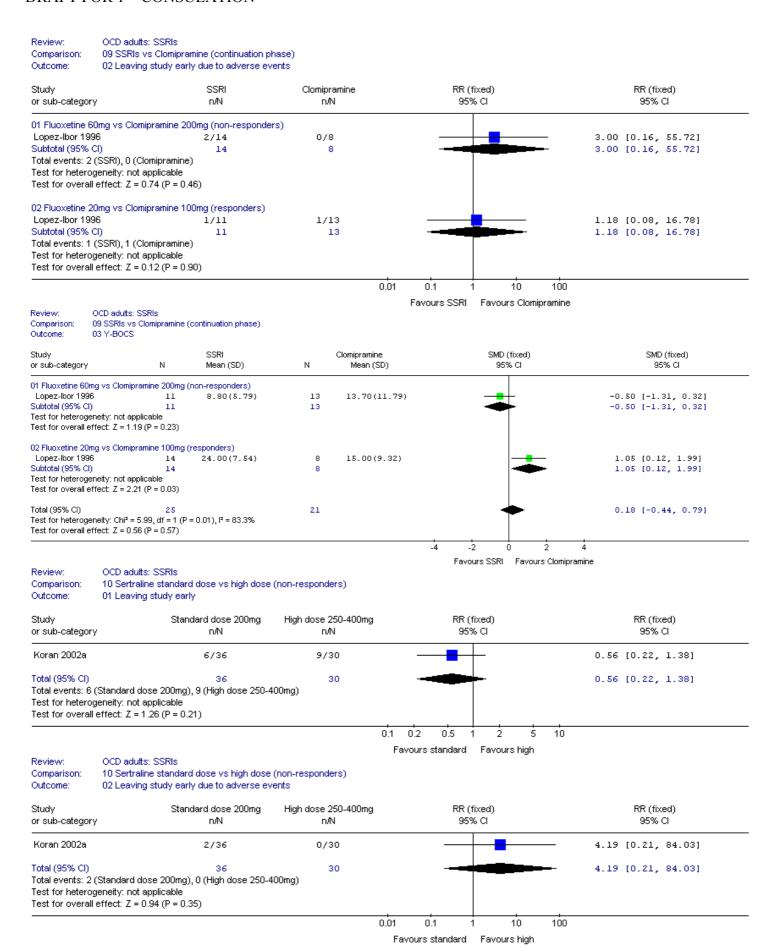
100

10

Favours Dose 1 Favours Dose 2

DRAFT FOR 1ST CONSULATION

Review: OCD adults: SSRIs 08 SSRIs at different doses (continuation phase) Comparison: Outcome: 03 Non-responders Dose 1 Dose 2 RR (fixed) RR (fixed) Study or sub-category n/N n/N 95% CI 95% CI 01 Fluoxetine 40mg v Fluoxetine 20mg Beasley 1992 12/21 14/23 0.94 [0.57, 1.54] Subtotal (95% CI) 23 0.94 [0.57, 1.54] Total events: 12 (Dose 1), 14 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 0.25 (P = 0.80) 02 Fluoxetine 60mg v Fluoxetine 20mg Beasley 1992 11/26 14/23 0.70 [0.40, 1.21] Subtotal (95% CI) 0.70 [0.40, 1.21] 23 Total events: 11 (Dose 1), 14 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.28 (P = 0.20)03 Fluoxetine 60mg v Fluoxetine 40mg 11/26 Beasley 1992 12/21 0.74 [0.41, 1.32] Subtotal (95% CI) 0.74 [0.41, 1.32] 26 Total events: 11 (Dose 1), 12 (Dose 2) Test for heterogeneity: not applicable Test for overall effect: Z = 1.01 (P = 0.31) 0.2 0.5 ż 5 Favours Dose 1 Favours Dose 2 OCD adults: SSRIs Review: Comparison: 08 SSRIs at different doses (continuation phase) 04 Y-BOCS Outcome: SMD (fixed) SMD (fixed) Dose 2 or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CL 01 Fluoxetine 40mg v Fluoxetine 20mg Beasley 1992 9.40(6.00) 23 9.80(7.30) -0.06 [-0.65, 0.53] Subtotal (95% CI) 21 23 -0.06 [-0.65, 0.53] Test for heterogeneity: not applicable Test for overall effect: Z = 0.19 (P = 0.85) 02 Fluoxetine 60mg v Fluoxetine 20mg Beasley 1992 26 7.00(5.40) 23 9.80(7.30) -0.43 [-1.00, 0.13] Subtotal (95% CI) -0.43 [-1.00, 0.13] 26 23 Test for heterogeneity: not applicable Test for overall effect: Z = 1.49 (P = 0.14) 03 Fluoxetine 60mg v Fluoxetine 40mg Beasley 1992 26 7.00(5.40) 21 9.40(6.00) -0.42 [-1.00, 0.17] Subtotal (95% CI) -0.42 [-1.00, 0.17] Test for heterogeneity: not applicable Test for overall effect: Z = 1.40 (P = 0.16) Ó Favours Dose 1 Favours Dose 2 Review: OCD adults: SSRIs Comparison: 09 SSRIs v Clomipramine (continuation phase) Outcome: 01 Leaving study early Study SSRI Clomipramine RR (fixed) RR (fixed) or sub-category n/N 95% CI 95% CI n/N 01 Fluoxetine 60mg vs Clomipramine 200mg (non-responders) Lopez-Ibor 1996 3/8 1.14 [0.39, 3.36] 6/14 Subtotal (95% CI) 1.14 [0.39, 3.36] Total events: 6 (SSRI), 3 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 0.24 (P = 0.81) 02 Fluoxetine 20mg vs Clomipramine 100mg (responders) Lopez-Ibor 1996 0.59 [0.19, 1.83] 3/11 6/13 Subtotal (95% CI) 0.59 [0.19, 1.83] 11 13 Total events: 3 (SSRI), 6 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 0.91 (P = 0.36) 0.1 0.2 0.5 ż 5 10 Favours SSRI Favours Clomipramine



Review: OCD adults: SSRIs 10 Sertraline standard dose vs high dose (non-responders) Comparison: Outcome: 03 Non-responders Standard dose 200mg High dose 250-400mg RR (fixed) RR (fixed) 95% CI or sub-category nΝ 95% CI Koran 2002a 18/30 1.11 [0.77, 1.61] 24/36 Total (95% CI) 36 30 1.11 [0.77, 1.61] Total events: 24 (Standard dose 200mg), 18 (High dose 250-400mg) Test for heterogeneity: not applicable Test for overall effect: Z = 0.55 (P = 0.58) 0.1 0.2 0.5 10 Favours standard Favours high Review: OCD adults: SSRIs 11 SSRI vs Placebo (maintenance) Comparison: 01 Leaving the study early Outcome: Study SSRI RR (fixed) RR (fixed) Placebo or sub-category n/N n/N 95% CI 95% CI 01 Paroxetine Ansseau 1995 19/51 7/12 0.64 [0.35, 1.16] Subtotal (95% CI) 51 12 0.64 [0.35, 1.16] Total events: 19 (SSRI), 7 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.47 (P = 0.14) 0.2 0.5 5 10 Favours SSRI Favours Placebo Review: OCD adults: SSRIs Comparison: 11 SSRI vs Placebo (maintenance) Outcome: 02 Leaving the study early due to adverse events SSRI Study Placebo RR (fixed) RR (fixed) n/N 95% CI 95% CI or sub-category nΝ 01 Paroxetine Ansseau 1995 8/51 2/12 0.94 [0.23, 3.88] Subtotal (95% CI) 0.94 [0.23, 3.88] Total events: 8 (SSRI), 2 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.08 (P = 0.93) ż 5 10 0.1 0.2 0.5 Favours SSRI Favours Placebo OCD adults: SSRIs Review: 11 SSRI vs Placebo (maintenance) Comparison: Outcome: 03 Adverse events Study SSRI Placebo RR (fixed) RR (fixed) or sub-category n/N n/N 95% CI 95% CI 01 Paroxetine Ansseau 1995 42/51 8/12 1.24 [0.81, 1.88] 1.24 [0.81, 1.88] Subtotal (95% CI) 51 12 Total events: 42 (SSRI), 8 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.99 (P = 0.32) 0.2 0.5 Favours SSRI Favours Placebo Review: OCD adults: SSRIs Comparison: 11 SSRI vs Placebo (maintenance) 04 Severe adverse events Outcome: SSRI RR (fixed) RR (fixed) Study Placebo or sub-category 95% CI 95% CI n/N n/N 01 Paroxetine Ansseau 1995 18/51 3/12 1.41 [0.49, 4.03] Subtotal (95% CI) 12 1.41 [0.49, 4.03] 51 Total events: 18 (SSRI), 3 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.64 (P = 0.52) 0.1 0.2 0.5 2 5 10

Favours SSRI Favours Placebo

Total events: 8 (SSRI), 6 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 1.38 (P = 0.17)

Review: OCD adults: SSRIs 11 SSRI vs Placebo (maintenance) Comparison: Outcome: 05 Non-responders (Y-BOCS 25% reduction) SSRI Placebo RR (fixed) RR (fixed) Study or sub-category n/Ν 95% CI 95% CI 01 Paroxetine Ansseau 1995 8/51 3/12 0.63 [0.20, 2.02] Subtotal (95% CI) 51 12 0.63 [0.20, 2.02] Total events: 8 (SSRI), 3 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.78 (P = 0.43) 0.1 0.2 0.5 5 Favours SSRI Favours Placebo OCD adults: SSRIs Review 11 SSRI vs Placebo (maintenance) Comparison: 06 Y-BOCS Outcome: Study SSRI Placebo SMD (fixed) SMD (fixed) Mean (SD) Ν Mean (SD) or sub-category Ν 95% CI 95% CI 01 Paroxetine Ansseau 1995 51 -14.70(7.20) 12 -11.00(6.90) -0.51 [-1.15, 0.12] Subtotal (95% CI) 51 12 -0.51 [-1.15, 0.12] Test for heterogeneity; not applicable Test for overall effect: Z = 1.58 (P = 0.11) -10 -5 Π 10 Favours SSRI Favours Placebo OCD adults: SSRIs Review: Comparison: 11 SSRI vs Placebo (maintenance) Outcome 07 NIMH-OCS Study SSRI Placebo SMD (fixed) SMD (fixed) or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Paroxetine Ansseau 1995 -5.20(2.60) 12 -3.60(2.60) -0.61 [-1.25, 0.03] 51 Subtotal (95% CI) 12 -0.61 [-1.25, 0.03] Test for heterogeneity: not applicable Test for overall effect: Z = 1.87 (P = 0.06) -10 Ó 10 Favours SSRI Favours Placebo OCD adults: SSRIs Review: Comparison: 12 SSRI vs Clomipramine (maintenance) Outcome: 01 Leaving the study early RR (fixed) Study SSRI Clomipramine RR (fixed) 95% CI 95% CI or sub-category n/N n/N 01 Paroxetine Ansseau 1995 19/51 8/20 0.93 [0.49, 1.77] Subtotal (95% CI) 0.93 [0.49, 1.77] 20 Total events: 19 (SSRI), 8 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 0.22 (P = 0.83) 0.1 0.2 0.5 2 5 10 Favours SSRI Favours Clomipramine Review: OCD adults: SSRIs 12 SSRI vs Clomipramine (maintenance) Comparison: 02 Leaving the study early due to adverse events Outcome: Study SSRI Clomipramine RR (fixed) RR (fixed) n/N 95% CI 95% CI or sub-category n/N 01 Paroxetine Ansseau 1995 0.52 [0.21, 1.32] 8/51 6/20 Subtotal (95% CI) 51 20 0.52 [0.21, 1.32]

0.1 0.2

0.2 0.5 Favours SSRI

Favours Clomipramine

01 Paroxetine

Ansseau 1995

Subtotal (95% CI)

Test for heterogeneity: not applicable

51

-5.20(2.60)

19

Review: OCD adults: SSRIs 12 SSRI vs Clomipramine (maintenance) Comparison: Outcome: 03 Adverse events SSRI Clomipramine RR (fixed) RR (fixed) Study or sub-category n/Ν n/N 95% CI 95% CI 01 Paroxetine Ansseau 1995 42/51 15/20 1.10 [0.83, 1.46] Subtotal (95% CI) 51 20 1.10 [0.83, 1.46] Total events: 42 (SSRI), 15 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 0.65 (P = 0.52) 0.1 0.2 0.5 2 5 10 Favours SSRI Favours Clomipramine Review: OCD adults: SSRIs 12 SSRI vs Clomipramine (maintenance) Comparison: 04 Severe adverse events Outcome: Study SSRI RR (fixed) RR (fixed) Clomipramine or sub-category n/N n/N 95% CI 95% CI 01 Paroxetine 3.53 [0.90, 13.84] Ansseau 1995 2/20 18/51 Subtotal (95% CI) 51 20 3.53 [0.90, 13.84] Total events: 18 (SSRI), 2 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 1.81 (P = 0.07) 0.01 0.1 100 Favours SSRI Favours Clomipramine OCD adults: SSRIs Review: Comparison: 12 SSRI vs Clomipramine (maintenance) Outcome: 05 Responders (Y-BOCS 25% reduction) Study SSRI Clomipramine RR (fixed) RR (fixed) n/N 95% CI 95% CI or sub-category n/N 01 Paroxetine Ansseau 1995 8/51 3/20 1.05 [0.31, 3.55] Subtotal (95% CI) 1.05 [0.31, 3.55] 51 20 Total events: 8 (SSRI), 3 (Clomipramine) Test for heterogeneity: not applicable Test for overall effect: Z = 0.07 (P = 0.94) 10 0.1 0.2 0.5 2 5 Favours SSRI Favours Clomipramine Review: OCD adults: SSRIs Comparison: 12 SSRI vs Clomipramine (maintenance) 06 Y-BOCS Outcome SSRI Clomipramine SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Paroxetine Ansseau 1995 51 -14.70(7.20) 20 -14.60(7.10) -0.01 [-0.53, 0.50] Subtotal (95% CI) 51 20 -0.01 [-0.53, 0.50] Test for heterogeneity: not applicable Test for overall effect: Z = 0.05 (P = 0.96) -10 -5 Ò Favours SSRI Favours Clomipramine Review: OCD adults: SSRIs Comparison: 12 SSRI vs Clomipramine (maintenance) Outcome 07 NIMH-OCS Study SSRI SMD (fixed) SMD (fixed) Clomipramine Mean (SD) Ν Mean (SD) 95% CI or sub-category

t for overall effect: Z = 1.46 (P = 0.14)				<u> </u>		
	-10		5 () ;) 1	10
		Favo	urs SSRI	Favours	Clomipram	nine

-0.40 [-0.93, 0.14]

-0.40 [-0.93, 0.14]

-4.20(2.20)

Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

Outcome: 01 Leaving the study early

Study or sub-category	Paroxetine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Paroxetine at 2 months				
Ansseau 1995	0/14	3/18 -		0.18 [0.01, 3.24]
Subtotal (95% CI)	14	18 -		0.18 [0.01, 3.24]
Total events: 0 (Paroxetine), 3	(Placebo)		_	
Test for heterogeneity: not app	licable			
Test for overall effect: $Z = 1.16$	6 (P = 0.25)			
02 Paroxetine at 6 months				
Bailer 1995	9/20	16/24	-	0.68 [0.39, 1.18]
Subtotal (95% CI)	20	24	-	0.68 [0.39, 1.18]
Total events: 9 (Paroxetine), 16	(Placebo)		- 1	
Test for heterogeneity: not app	licable			
Test for overall effect: $Z = 1.37$	(P = 0.17)			
Total (95% CI)	34	42	•	0.59 [0.33, 1.04]
Total events: 9 (Paroxetine), 19	(Placebo)		-	
Test for heterogeneity: $Chi^2 = 0$		6		
Test for overall effect: $Z = 1.83$				
		0.0	1 0.1 1 10	100
		F	avours Paroxetine Favours Plac	ebo

Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)
Outcome: 02 Leaving the study early due to adverse events

Study or sub-category	Paroxetine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Paroxetine at 6 months				
Bailer 1995	0/20	9/24		0.06 [0.00, 1.01]
Subtotal (95% CI)	20	24		0.06 [0.00, 1.01]
Total events: 0 (Paroxetine),	9 (Placebo)			·
Test for heterogeneity: not ap	pplicable			
Test for overall effect: $Z = 1$.	95 (P = 0.05)			
			0.001 0.01 0.1 1 10	100 1000

Favours Paroxetine Favours Placebo

Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

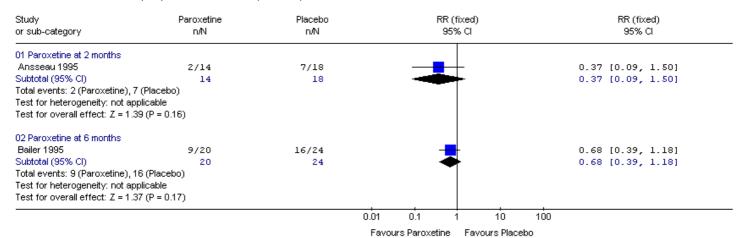
Outcome: 03 Full relapse (Y-BOCS and CGI Severity increase)

Study or sub-category	Paroxetine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% CI
01 Paroxetine at 6 months				
Bailer 1995	1/20	6/24		0.20 [0.03, 1.53]
Subtotal (95% CI)	20	24		0.20 [0.03, 1.53]
Total events: 1 (Paroxetine),	6 (Placebo)		 -	
Test for heterogeneity: not a	pplicable			
Test for overall effect: Z = 1	.55 (P = 0.12)			
		0.0	1 0.1 1 10	100
		0.0	1 0.1 1 10	100
		F	avours Paroxetine Favours Place	bo

Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

Outcome: 04 Partial relapse (Y-BOCS or CGI Severity increase)



Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

Outcome: 05 Adverse events

Study or sub-category	Paroxetine n/N	Placebo n/N		RR (fixed) 95% Cl		RR (fixed) 95% Cl
01 Paroxetine at 2 months						
Ansseau 1995	8/14	9/18				1.14 [0.60, 2.18]
Subtotal (95% CI)	14	18		-		1.14 [0.60, 2.18]
Total events: 8 (Paroxetine),	9 (Placebo)			_		
Test for heterogeneity: not a	pplicable					
Test for overall effect: Z = 0	.40 (P = 0.69)					
			0.1 0.2	0.5 1 2	5 10	

Favours Paroxetine Favours Placebo

Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

Outcome: 06 Severe adverse events

Study or sub-category	Paroxetine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Paroxetine at 2 months				
Ansseau 1995	1/14	4/18		0.32 [0.04, 2.57]
Subtotal (95% CI)	14	18		0.32 [0.04, 2.57]
Total events: 1 (Paroxetine),	4 (Placebo)			•
Test for heterogeneity: not a	pplicable			
Test for overall effect: Z = 1.	• •			
			0.01 0.1 1 10	100
			Favours Paroxetine Favours Placeb	0

Review: OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

Outcome: 07 Y-BOCS

Study or sub-category	N	Paroxetine Mean (SD)	N	Placebo Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% CI
01 Paroxetine at 2 months						
Ansseau 1995	12	0.80(1.60)	12	0.90(3.20)	<u> </u>	-0.04 [-0.84, 0.76]
Subtotal (95% CI)	12		12		•	-0.04 [-0.84, 0.76]
Test for heterogeneity: not a	applicable				Ī	·
Test for overall effect: $Z = 0$	0.09 (P = 0.93)					
02 Paroxetine at 6 months						
Bailer 1995	12	-3.50(3.60)	8	0.88(3.59)	-	-1.17 [-2.15, -0.19]
Subtotal (95% CI)	12		8		•	-1.17 [-2.15, -0.19]
Test for heterogeneity: not a	applicable				-	
Test for overall effect: $Z = 2$	2.33 (P = 0.02)					
Total (95% CI)	24		20		•	-0.49 [-1.11, 0.13]
Test for heterogeneity: Chi ²	= 3.05, df = 1 (P	= 0.08), I ² = 67.2%			1	
Test for overall effect: $Z = 1$	1.54 (P = 0.12)					
				-1	0 -5 0 5	10

Favours Paroxetine Favours Placebo

OCD adults: SSRIs

Comparison: 13 SSRI vs Placebo (relapse prevention)

Outcome: 08 NIMH-OC

Review:

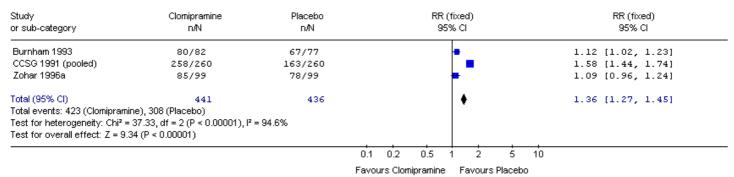
Study or sub-category	N	Paroxetine Mean (SD)	N	Placebo Mean (SD)			MD (fixed) 95% CI)		SMD (fixed) 95% Cl
01 Paroxetine at 2 months										
Ansseau 1995	11	0.20(0.90)	9	1.30(2.30)			-			-0.63 [-1.54, 0.28]
Subtotal (95% CI)	11		9				•			-0.63 [-1.54, 0.28]
Test for heterogeneity: not app	licable						7			
Test for overall effect: Z = 1.36	S (P = 0.17)									
02 Paroxetine at 6 months										
Bailer 1995	12	-0.67(1.66)	8	0.38(1.67)			-			-0.60 [-1.52, 0.31]
Subtotal (95% CI)	12		8				•			-0.60 [-1.52, 0.31]
Test for heterogeneity: not app	licable									
Test for overall effect: Z = 1.29	9 (P = 0.20)									
Total (95% CI)	23		17				•			-0.62 [-1.26, 0.03]
Test for heterogeneity: Chi ² = 0	1.00, df = 1 (F)	P = 0.97), I ² = 0%								
Test for overall effect: Z = 1.87	(P = 0.06)									
					-10	-5	-	5	10	
					Favours	Paroxetii	ne Fav	ours Place	ebo	

Clomipramine (OCD, adults)

Review: OCD adults: Clomipramine

Comparison: 01 Clomipramine vs placebo: acute phase

Outcome: 01 Adverse events



Review: OCD adults: Clomipramine

01 Clomipramine vs placebo: acute phase Comparison:

Outcome: 02 Leaving study early

Study or sub-category	Clomipramine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Burnham 1993	28/82	20/77	-	1.31 [0.81, 2.13]
CCSG 1991(1)	17/118	13/121	- •	1.34 [0.68, 2.64]
CCSG 1991(2)	14/142	12/139	- 	1.14 [0.55, 2.38]
Stein 1992	7/21	2/23	-	→ 3.83 [0.89, 16.44]
Zohar 1996a	34/99	39/99	-	0.87 [0.60, 1.26]
Total (95% CI)	462	459	•	1.15 [0.90, 1.47]
Total events: 100 (Clomipra	mine), 86 (Placebo)		'	
Test for heterogeneity: Chir	$^{2} = 5.32$, df = 4 (P = 0.26), $I^{2} = 24.9$	9%		
Test for overall effect: Z =	1.11 (P = 0.27)			
		0.1	0.2 0.5 1 2 5	10
		Favo	ours Clomipramine Favours Placebo	

OCD adults: Clomipramine Review:

Comparison: 01 Clomipramine vs placebo; acute phase Outcome: 03 Leaving study early due to adverse events

Study or sub-category	Clomipramine n/N	Placebo n <i>l</i> N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Burnham 1993	17/82	8/77		2.00 [0.91, 4.36]
Zohar 1996a	17/99	6/99		- 2.83 [1.17, 6.89]
Total (95% CI)	181	176	-	2.35 [1.31, 4.22]
Total events: 34 (Clomipram	nine), 14 (Placebo)			
Test for heterogeneity: Chi²	$= 0.34$, df = 1 (P = 0.56), $I^2 = 0\%$			
Test for overall effect: Z = 3	2.86 (P = 0.004)			
		0.1	0.2 0.5 1 2 5	10

Favours Clomipramine Favours Placebo

OCD adults: Clomipramine Review:

01 Clomipramine vs placebo: acute phase Comparison:

Outcome: 04 Non-responders (Y-BOCS)

Study or sub-category	Clomipramine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Burnham 1993	42/82	45/77		0.88 [0.66, 1.16]
Zohar 1996a	47/99	64/99	-	0.73 [0.57, 0.95]
Total (95% CI)	181	176	•	0.79 [0.66, 0.96]
Total events: 89 (Clomipram	ine), 109 (Placebo)		-	
Test for heterogeneity: Chi²	$= 0.83$, df = 1 (P = 0.36), $I^2 = 0\%$			
Test for overall effect: Z = 2	2.40 (P = 0.02)			
			0.1 0.2 0.5 1 2 5	10

Favours Clomipramine Favours Placebo

OCD adults: Clomipramine Comparison:

01 Clomipramine vs placebo: acute phase

Outcome: 05 Non-responders (CGI)

Study or sub-category	Clomipramine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Stein 1992	14/21	17/23	+	0.90 [0.61, 1.33]
Total (95% CI) Total events: 14 (Clomipran Test for heterogeneity: not Test for overall effect: Z =	applicable	23	+	0.90 [0.61, 1.33]
		0.1	0.2 0.5 1 2	5 10
		Favo	urs Clomipramine - Favours Pla	acebo

Review: OCD adults: Clomipramine

Comparison: 01 Clomipramine vs placebo: acute phase

Outcome: 06 Non-responders (all)

Study or sub-category	Clomipramine n/N	Placebo n/N			,	(fixed) % Cl			RR (fixed) 95% Cl
Burnham 1993	42/82	45/77			-	-			0.88 [0.66, 1.16]
Stein 1992	14/21	17/23			-	<u> </u>			0.90 [0.61, 1.33]
Zohar 1996a	47/99	64/99			-	-			0.73 [0.57, 0.95]
Total (95% CI)	202	199			•				0.81 [0.68, 0.96]
Total events: 103 (Clomipra	mine), 126 (Placebo)				•				•
Test for heterogeneity: Chi ²	= 1.17, df = 2 (P = 0.56), l ² = 0%								
Test for overall effect: Z = :									
			0.1	0.2	0.5	1 2	5	10	

Favours Clomipramine Favours placebo

Review: OCD adults: Clomipramine

Comparison: 01 Clomipramine vs placebo: acute phase

Outcome: 07 Non-remitters

Study or sub-category	Clomipramine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
CCSG 1991 (pooled)	136/260	252/260	-	0.54 [0.48, 0.61]
Total (95% CI) Total events: 136 (Clomipramir Test for heterogeneity: not ap Test for overall effect: Z = 10	plicable	260	•	0.54 [0.48, 0.61]
			0.1 0.2 0.5 1 2 5	5 10

Favours Clomipramine Favours placebo

Review: OCD adults: Clomipramine

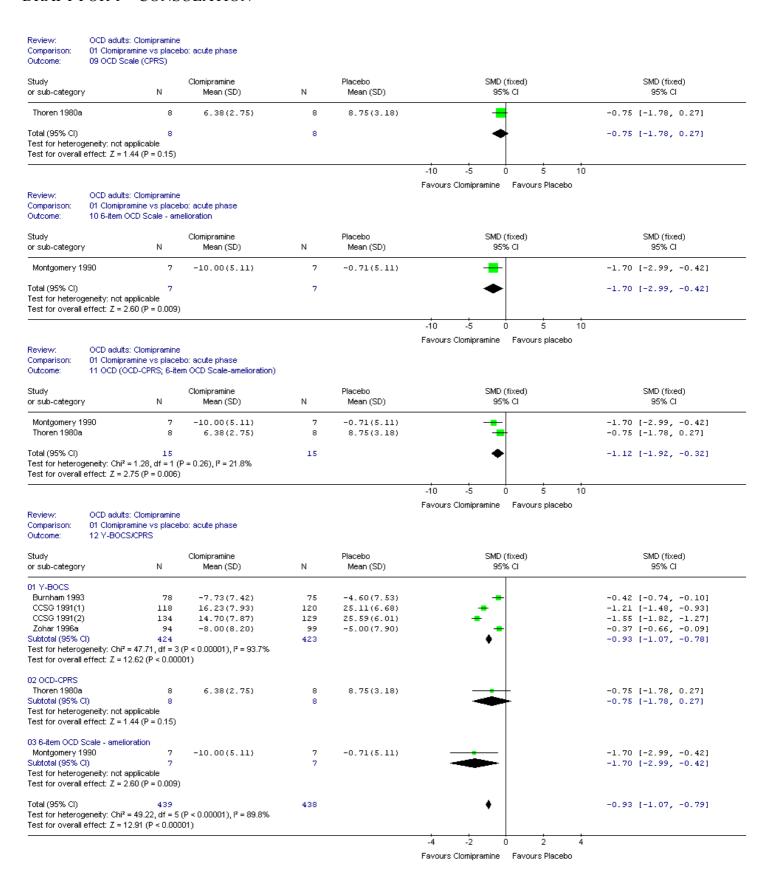
Comparison: 01 Clomipramine vs placebo: acute phase

Outcome: 08 Y-BOCS

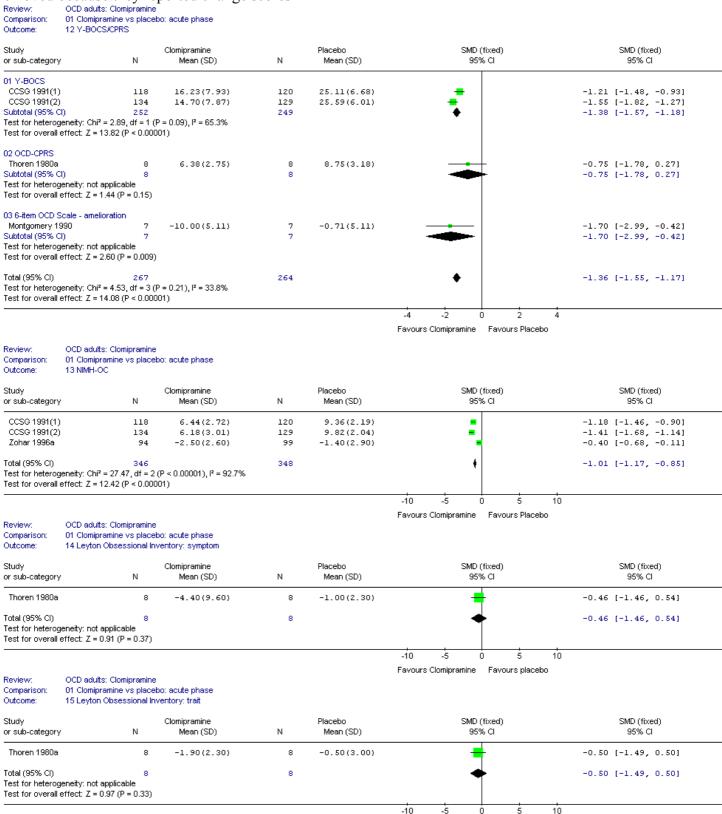
Study or sub-category	N	Clomipramine Mean (SD)	N	Placebo Mean (SD)		SMD (fixed) 95% Cl			SMD (fixed) 95% CI	
Burnham 1993	78	-7.73(7.42)	75	-4.60(7.53)		_	-			-0.42 [-0.74, -0.10]
CCSG 1991(1)	118	16.23(7.93)	120	25.11(6.68)		-				-1.21 [-1.48, -0.93]
CCSG 1991(2)	134	14.70(7.87)	129	25.59(6.01)		-				-1.55 [-1.82, -1.27]
Zohar 1996a	94	-8.00(8.20)	99	-5.00(7.90)			-			-0.37 [-0.66, -0.09]
Total (95% CI)	424		423			•				-0.93 [-1.07, -0.78]
Test for heterogeneity: Ch	ni ² = 47.71, df = 3 ($P < 0.00001$), $I^2 = 93.7\%$				•				,
Test for overall effect: Z =	= 12.62 (P < 0.0000	01)								
					-4	-2	0	2	4	

Favours Clomipramine Favours Placebo

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Removing heterogeneity from Clomipramine v Placebo (Y-BOCS/CPRS): Burnham1993 and Zohar1996a removed because they reported change scores

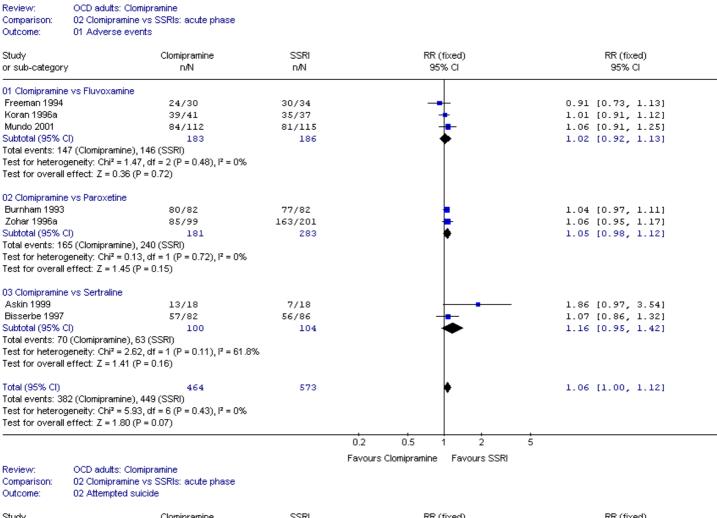


Favours Clomipramine

Favours placebo

Review: OCD adults: Clomipramine Comparison: 01 Clomipramine vs placebo: acute phase Outcome 16 Leyton Obsessional Inventory: resistance SMD (fixed) Study Placebo SMD (fixed) Clomipramine or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI Thoren 1980a 8 -13.00(19.60) 8 -4.30(18.60) -0.43 [-1.43, 0.56] Total (95% CI) -0.43 [-1.43, 0.56] Test for heterogeneity: not applicable Test for overall effect: Z = 0.85 (P = 0.40) -10 -5 ò 10 Favours Clomipramine Favours placebo OCD adults: Clomipramine Review: Comparison 01 Clomipramine vs placebo: acute phase 17 Leyton Obsessional Inventory: interference Outcome SMD (fixed) SMD (fixed) Study Clomipramine Placebo or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI Thoren 1980a -12.30(24.00) -8.40(15.90) -0.18 [-1.16, 0.80] Total (95% CI) -0.18 [-1.16, 0.80] Test for heterogeneity: not applicable Test for overall effect: Z = 0.36 (P = 0.72) -10 -5 10 0 Favours Clomipramine Favours placebo Review: OCD adults: Clomipramine Comparison: 01 Clomipramine vs placebo; acute phase Outcome 18 Self-Rating Obsessive-Compulsive Personality Inventory Study Clomipramine Placebo SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI Stein 1992 21 45.17(7.36) 23 49.31(7.36) -0.55 [-1.16, 0.05] Total (95% CI) 21 23 -0.55 [-1.16, 0.05] Test for heterogeneity; not applicable Test for overall effect: Z = 1.79 (P = 0.07) -10 -5 ń 10 Favours Clomipramine Favours Placebo OCD adults: Clomipramine Review: 01 Clomipramine vs placebo: acute phase Comparison: Outcome 19 Montgomery-Asberg Depression Rating Scale SMD (fixed) SMD (fixed) Study Clomipramine Placebo or sub-category Ν Ν Mean (SD) 95% CI Zohar 1996a 94 -2.40(7.30) 99 -0.60(7.90) -0.24 [-0.52, 0.05] Total (95% CI) -0.24 [-0.52, 0.05] Test for heterogeneity: not applicable Test for overall effect: Z = 1.63 (P = 0.10) 10 Favours Clomipramine Favours Placebo OCD adults: Clomipramine Review: 01 Clomipramine vs placebo: acute phase Comparison: 20 Clinical Global Impressions: severity of illness Outcome SMD (fixed) SMD (fixed) Study Clomipramine Placebo Ν Mean (SD) 95% CI or sub-category Ν Mean (SD) 95% CI Zohar 1996a -1.10(1.20) 99 -0.70(1.30) -0.32 [-0.60, -0.03] Total (95% CI) 99 -0.32 [-0.60, -0.03] Test for heterogeneity: not applicable Test for overall effect: Z = 2.20 (P = 0.03) -10 10 -5 0 Favours Clomipramine Favours Placebo Review: OCD adults: Clomipramine Comparison: 01 Clomipramine vs placebo: acute phase 21 Symptom Checklist-90 Outcome SMD (fixed) SMD (fixed) Study Placebo or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI Zohar 1996a -31.90(39.90) 77 -19.50(37.30) -0.32 [-0.64, 0.00] Total (95% CI) 77 -0.32 [-0.64, 0.00] Test for heterogeneity: not applicable Test for overall effect: Z = 1.95 (P = 0.05) -10 -5 Ó 5 10

Favours Clomipramine Favours Placebo

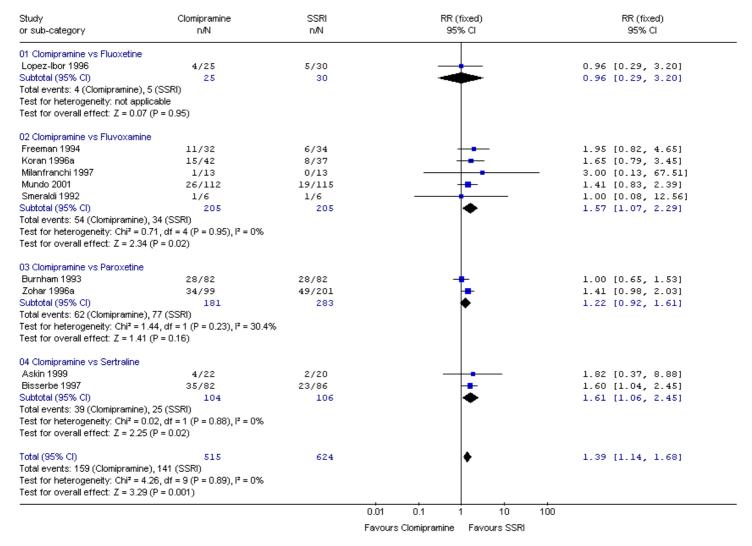


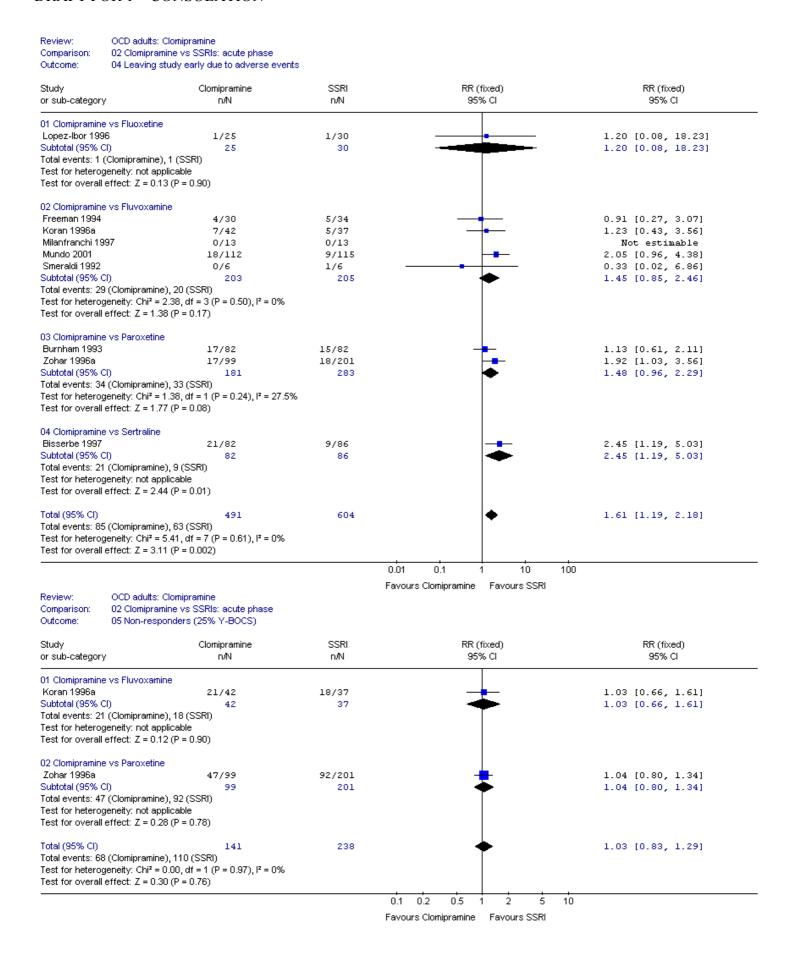
Study SSRI RR (fixed) RR (fixed) Clomipramine 95% CI or sub-category n/Ν 95% CI n/N 01 Clomipramine vs Sertraline Bisserbe 1997 3/82 1/86 3.15 [0.33, 29.64] Subtotal (95% CI) 86 3.15 [0.33, 29.64] Total events: 3 (Clomipramine), 1 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 1.00 (P = 0.32)0.01 0.1 100 10 Favours Clomipramine Favours SSRI

Review: OCD adults: Clomipramine

Comparison: 02 Clomipramine vs SSRIs: acute phase

Outcome: 03 Leaving study early

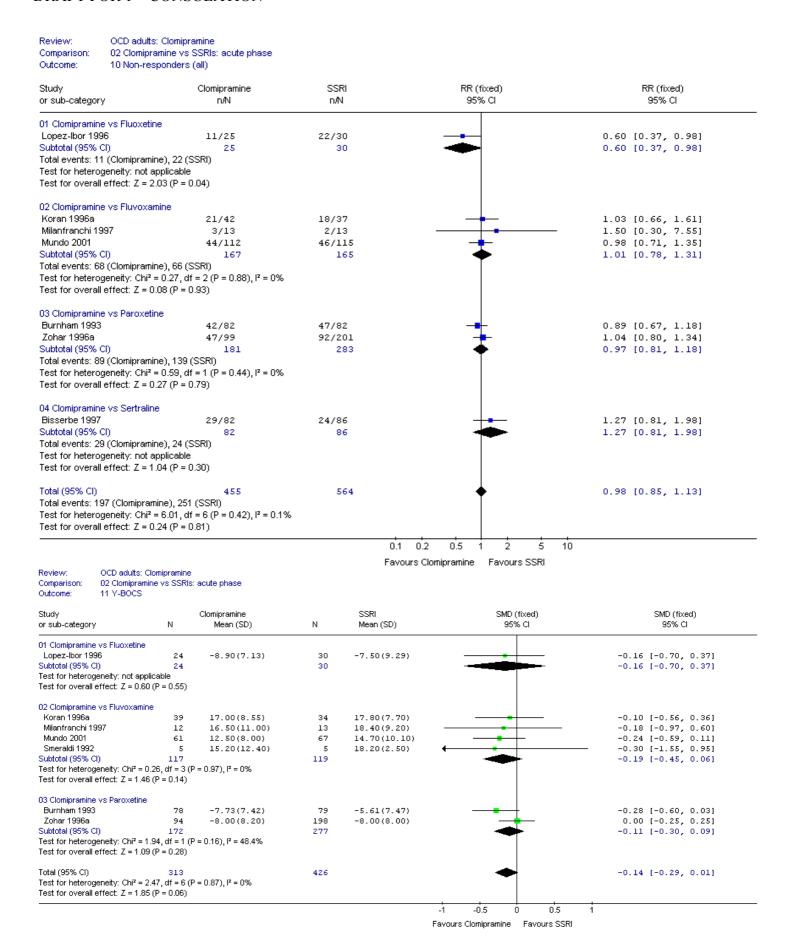




Review: OCD adults: Clomipramine 02 Clomipramine vs SSRIs; acute phase Comparison: Outcome: 06 Non-responders (35% Y-BOCS) SSRI RR (fixed) RR (fixed) Study Clomipramine or sub-category nΝ n/N 95% CI 95% CI 01 Clomipramine vs Fluvoxamine Mundo 2001 44/112 46/115 0.98 [0.71, 1.35] Subtotal (95% CI) 112 115 0.98 [0.71, 1.35] Total events: 44 (Clomipramine), 46 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.11 (P = 0.91) 0.1 0.2 0.5 2 5 10 Favours Clomipramine Favours SSRI Review: OCD adults: Clomipramine Comparison: 02 Clomipramine vs SSRIs: acute phase Outcome: 07 Non-responders (CGI; 25% Y-BOCS) Study Clomipramine SSRI RR (fixed) RR (fixed) or sub-category n/Ν n/N 95% CI 95% CI 01 Clomipramine vs Fluoxetine Lopez-Ibor 1996 11/25 22/30 0.60 [0.37, 0.98] Subtotal (95% CI) 25 30 0.60 [0.37, 0.98] Total events: 11 (Clomipramine), 22 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 2.03 (P = 0.04) 02 Clomipramine vs Paroxetine 0.89 [0.67, 1.18] Burnham 1993 42/82 47/82 Subtotal (95% CD 0.89 [0.67, 1.18] 82 Total events: 42 (Clomipramine), 47 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.78 (P = 0.43) Total (95% CI) 0.81 [0.63, 1.03] 112 107 Total events: 53 (Clomipramine), 69 (SSRI) Test for heterogeneity: $Chi^2 = 1.90$, df = 1 (P = 0.17), $I^2 = 47.3\%$ Test for overall effect: Z = 1.73 (P = 0.08) 0.2 0.5 5 10 Favours Clomipramine Favours SSRI OCD adults: Clomipramine Review: 02 Clomipramine vs SSRIs; acute phase Comparison: Outcome: 09 Non-responders (CGI-I) SSRI RR (fixed) RR (fixed) Study Clomipramine or sub-category n/N n/N 95% CI 95% CI 01 Clomipramine vs Fluvoxamine Milanfranchi 1997 3/13 2/13 1.50 [0.30, 7.55] Subtotal (95% CI) 1.50 [0.30, 7.55] 13 Total events: 3 (Clomipramine), 2 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.49 (P = 0.62) 02 Clomipramine vs Sertraline Bisserbe 1997 29/82 24/86 1.27 [0.81, 1.98] Subtotal (95% CI) 86 1.27 [0.81, 1.98] Total events: 29 (Clomipramine), 24 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 1.04 (P = 0.30) Total (95% CI) 99 1.29 [0.83, 1.98] Total events: 32 (Clomipramine), 26 (SSRI) Test for heterogeneity: $Chi^2 = 0.04$, df = 1 (P = 0.84), $I^2 = 0\%$ Test for overall effect: Z = 1.14 (P = 0.25) 0.2 10 0.5 5 Favours Clomipramine

Favours SSRI

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Review: OCD adults: Clomipramine

02 Clomipramine vs SSRIs: acute phase 12 NIMH-OC Comparison:

Outcome:

tudy r sub-category	N	Clomipramine Mean (SD)	N	SSRI Mean (SD)	SMD (fixed) 95% CI	SMD (fixed) 95% CI	
1 Clomipramine vs Fluvoxamin	ie						
Mundo 2001	105	5.90(2.80)	112	5.90(3.10)		0.00 [-0.27, 0.27]	
ubtotal (95% CI)	105		112			0.00 [-0.27, 0.27]	
est for heterogeneity: not app	licable				T		
est for overall effect: $Z = 0.00$	(P = 1.00)						
2 Clomipramine vs Paroxetine							
Burnham 1993	78	-2.06(2.03)	79	-1.42(2.04)		-0.31 [-0.63, 0.00]	
Zohar 1996a	94	-2.50(2.60)	198	-2.50(2.90)		0.00 [-0.25, 0.25]	
ubtotal (95% CI)	172		277		•	-0.12 [-0.31, 0.08]	
est for heterogeneity: Chi² = 2	.36, df = 1 (P	' = 0.12), I ² = 57.6%			-		
est for overall effect: $Z = 1.20$) (P = 0.23)						
otal (95% CI)	277		389		•	-0.08 [-0.23, 0.08]	
est for heterogeneity: Chi² = 2 est for overall effect: Z = 0.97		= 0.24), I ² = 30.0%					

Review:

OCD adults: Clomipramine 02 Clomipramine vs SSRIs: acute phase Comparison:

Outcome: 13 Comprehensive Psychopathological Rating Scale: obsessive-compulsive

Study or sub-category	N	Clomipramine Mean (SD)	N	SSRI Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Clomipramine vs Fluoxe	tine					
Lopez-lbor 1996	24	-10.90(7.33)	30	-8.10(7.64)		-0.37 [-0.91, 0.17]
Subtotal (95% CI)	24		30			-0.37 [-0.91, 0.17]
Test for heterogeneity: not	t applicable				_	
Test for overall effect: Z =	1.33 (P = 0.18)					
					1 05 0 05	1

Review: OCD adults: Clomipramine

02 Clomipramine vs SSRIs; acute phase 14 Hamilton Rating Scale for Depression Comparison: Outcome:

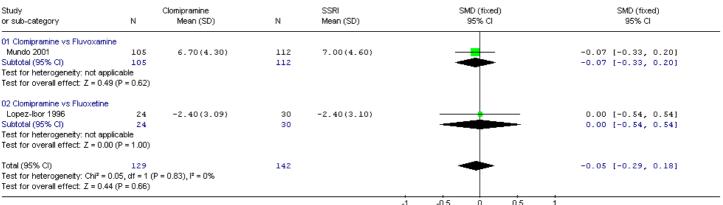
Study or sub-category	N	Clomipramine Mean (SD)	N	SSRI Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% CI
01 Clomipramine vs Fluoxeti	ine					
Lopez-lbor 1996	24	-9.40(7.71)	30	-7.50(5.93)		-0.28 [-0.82, 0.26]
Subtotal (95% CI)	24		30			-0.28 [-0.82, 0.26]
Test for heterogeneity: not :	applicable				_ _ _	
Test for overall effect: Z = 1	1.00 (P = 0.32)					
02 Clomipramine vs Fluvoxa	amine					
Koran 1996a	39	5.80(4.70)	34	6.10(3.30)		-0.07 [-0.53, 0.39]
Mundo 2001	105	7.00(4.50)	112	7.70(6.00)		-0.13 [-0.40, 0.14]
Subtotal (95% CI)	144		146			-0.12 [-0.35, 0.11]
Test for heterogeneity: Chi ²	= 0.05, df $= 1$ (l	P = 0.83), I ² = 0%			-	
Test for overall effect: $Z = 0$	0.99 (P = 0.32)					
Total (95% CI)	168		176			-0.14 [-0.35, 0.07]
Test for heterogeneity: Chi²	= 0.33, df $= 2$ (l	P = 0.85), I ² = 0%			-	•
Test for overall effect: Z = 1	1.30 (P = 0.19)					
				-	1 -0.5 0 0.5	1

Favours Clomipramine Favours SSRI

Favours Clomipramine Favours SSRI

Review: OCD adults: Clomipramine Comparison: 02 Clomipramine vs SSRIs: acute phase Outcome 15 Montgomery-Asberg Depression Rating Scale SMD (fixed) SMD (fixed) Study SSRI or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI 01 Clomipramine vs Fluoxetine Lopez-lbor 1996 24 -13.80(9.09) 30 -10.10(8.20) -0.42 [-0.97, 0.12] Subtotal (95% CI) 24 30 -0.42 [-0.97, 0.12] Test for heterogeneity: not applicable Test for overall effect: Z = 1.53 (P = 0.13) Smeraldi 1992 5 9.60(10.30) 5 11.80(6.80) -0.23 [-1.47, 1.02] Subtotal (95% CI) 5 -0.23 [-1.47, 1.02] Test for heterogeneity: not applicable Test for overall effect: Z = 0.36 (P = 0.72) 03 Clomipramine vs Paroxetine Zohar 1996a 94 -2.40(7.30) 198 -3.40(7.90)0.13 [-0.12, 0.38] Subtotal (95% CI) 0.13 [-0.12, 0.38] Test for heterogeneity: not applicable Test for overall effect: Z = 1.03 (P = 0.30) 233 0.03 [-0.19, 0.25] Test for heterogeneity: Chi² = 3.47, df = 2 (P = 0.18), l² = 42.4% Test for overall effect: Z = 0.24 (P = 0.81) Favours Clomipramine Favours SSRI OCD adults: Clomipramine Review: Comparison: 02 Clomipramine vs SSRIs: acute phase 16 Depression (HRSD; MADRS) Outcome SMD (fixed) SMD (fixed) Study Clomipramine SSRI Mean (SD) 95% CI 95% CI or sub-category Ν Mean (SD) 01 Clomipramine vs Fluvoxamine Koran 1996a 39 5.80(4.70) 34 6.10(3.30) -0.07 [-0.53, 0.39] Mundo 2001 -0.13 [-0.40, 0.14] 105 7.00(4.50) 112 7.70(6.00) Smeraldi 1992 9.60(10.30) 11.80(6.80) -0.23 [-1.47, 1.02] 5 Subtotal (95% CI) 149 151 -0.12 [-0.35, 0.11] Test for heterogeneity: $Chi^2 = 0.08$, df = 2 (P = 0.96), $I^2 = 0\%$ Test for overall effect: Z = 1.04 (P = 0.30)02 Clomipramine vs Paroxetine Zohar 1996a -2.40(7.30) 198 -3.40(7.90) 0.13 [-0.12, 0.38] Subtotal (95% CI) 94 198 0.13 [-0.12, 0.38] Test for heterogeneity: not applicable Test for overall effect: Z = 1.03 (P = 0.30) Total (95% CI) 349 -0.01 [-0.17, 0.16] Test for heterogeneity: Chi² = 2.21, df = 3 (P = 0.53), l² = 0% Test for overall effect: Z = 0.06 (P = 0.95) -2 Ò Favours Clomipramine Favours SSRI OCD adults: Clomipramine Review: Comparison: 02 Clomipramine vs SSRIs; acute phase Outcome 17 Clinical Anxiety Scale SSRI SMD (fixed) SMD (fixed) Study or sub-category Ν Mean (SD) N Mean (SD) 95% CI 95% CI 01 Clomipramine vs Fluvoxamine Mundo 2001 6.70(4.30) 112 7.00(4.60) -0.07 [-0.33, 0.20] 105 Subtotal (95% CI) -0.07 [-0.33, 0.20] 112 Test for heterogeneity: not applicable Test for overall effect: Z = 0.49 (P = 0.62) -0.5 0.5 Ó Favours Clomipramine Favours SSRI Review: OCD adults: Clomipramine 02 Clomipramine vs SSRIs; acute phase Comparison: Outcome 18 Covi Anxiety Scale SSRI SMD (fixed) SMD (fixed) Study Clomipramine or sub-category Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Clomipramine vs Fluoxetine Lopez-Ibor 1996 24 -2.40(3.09) 30 -2.40(3.10) 0.00 [-0.54, 0.54] 0.00 [-0.54, 0.54] Subtotal (95% CI) 30 Test for heterogeneity: not applicable Test for overall effect: Z = 0.00 (P = 1.00) 10 Ó Favours Clomipramine Favours SSRI

Review: OCD adults: Clomipramine
Comparison: 02 Clomipramine vs SSRIs: acute phase
Outcome: 19 Anxiety (Clinical Anxiety Scale; Covi Anxiety Scale)



Review: OCD adults: Clomipramine

Comparison: 02 Clomipramine vs SSRIs: acute phase Outcome: 20 Clinical Global Impressions: global improvement

SMD (fixed) SMD (fixed) Study Clomipramine SSRI or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Clomipramine vs Fluoxetine Lopez-lbor 1996 24 -2.60(1.19) 30 -2.60(1.13) 0.00 [-0.54, 0.54] Subtotal (95% CI) 0.00 [-0.54, 0.54] Test for heterogeneity: not applicable Test for overall effect: Z = 0.00 (P = 1.00) 02 Clomipramine vs Fluvoxamine Mundo 2001 105 2.30(1.00) 112 2.30(1.00) 0.00 [-0.27, 0.27] Subtotal (95% CI) 105 112 0.00 [-0.27, 0.27] Test for heterogeneity: not applicable Test for overall effect: Z = 0.00 (P = 1.00) Total (95% CI) 142 0.00 [-0.24, 0.24] 129 Test for heterogeneity: $Chi^2 = 0.00$, df = 1 (P = 1.00), $I^2 = 0\%$ Test for overall effect: Z = 0.00 (P = 1.00) -0.5 0.5

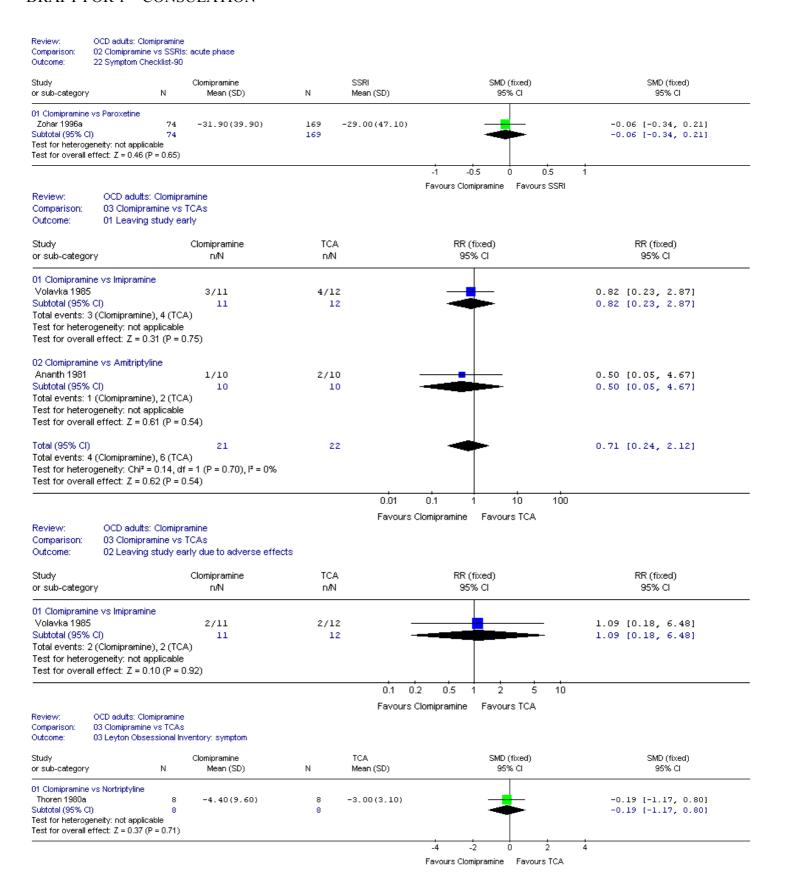
Favours Clomipramine Favours SSRI

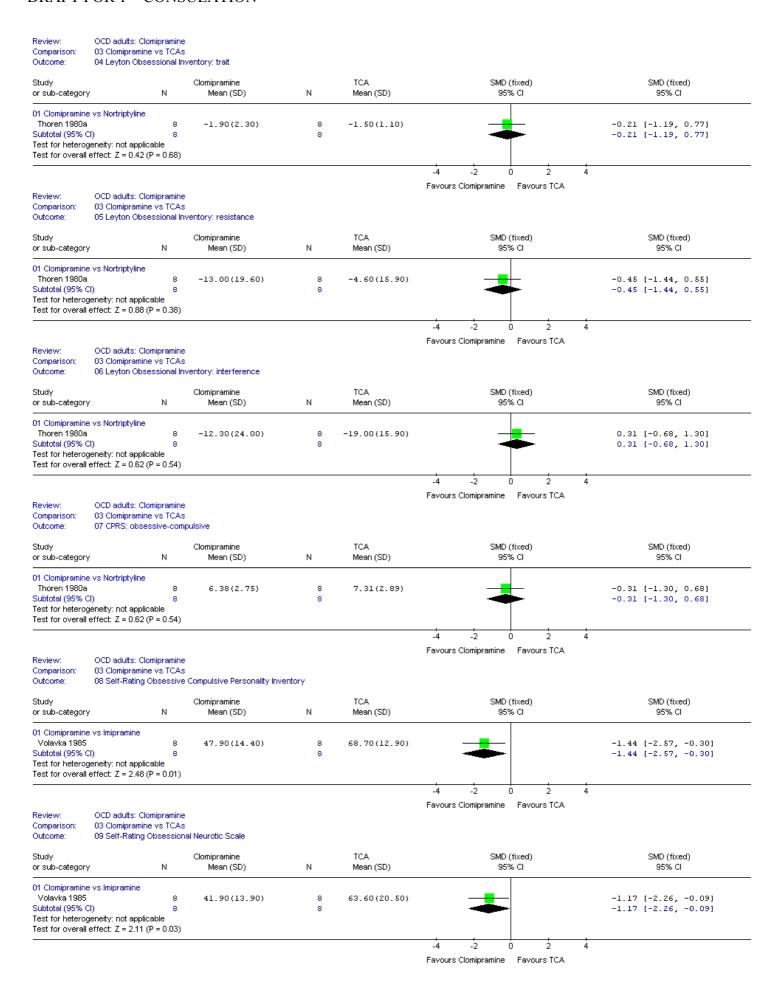
Favours Clomipramine Favours SSRI

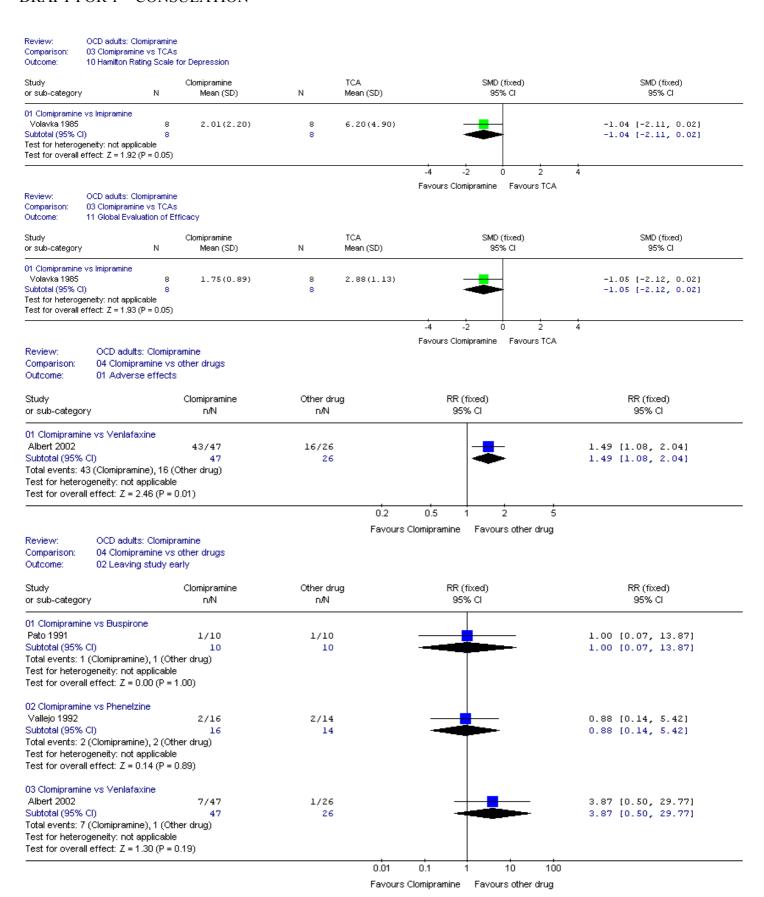
Review: OCD adults: Clomipramine Comparison: 02 Clomipramine vs SSRIs:

Comparison: 02 Clomipramine vs SSRIs: acute phase Outcome: 21 Clinical Global Impressions: severity of illness

Study or sub-category	N	Clomipramine Mean (SD)	N	SSRI Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Clomipramine vs Fluox	retine					
Lopez-lbor 1996	24	-1.90(1.14)	30	-0.90(1.23)		-0.83 [-1.39, -0.27]
Subtotal (95% CI)	24		30		•	-0.83 [-1.39, -0.27]
Test for heterogeneity: no	ot applicable				-	
Test for overall effect: Z	= 2.89 (P = 0.004)	1				
02 Clomipramine vs Fluvo	oxamine					
Mundo 2001	105	3.20(1.20)	112	3.40(1.30)		-0.16 [-0.43, 0.11]
Subtotal (95% CI)	105		112		*	-0.16 [-0.43, 0.11]
Test for heterogeneity: no	ot applicable					
Test for overall effect: Z	= 1.17 (P = 0.24)					
03 Clomipramine vs Paro:	xetine					
Zohar 1996a	94	-1.10(1.20)	194	-1.20(1.40)	+	0.07 [-0.17, 0.32]
Subtotal (95% CI)	94		194		•	0.07 [-0.17, 0.32]
Test for heterogeneity: no	ot applicable				ľ	
Test for overall effect: Z						
Total (95% CI)	223		336		•	-0.11 [-0.28, 0.06]
Test for heterogeneity: C	$hi^2 = 8.57$, $df = 2$ (P = 0.01), I ² = 76.7%			1	
Test for overall effect: Z	= 1.23 (P = 0.22)					
					-4 -2 0	2 4
				_		
				- F	avours Clomipramine 🔝 Favo	urs SSRI







Review: OCD adults: Clomipramine Comparison: 04 Clomipramine vs other drugs

Outcome: 03 Leaving study early due to adverse effects

Study or sub-category	Clomipramine n/N	Other drug n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
	e			
Pato 1991	1/10	0/10		3.00 [0.14, 65.90]
Subtotal (95% CI)	10	10		3.00 [0.14, 65.90]
Total events: 1 (Clomipramine), 0 (Other drug)			·
Test for heterogeneity: not ap	pplicable			
Test for overall effect: $Z = 0$.	70 (P = 0.49)			
02 Clomipramine vs Phenelzin	ne			
Vallejo 1992	1/16	0/14		2.65 [0.12, 60.21]
Subtotal (95% CI)	16	14		2.65 [0.12, 60.21]
Total events: 1 (Clomipramine), 0 (Other drug)			•
Test for heterogeneity: not ag	pplicable			
Test for overall effect: $Z = 0.0$	61 (P = 0.54)			
03 Clomipramine vs Venlafax	ine			
Albert 2002	5/47	0/26		6.19 [0.36, 107.66]
Subtotal (95% CI)	47	26		6.19 [0.36, 107.66]
Fotal events: 5 (Clomipramine), 0 (Other drug)			
Test for heterogeneity: not ap	pplicable			
Test for overall effect: Z = 1.:	•			
		0.00	1 0.01 0.1 1 10 100	1000
		Favo	ours Clomipramine Favours other o	drua

Review: OCD adults: Clomipramine Comparison: 04 Clomipramine vs other drugs

Outcome: 04 Non-responders

Study or sub-category	Clomipramine n/N	Other drug n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Clomipramine vs Venlafa	xine			
Albert 2002	27/47	17/26		0.88 [0.61, 1.28]
Subtotal (95% CI)	47	26		0.88 [0.61, 1.28]
Total events: 27 (Clomiprami	ine), 17 (Other drug)		 -	·
Test for heterogeneity: not a	applicable			
Test for overall effect: Z = 0	0.68 (P = 0.50)			
			15 0.7 1 1.5	2

Favours Clomipramine Favours other drug

Review: OCD adults: Clomipramine Comparison: 04 Clomipramine vs other drugs

Outcome: 05 Y-BOCS

Study or sub-category	N	Clomipramine Mean (SD)	N	Other drug Mean (SD)	SMD (fixed) 95% Cl	SMD (fixed) 95% CI	
01 Clomipramine vs Buspirone							
Pato 1991	9	17.67(4.97)	9	16.78(6.46)	_ _	0.15 [-0.78, 1.07]	
Subtotal (95% CI)	9		9			0.15 [-0.78, 1.07]	
est for heterogeneity: not app	licable				T-		
Fest for overall effect: Z = 0.31	1 (P = 0.76)						
02 Clomipramine vs Venlafaxin	e						
Albert 2002	47	17.30(6.15)	26	18.36(7.11)		-0.16 [-0.64, 0.32]	
Subtotal (95% CI)	47		26		•	-0.16 [-0.64, 0.32]	
est for heterogeneity: not app	licable				1		
Fest for overall effect: $Z = 0.66$	6 (P = 0.51)						
				-4	-2 0 2	4	

Review: OCD adults: Clomipramine Favours other drugs

OCD adults: Clomipramine vs. other drugs

Outcome: 06 NIMH-OC

Study or sub-category	N	Clomipramine Mean (SD)	N	Other drug Mean (SD)			D (fixed) 15% Cl			SMD (fixed) 95% Cl
01 Clomipramine vs Buspiror	ne									
Pato 1991	9	5.22(1.20)	9	5.11(1.27)		_	_			0.08 [-0.84, 1.01]
Subtotal (95% CI)	9		9			-	•			0.08 [-0.84, 1.01]
Test for heterogeneity: not a	applicable						Ī			
Test for overall effect: $Z = 0$	0.18 (P = 0.86)									
-					-4	-2	0	2	4	
					Favours	Clomipramine	e Favo	urs other	drug	

Review: OCD adults: Clomipramine Comparison: 04 Clomipramine vs other drugs Outcome 07 Maudsley Obsessive-Compulsive Inventory SMD (fixed) SMD (fixed) Study Other drug or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Clomipramine vs Phenelzine Vallejo 1992 12.10(4.70) 12 10.10(6.90) 0.33 [-0.44, 1.11] 14 Subtotal (95% CI) 12 0.33 [-0.44, 1.11] Test for heterogeneity: not applicable Test for overall effect: Z = 0.84 (P = 0.40) Ó Favours Clomipramine Favours other drug OCD adults: Clomipramine Review: Comparison: 04 Clomipramine vs other drugs Outcome 08 Hamilton Rating Scale for Depression SMD (fixed) Study SMD (fixed) Clomipramine Other drug Mean (SD) Mean (SD) 95% CI 95% CI or sub-category 01 Clomipramine vs Buspirone -0.09 [-1.02, 0.83] -0.09 [-1.02, 0.83] Pato 1991 9 9.33(4.58) 9 9.89(6.75) Subtotal (95% CI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.20 (P = 0.84) 02 Clomipramine vs Phenelzine Vallejo 1992 14 11.50(6.90) 12 7.00(5.70) 0.68 [-0.11, 1.48] Subtotal (95% CI) 12 0.68 [-0.11, 1.48] Test for heterogeneity: not applicable Test for overall effect: Z = 1.68 (P = 0.09)Favours Clomipramine Favours other drug OCD adults: Clomipramine Review: Comparison: 04 Clomipramine vs other drugs Outcome 09 Hamilton Rating Scale for Anxiety SMD (fixed) SMD (fixed) Study Clomipramine Other drug or sub-category Mean (SD) Mean (SD) 01 Clomipramine vs Phenelzine Valleio 1992 0.88 [0.07, 1.69] 0.88 [0.07, 1.69] 14 14.10(8.70) 12 7.00(6.60) Subtotal (95% CI) 14 Test for heterogeneity: not applicable Test for overall effect: Z = 2.12 (P = 0.03) -2 Favours Clomipramine Favours other drug Review: OCD adults: Clomipramine Comparison: 05 Intravenous Clomipramine vs IV placebo Outcome: 01 Leaving study early IV Placebo RR (fixed) RR (fixed) Study IV Clomipramine or sub-category n/Ν n/N 95% CI 95% CI Fallon 1998 2/25 0.43 [0.04, 4.48] 1/29 Total (95% CI) 29 25 0.43 [0.04, 4.48] Total events: 1 (IV Clomipramine), 2 (IV Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.70 (P = 0.48) 0.01 10 100 0.1 Favours Clomipramine Favours Placebo Review: OCD adults: Clomipramine Comparison: 05 Intravenous Clomipramine vs IV placebo Outcome: 02 Non-responders Study IV Clomipramine IV Placebo RR (fixed) RR (fixed) 95% CI 95% CI n/N or sub-category n/Ν Fallon 1998 23/29 25/25 0.79 [0.66, 0.96] Total (95% CI) 25 0.79 [0.66, 0.96] Total events: 23 (IV Clomipramine), 25 (IV Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 2.44 (P = 0.01) 0.5 0.7 1.5 Favours Clomipramine Favours Placebo

Test for overall effect: Z = 0.21 (P = 0.83)

OCD adults: Clomipramine Review: Comparison: 05 Intravenous Clomipramine vs IV placebo Outcome 03 Y-BOCS IV Placebo SMD (fixed) SMD (fixed) Study IV Clomipramine or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI Fallon 1998 28 25.20(7.00) 23 26.10(5.00) -0.14 [-0.70, 0.41] Total (95% CI) 23 -0.14 [-0.70, 0.41] Test for heterogeneity: not applicable Test for overall effect: Z = 0.51 (P = 0.61) -0.5 ò 0.5 Favours Clomipramine Favours Placebo Review: OCD adults: Clomipramine Comparison 05 Intravenous Clomipramine vs IV placebo 04 NIMH-OC IV Placebo SMD (fixed) SMD (fixed) Study IV Clomipramine Ν or sub-category Ν Mean (SD) Mean (SD) 95% CI 95% CI Fallon 1998 28 10.40(2.00) 23 10.80(1.00) -0.24 [-0.80, 0.31] Total (95% CI) 23 -0.24 [-0.80, 0.31] 28 Test for heterogeneity: not applicable Test for overall effect: Z = 0.86 (P = 0.39) -0.5 0.5 Ó Favours Clomipramine Favours Placebo Review: OCD adults: Clomipramine 05 Intravenous Clomipramine vs IV placebo Comparison: Outcome: 05 Clinical Global Impressions: severity Study IV Clomipramine IV Placebo SMD (fixed) SMD (fixed) Ν Ν Mean (SD) or sub-category Mean (SD) 95% CI 95% CI Fallon 1998 28 5.30(1.00) 23 5.70(5.00) -0.11 [-0.67, 0.44] Total (95% CI) 28 23 -0.11 [-0.67, 0.44] Test for heterogeneity; not applicable Test for overall effect: Z = 0.41 (P = 0.68) -0.5 Ó 0.5 Favours Clomipramine Favours Placebo OCD adults: Clomipramine Review: Comparison: 05 Intravenous Clomipramine vs IV placebo Outcome 06 Hamilton Rating Scale for Depression IV Clomipramine IV Placebo SMD (fixed) SMD (fixed) Study or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI Fallon 1998 28 12.00(6.00) 23 12.70(7.00) -0.11 [-0.66, 0.45] Total (95% CI) 28 -0.11 [-0.66, 0.45] Test for heterogeneity: not applicable Test for overall effect: Z = 0.38 (P = 0.71) -0.5 Favours Clomipramine Favours Placebo Review: OCD adults: Clomipramine Comparison: 06 Intravenous Clomipramine vs oral Clomipramine Outcome: 01 Adverse effects Oral Clomipramine RR (fixed) RR (fixed) Study IV Clomipramine 95% CI 95% CI or sub-category n/N n/N Koran 1997 4/7 5/8 0.91 [0.40, 2.11] 0.91 [0.40, 2.11] Total (95% CI) 8 Total events: 4 (IV Clomipramine), 5 (Oral Clomipramine) Test for heterogeneity: not applicable

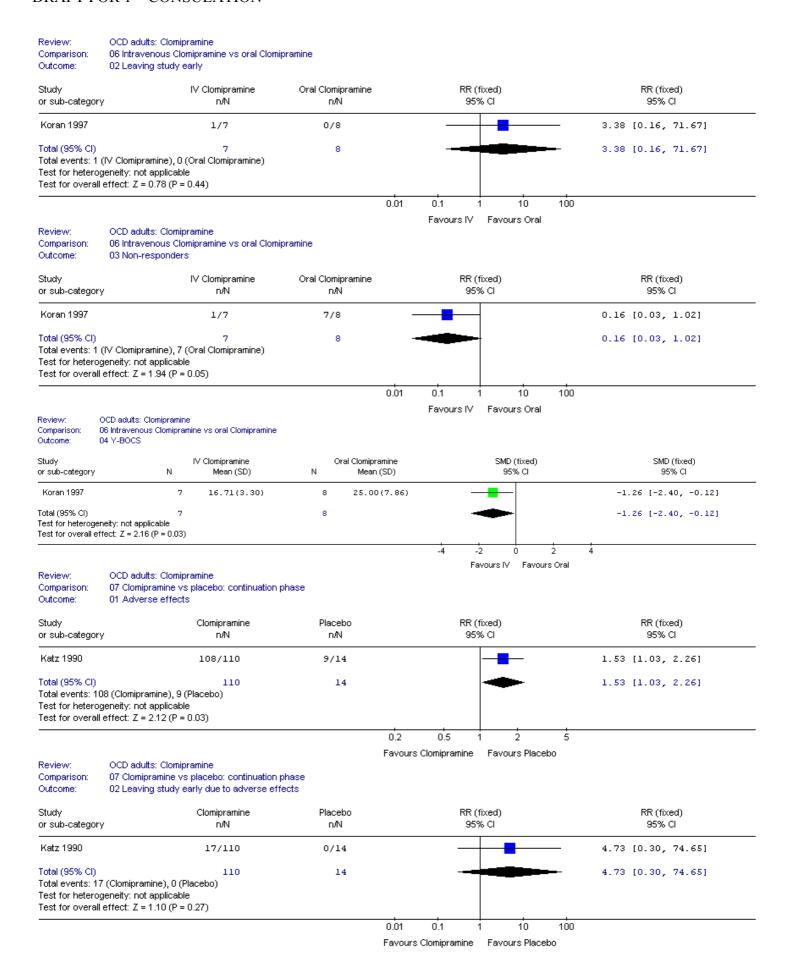
0.2

0.5

Favours IV

5

Favours Oral



Review: OCD adults: Clomipramine Comparison: 07 Clomipramine vs placebo: continuation phase Outcome 03 NIMH-OC SMD (fixed) SMD (fixed) Study Clomipramine Placebo or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI Katz 1990 101 5.10(2.70) 12 9.00(2.50) -1.44 [-2.07. -0.82] Total (95% CI) 12 -1.44 [-2.07, -0.82] Test for heterogeneity: not applicable Test for overall effect: Z = 4.51 (P < 0.00001) ò Favours Clomipramine Favours Placebo OCD adults: Clomipramine Review: Comparison 07 Clomipramine vs placebo: continuation phase 04 Physician's Global Evaluation SMD (fixed) SMD (fixed) Study Clomipramine Placebo Ν or sub-category Ν Mean (SD) Mean (SD) 95% CI 95% CI Katz 1990 101 1.89(0.94) 12 3.33(0.89) -1.53 [-2.16, -0.90] Total (95% CI) 12 -1.53 [-2.16. -0.90] 101 Test for heterogeneity: not applicable Test for overall effect: Z = 4.74 (P < 0.00001)Ó Favours Clomipramine Favours Placebo OCD adults: Clomipramine Comparison: 08 Clomipramine vs SSRIs: continuation phase 01 Leaving study early Outcome: Study Clomipramine SSRI RR (fixed) RR (fixed) or sub-category n/Ν n/N 95% CI 95% CI 01 Clomipramine 200mg vs Fluoxetine 60mg (non-responders) 0.88 [0.30, 2.58] Lopez-lbor 1996 6/14 3/8 Subtotal (95% CI) 14 0.88 [0.30, 2.58] Total events: 3 (Clomipramine), 6 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.24 (P = 0.81) 02 Clomipramine 100mg vs Fluoxetine 20mg (responders) Lopez-lbor 1996 3/11 1.69 [0.55, 5.24] 6/13 Subtotal (95% CI) 13 1.1 1.69 [0.55, 5.24] Total events: 6 (Clomipramine), 3 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.91 (P = 0.36) 0.2 0.5 5 10 Favours Clomipramine Favours SSRI Review: OCD adults: Clomipramine Comparison: 08 Clomipramine vs SSRIs: continuation phase Outcome: 02 Leaving study early due to adverse effects Study SSRI RR (fixed) RR (fixed) Clomipramine or sub-category n/Ν n/Ν 95% CL 95% CL 01 Clomipramine 200mg vs Fluoxetine 60mg (non-responders) Lopez-lbor 1996 0/8 2/14 0.33 [0.02, 6.19] Subtotal (95% CI) 0.33 [0.02, 6.19] 14 Total events: 0 (Clomipramine), 2 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.74 (P = 0.46) 02 Clomipramine 100mg vs Fluoxetine 20mg (responders) Lopez-lbor 1996 0.85 [0.06, 12.01] 1/13 1/11 Subtotal (95% CI) 13 0.85 [0.06, 12.01] 11 Total events: 1 (Clomipramine), 1 (SSRI) Test for heterogeneity: not applicable Test for overall effect: Z = 0.12 (P = 0.90)

0.01

0.1

Favours Clomipramine

10

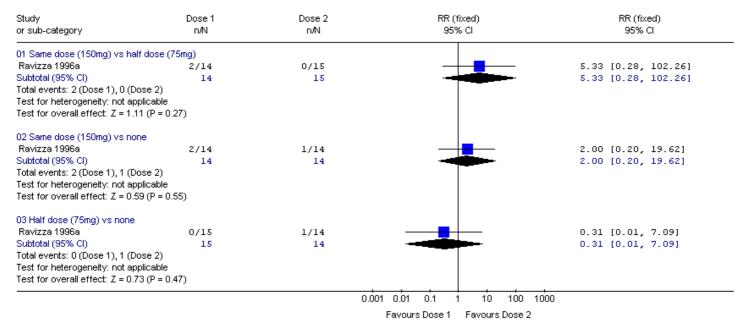
Favours SSRI

100

Review: OCD adults: Clomipramine

Comparison: 09 Clomipramine same dose vs half dose vs none: continuation/discontinuation

Outcome: 01 Leaving study early



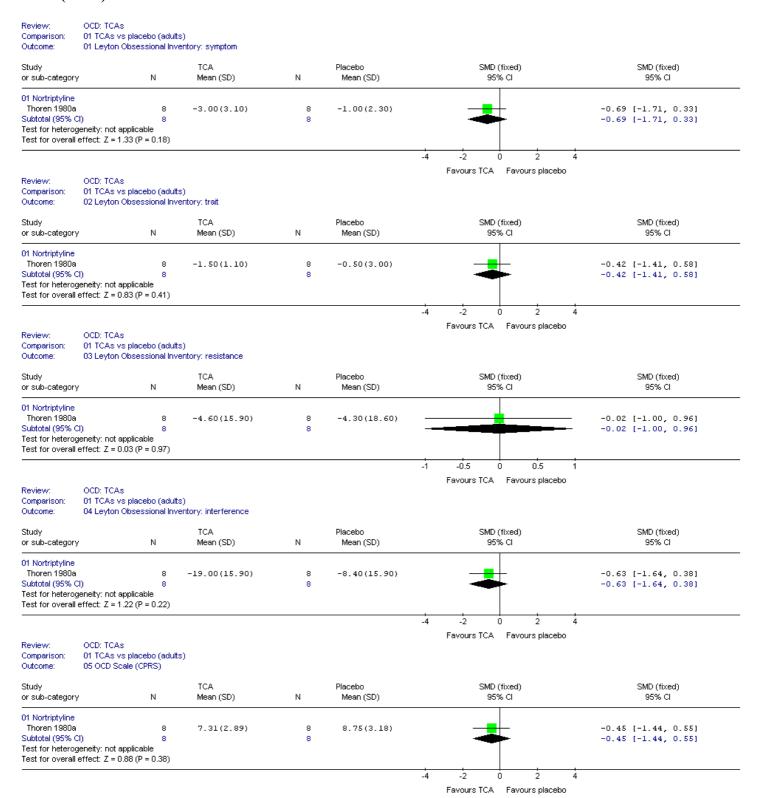
Review: OCD adults: Clomipramine

Comparison: 09 Clomipramine same dose vs half dose vs none: continuation/discontinuation

Outcome: 02 Relapse (CGI; 25% Y-BOCS)

Study or sub-category	Dose 1	Dose 2 n/N	RR (fixed) 95% Cl	RR (fixed) 95% CI
01 Same dose (150mg) vs half dose (<u> </u>	
Ravizza 1996a	5/14	4/15		1.34 [0.45, 4.00]
Subtotal (95% CI)	14	15		1.34 [0.45, 4.00]
Total events: 5 (Dose 1), 4 (Dose 2)				
Test for heterogeneity: not applicable				
Test for overall effect: Z = 0.52 (P = 0).60)			
02 Same dose (150mg) vs none				
Ravizza 1996a	5/14	11/14		0.45 [0.21, 0.97]
Subtotal (95% CI)	14	14	-	0.45 [0.21, 0.97]
Total events: 5 (Dose 1), 11 (Dose 2)				•
Test for heterogeneity: not applicable				
Test for overall effect: Z = 2.05 (P = 0				
	/			
03 Half dose (75mg) vs none				
Ravizza 1996a	4/15	11/14		0.34 [0.14, 0.82]
Subtotal (95% CI)	15	14		0.34 [0.14, 0.82]
Total events: 4 (Dose 1), 11 (Dose 2)				
Test for heterogeneity: not applicable				
Test for overall effect: Z = 2.40 (P = 0				
04 Continuation v discontinuation				
Ravizza 1996a	9/29	11/14		0.39 [0.22, 0.73]
Subtotal (95% CI)	29	14		0.39 [0.22, 0.73]
Total events: 9 (Dose 1), 11 (Dose 2)		14		0.35 (0.22, 0.73)
Test for heterogeneity: not applicable				
Test for overall effect: Z = 3.00 (P = 0				
rest for overall effect. Z = 3.00 (P = 0	1.003)			
		0.1	0.2 0.5 1 2 5	10
			Favours Dose 1 Favours Dose 2	2

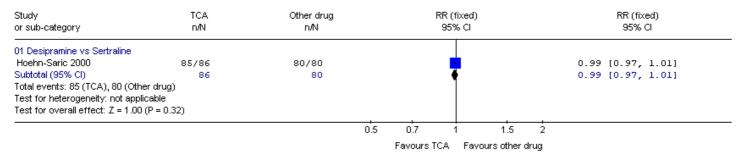
TCAs (OCD)



Review: OCD: TCAs

Comparison: 02 TCAs vs other drugs (adults)

Outcome: 01 Adverse effects

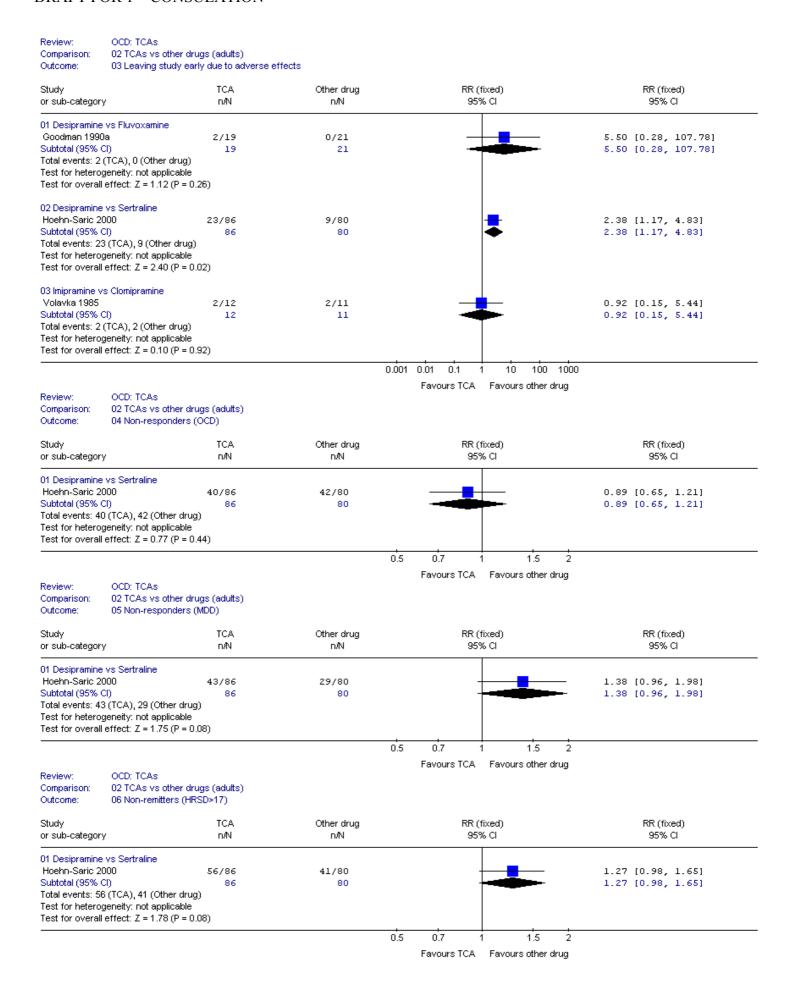


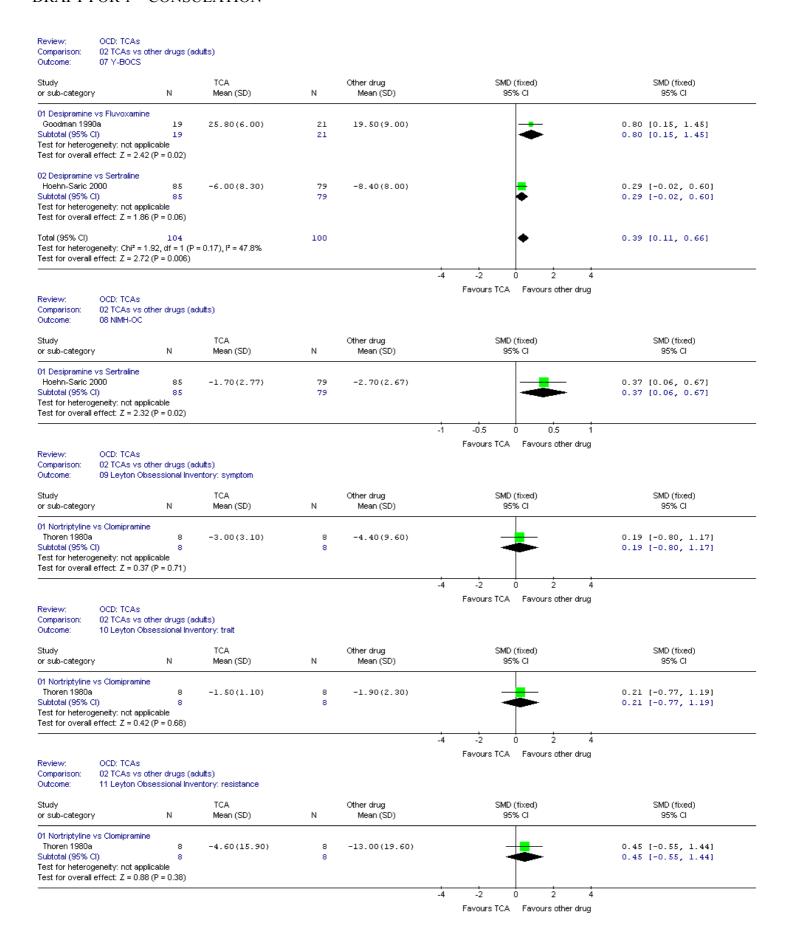
Review: OCD: TCAs

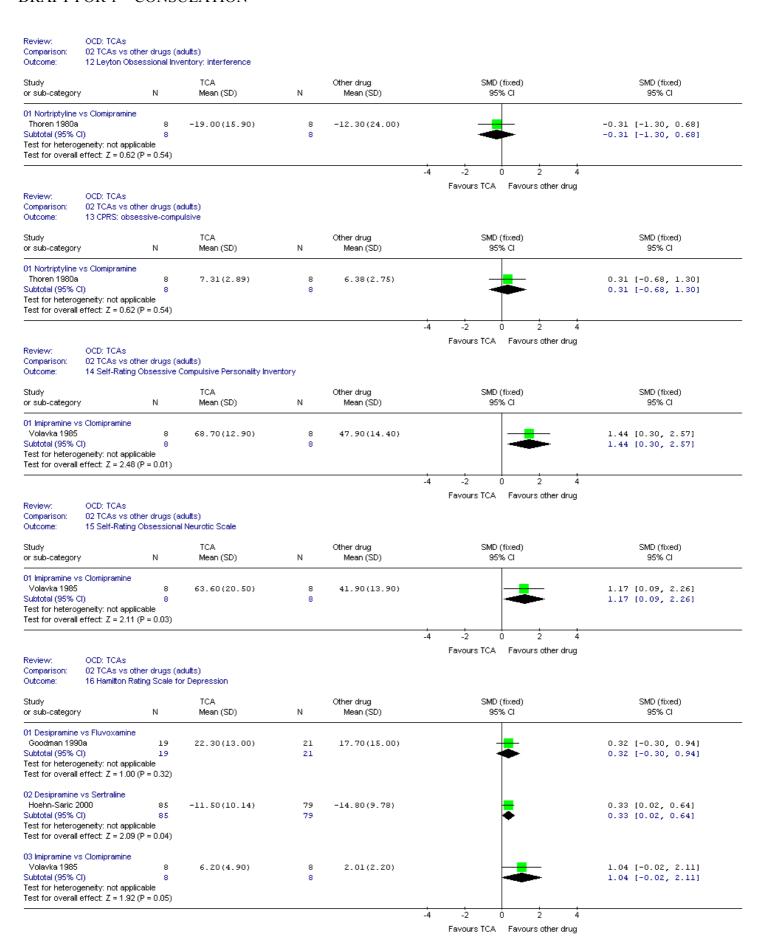
Comparison: 02 TCAs vs other drugs (adults)

Outcome: 02 Leaving study early

tudy r sub-category	TCA n/N	Other drug n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
1 Amitriptyline vs Clomipramine				
Ananth 1981	2/10	1/10		2.00 [0.21, 18.69]
ubtotal (95% CI)	10	10		2.00 [0.21, 18.69]
otal events: 2 (TCA), 1 (Other drug)	l			
est for heterogeneity: not applicable				
est for overall effect: Z = 0.61 (P = 0	0.54)			
2 Desipramine vs Fluvoxamine				
Goodman 1990a	6/19	2/21	+-	3.32 [0.76, 14.49]
Subtotal (95% CI)	19	21	-	3.32 [0.76, 14.49]
otal events: 6 (TCA), 2 (Other drug)	l			
est for heterogeneity: not applicable				
est for overall effect: Z = 1.59 (P = 0	0.11)			
3 Desipramine vs Sertraline				
Hoehn-Saric 2000	33/86	14/80	-	2.19 [1.27, 3.79]
ubtotal (95% CI)	86	80	◆	2.19 [1.27, 3.79]
otal events: 33 (TCA), 14 (Other dru	ıg)			
est for heterogeneity: not applicable				
est for overall effect: Z = 2.82 (P = 0	0.005)			
4 Imipramine vs Clomipramine				
Volavka 1985	4/12	3/11		1.22 [0.35, 4.28]
ubtotal (95% CI)	12	11		1.22 [0.35, 4.28]
otal events: 4 (TCA), 3 (Other drug)				
est for heterogeneity: not applicable				
est for overall effect: $Z = 0.31$ (P = 0	0.75)			
		0.01	0.1 1 10	100







OCD: TCAs Review: Comparison: Outcome: Study or sub-category 01 Imipramine vs Clomipramine Volavka 1985 Subtotal (95% CI) Review: OCD: TCAs Comparison: Outcome:

02 TCAs vs other drugs (adults) 17 Global Evaluation of Efficacy

SMD (fixed) SMD (fixed) TCA Other drug Mean (SD) Ν Mean (SD) 95% CI 95% CI 2.88(1.13) 1.75(0.89) 1.05 [-0.02, 2.12] 1.05 [-0.02, 2.12] Test for heterogeneity: not applicable Test for overall effect: Z = 1.93 (P = 0.05) ò

03 Desipramine substitution vs Clomipramine continuation (child/adolescent) 01 Leaving the study early (only during the 2-month substitution period)

Study or sub-category	Desipramine n/N	Clomipramine n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Leonard 1991a	1/10	0/11	-	3.27 [0.15, 72.23]
Total (95% CI) Total events: 1 (Desipramini Test for heterogeneity: not a Test for overall effect: Z = 0	applicable	11		3.27 [0.15, 72.23]
		0.01	0.1 1 10 10	00

Favours Desipramine Favours Clomipramine

Favours TCA Favours other drug

Review: OCD: TCAs

Comparison: 03 Desipramine substitution vs Clomipramine continuation (child/adolescent)

Outcome: 02 Relapse (Physician's Relapse Scale)

Study or sub-category	Desipramine n/N	Clomipramine n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Leonard 1991a	8/9	2/11	-	4.89 [1.37, 17.49]
Total (95% CI) Total events: 8 (Desipramini Test for heterogeneity: not a Test for overall effect: Z = 2	applicable	11	-	4.89 [1.37, 17.49]
		0.01	0.1 1 10	100

Favours Desipramine

Review: OCD: TCAs

03 Designamine substitution vs Clomipramine continuation (child/adolescent) Comparison: Outcome 03 Comprehensive Psychopathological Rating Scale: obsessive-compulsive

Study or sub-category	N	Desipramine Mean (SD)	N	Clomipramine Mean (SD)		S	MD (fixed) 95% Cl			SMD (fixed) 95% CI
Leonard 1991a	9	6.30(3.30)	11	5.20(4.00)			-			0.28 [-0.60, 1.17]
Total (95% CI) Test for heterogeneity: not Test for overall effect: Z =			11				-			0.28 [-0.60, 1.17]
					-4	-2	ö	2	4	

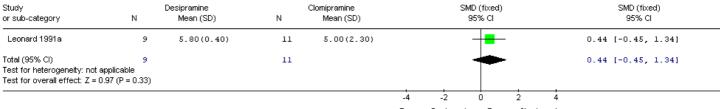
Favours Desipramine Favours Clomipramine

Favours Clomipramine

Review: OCD: TCAs

Comparison: 03 Desipramine substitution vs Clomipramine continuation (child/adolescent)

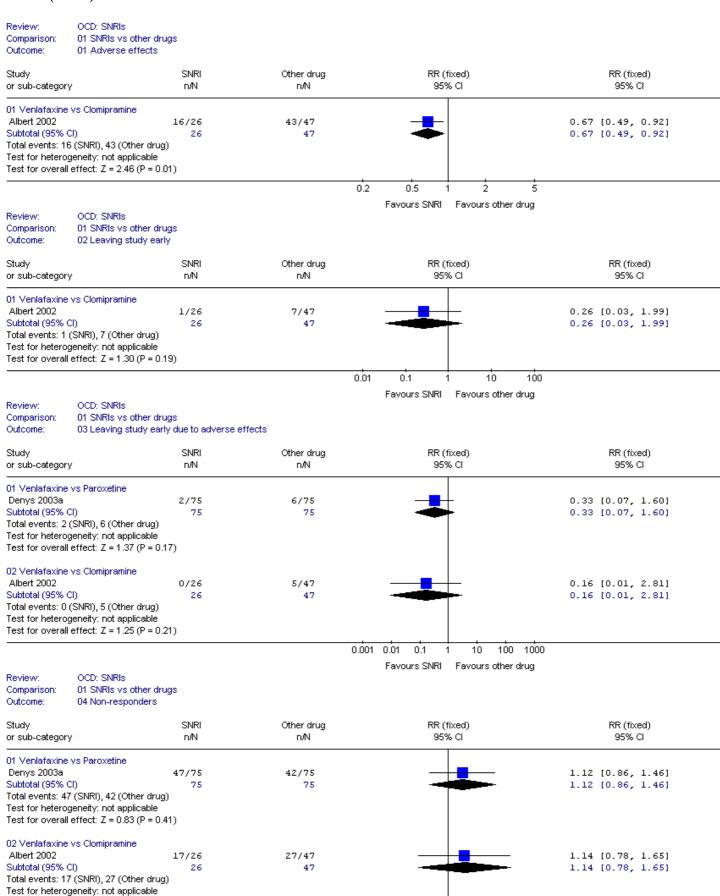
04 NIMH-OC Outcome



Favours Desipramine Favours Clomipramine

Test for overall effect: Z = 0.68 (P = 0.50)

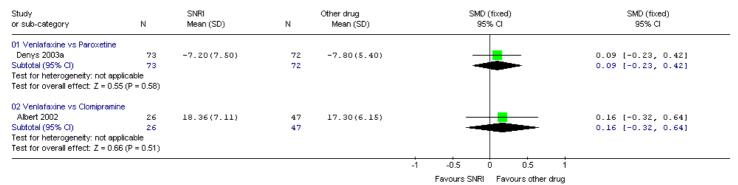
SNRIs (OCD)



Review: OCD: SNRIs

Comparison: 01 SNRIs vs other drugs

05 Y-BOCS Outcome:



Review: OCD: SNRIs

Comparison:

01 SNRIs vs other drugs 06 Hamilton Rating Scale for Depression Outcome:

Study or sub-category	N	SNRI Mean (SD)	N	Other drug Mean (SD)		SMD (fixed) 95% Cl	SMD (fixed) 95% Cl
01 Venlafaxine vs Paroxet	tine						
Denys 2003a	73	-2.80(5.60)	72	-3.50(4.60)	_		0.14 [-0.19, 0.46]
Subtotal (95% CI)	73		72		_		0.14 [-0.19, 0.46]
Test for heterogeneity: not	t applicable					 -	
Test for overall effect: $Z =$	0.82 (P = 0.41)						
					-0.5 -0.25	0 0.25	o.s
					Favours	SNRI Favours other dru	g

OCD: SNRIs Review:

Comparison: 01 SNRIs vs other drugs Outcome: 07 Hamilton Anxiety Scale

Study or sub-category	N	SNRI Mean (SD)	N	Other drug Mean (SD)		SMD (fi: 95% :			SMD (fixed) 95% Cl
01 Venlafaxine vs Paroxet									
Denys 2003a	73	-4.90(5.00)	72	-4.70(7.00)	_				-0.03 [-0.36, 0.29]
Subtotal (95% CI)	73		72		-				-0.03 [-0.36, 0.29]
Test for heterogeneity: not	t applicable								
Test for overall effect: Z =	0.20 (P = 0.84)								
					-0.5	-0.25 0	0.25	0.5	
					Fa	vours SNRI	Favours othe	r drug	

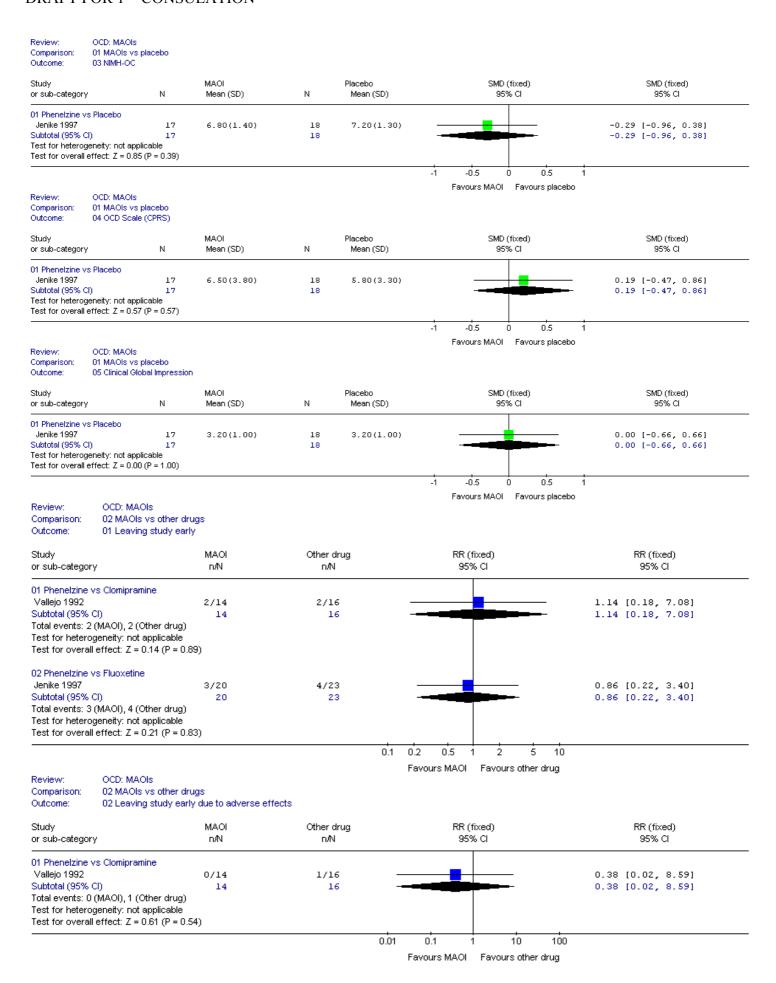
MAOIs (OCD)

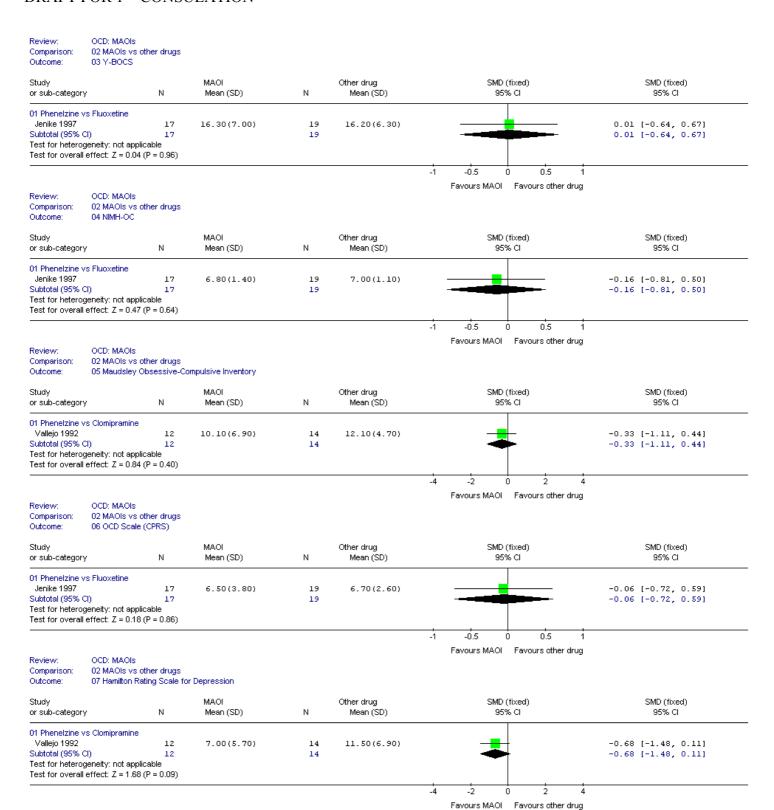
Review: OCD: MAOIs Comparison: 01 MAOIs vs placebo Outcome: 01 Leaving study early

Study or sub-category	MAOI n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Phenelzine vs Placebo				
Jenike 1997	3/20	3/21		— 1.05 [0.24, 4.61]
Subtotal (95% CI)	20	21		- 1.05 [0.24, 4.61]
Total events: 3 (MAOI), 3 (Place	cebo)			
Test for heterogeneity; not ap-	plicable			
Test for overall effect: $Z = 0.0$	06 (P = 0.95)			
		0.2	0.5 1 2	5
			Favours MAOI Favours placebo	0

Review: OCD: MAOIs 01 MAOIs vs placebo 02 Y-BOCS Comparison: Outcome:

Study or sub-category	N	MAOI Mean (SD)	N	Placebo Mean (SD)			D (fixed 15% CI)		SMD (fixed) 95% Cl
01 Phenelzine vs Placebo										
Jenike 1997	17	16.30(7.00)	18	18.70(6.10)		_				-0.36 [-1.03, 0.31]
Subtotal (95% CI)	17		18			-				-0.36 [-1.03, 0.31]
Test for heterogeneity: not	applicable						-			
Test for overall effect: $Z =$	1.05 (P = 0.29)									
					-4	-2	0	<u>;</u>	4	
					F	avours MAC	l Fav	ours place	ebo	

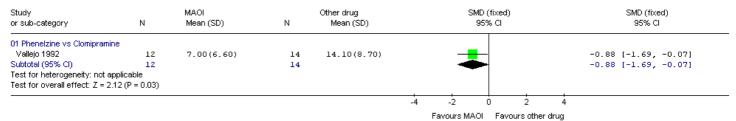




Review: OCD: MAOIs

Comparison: 02 MAOIs vs other drugs

Outcome: 08 Hamilton Rating Scale for Anxiety



Review: OCD: MAOIs

Comparison: 02 MAOIs vs other drugs Outcome: 09 Clinical Global Impression

Study or sub-category	N	MAOI Mean (SD)	N	Other drug Mean (SD)			(fixed) % CI			SMD (fixed) 95% Cl
01 Phenelzine vs Fluoxetine	Э									
Jenike 1997	17	3.20(1.00)	19	3.10(1.00)			-			0.10 [-0.56, 0.75]
Subtotal (95% CI)	17		19						-	0.10 [-0.56, 0.75]
Test for heterogeneity: not	applicable									
Test for overall effect: $Z =$	0.29 (P = 0.77)									
					-1	-0.5	0	0.5	i	
					F	avours MAOI	Favo	ours other	drug	

Anxiolytics (OCD)

Review: OCD: anxiolytics

Comparison: 01 Anxiolytics vs placebo Outcome: 01 Leaving study early

Study or sub-category	Anxiolytic n/N	Placebo n/N	RR (fixed) 95% Cl		RR (fixed) 95% Cl
01 Clonazepam					
Hollander 2003c	5/17	4/10			0.74 [0.26, 2.12]
Subtotal (95% CI)	17	10		- -	0.74 [0.26, 2.12]
Total events: 5 (Anxiolytic),	4 (Placebo)				
Test for heterogeneity: not a	applicable				
Test for overall effect: Z = 0	.57 (P = 0.57)				
			0.2 0.5 1	2 5	

Favours anxiolytic

Favours placebo

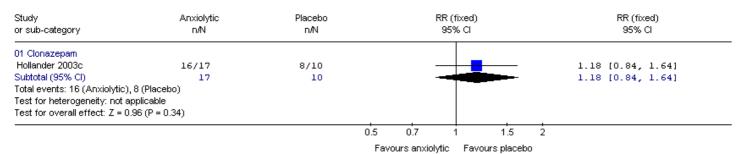
Review: OCD: anxiolytics

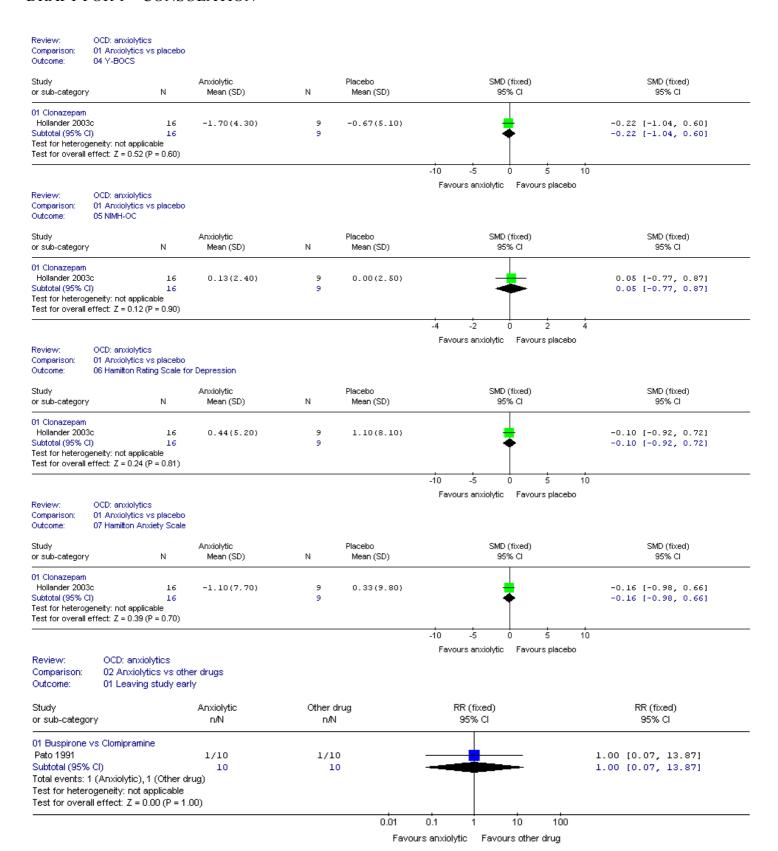
Comparison: 01 Anxiolytics vs placebo

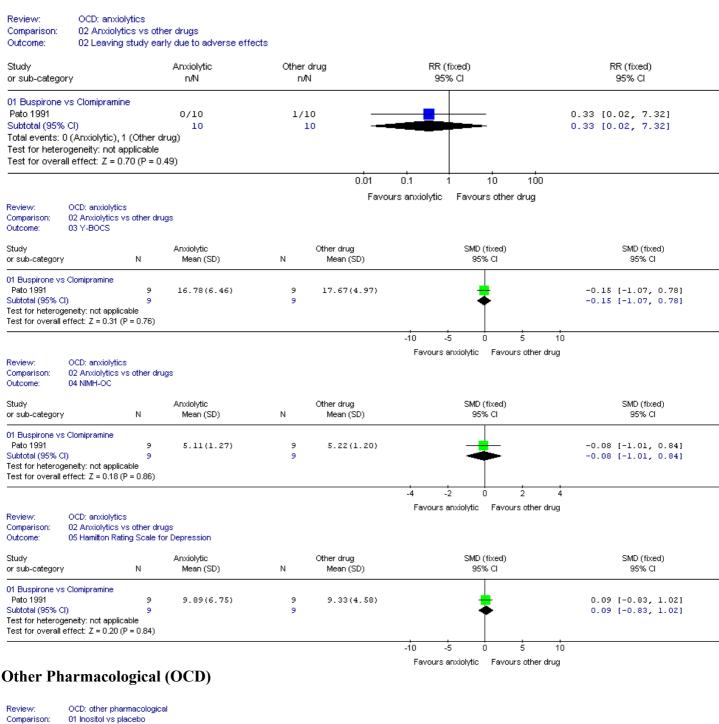
Outcome: 02 Leaving study early due to adverse effects

Study	Anxiolytic	Placebo		RR (fixed)						RR (fixed)	
or sub-category ————————————————————————————————————	n/N	n/N		95% CI			95% CI				
01 Clonazepam											
Hollander 2003c	3/17	2/10						_		0.88 [0.18, 4.41]	
Subtotal (95% CI)	17	10		_				_		0.88 [0.18, 4.41]	
Total events: 3 (Anxiolytic), 2	(Placebo)					\neg					
Test for heterogeneity: not ap	plicable										
Test for overall effect: $Z = 0$:	15 (P = 0.88)										
			0.1	0.2	0.5	1	2	5	10		
			Fa	avours	anxiolyti	ic F	avours	placeb	0		

Review: OCD: anxiolytics Comparison: 01 Anxiolytics vs placebo Outcome: 03 Non-responders

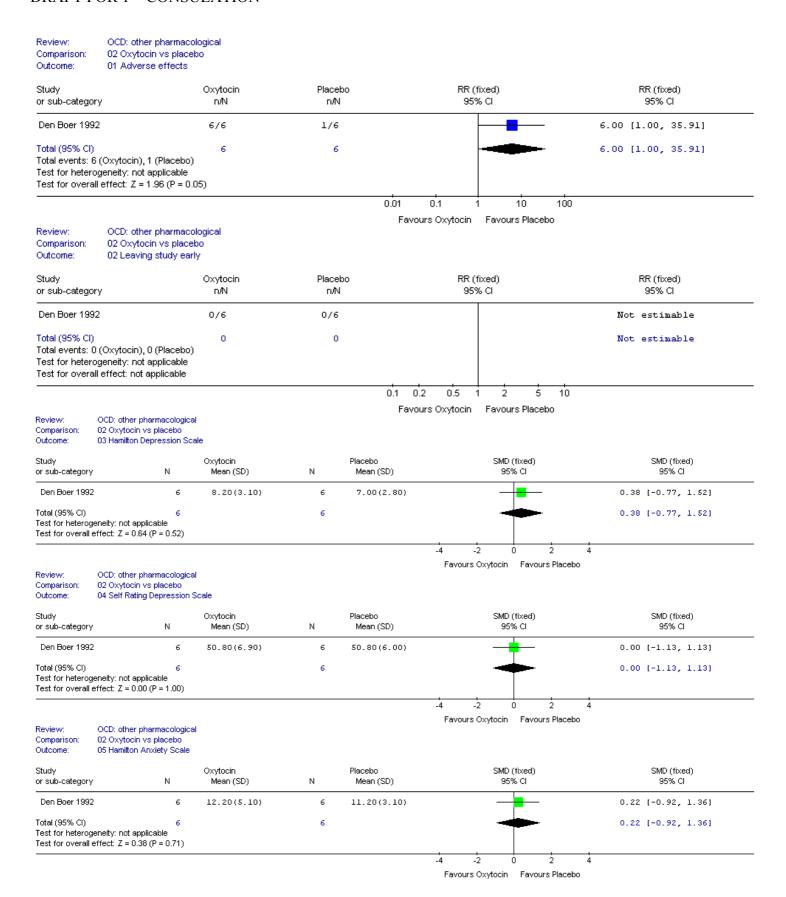




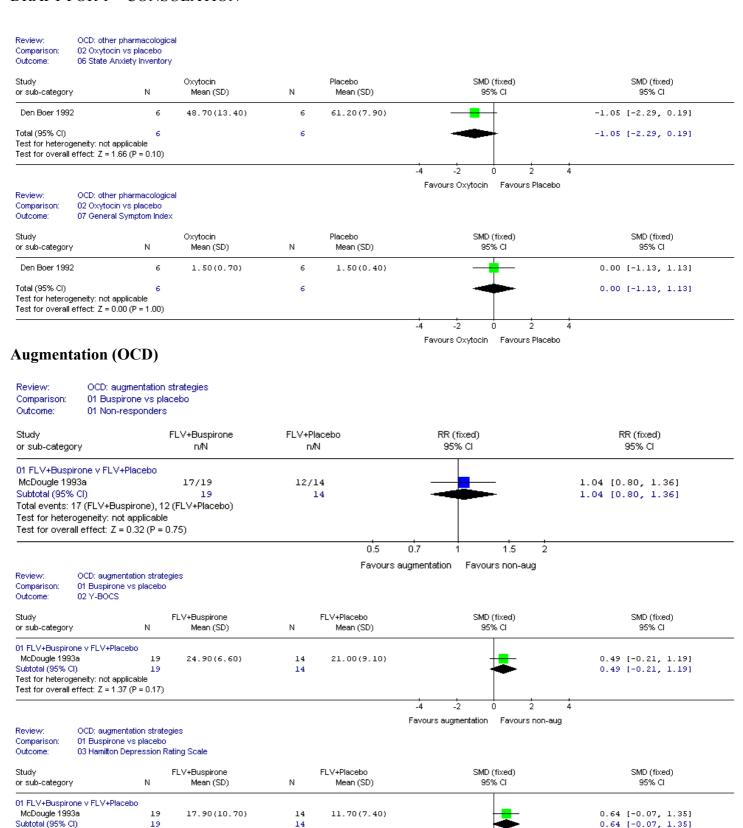


01 Y-BOCS

Study or sub-category	N	Inositol Mean (SD)	N	Placebo Mean (SD)			(fixed) 5% CI			SMD (fixed) 95% Cl
Fux 1996	7	17.57(9.60)	6	20.00(5.20)		-	_			-0.29 [-1.38, 0.81]
Total (95% CI) Test for heterogeneity: not Test for overall effect: Z =			6			-				-0.29 [-1.38, 0.81]
					-4	-2	Ó	2	4	
					Fa	vours Inositol	Favo	urs Place	bo	



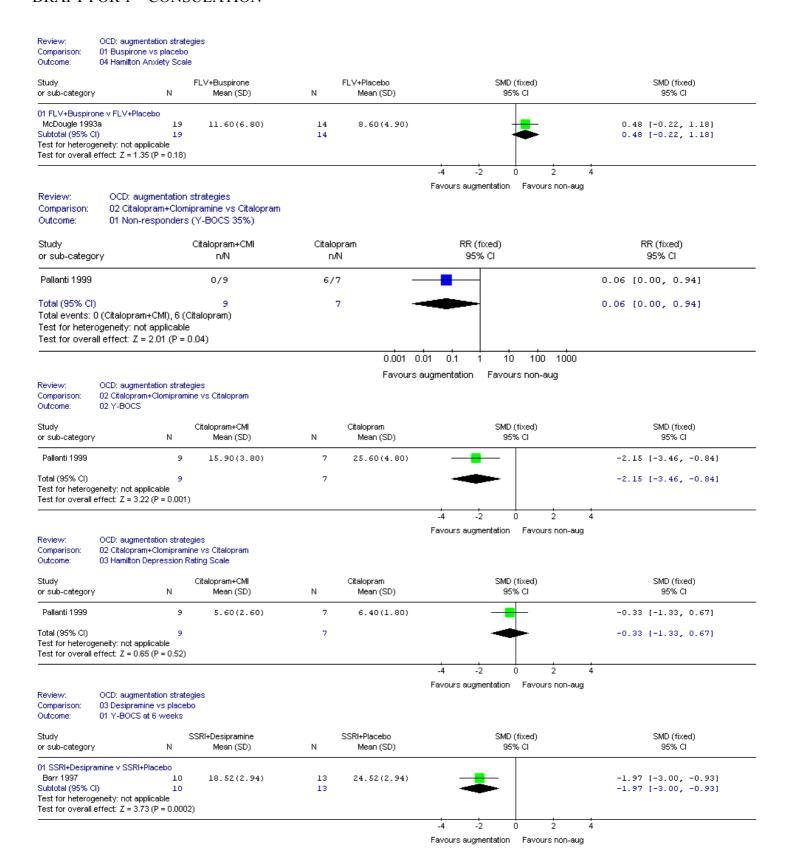
Test for heterogeneity: not applicable Test for overall effect: Z = 1.77 (P = 0.08)

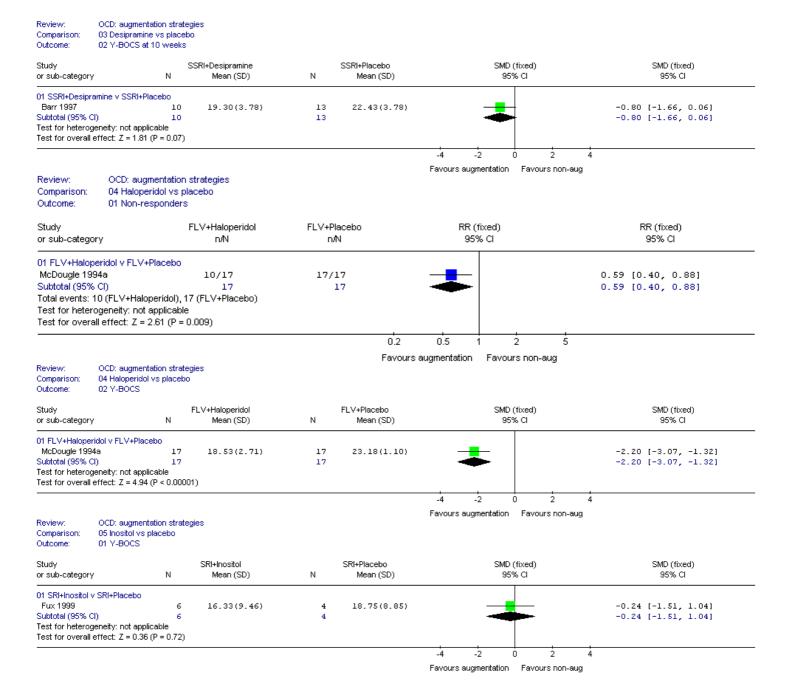


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Favours non-aug

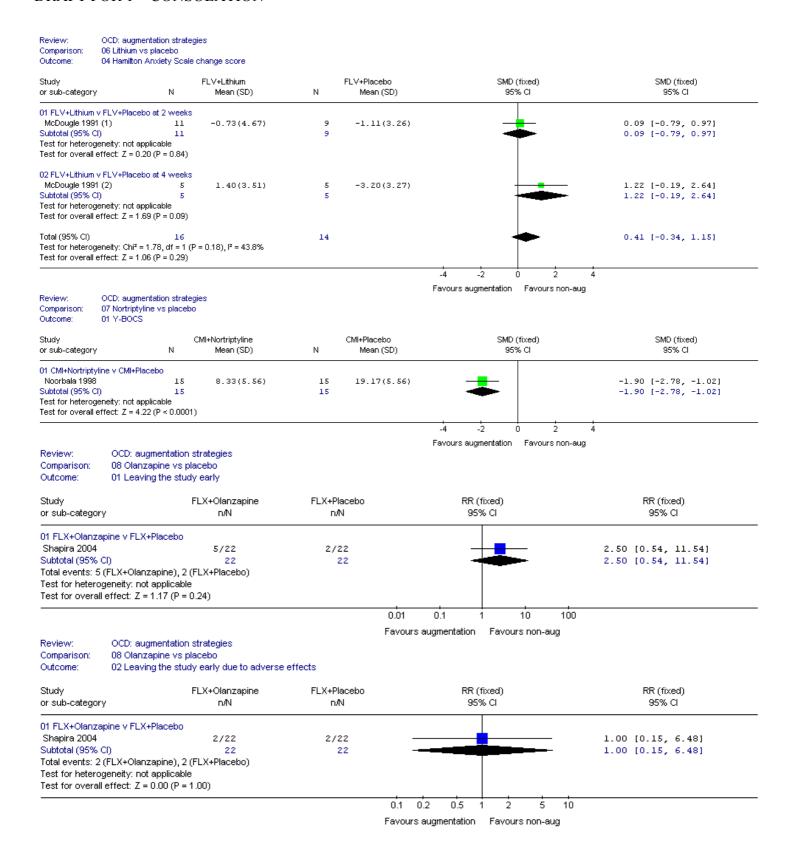
Favours augmentation

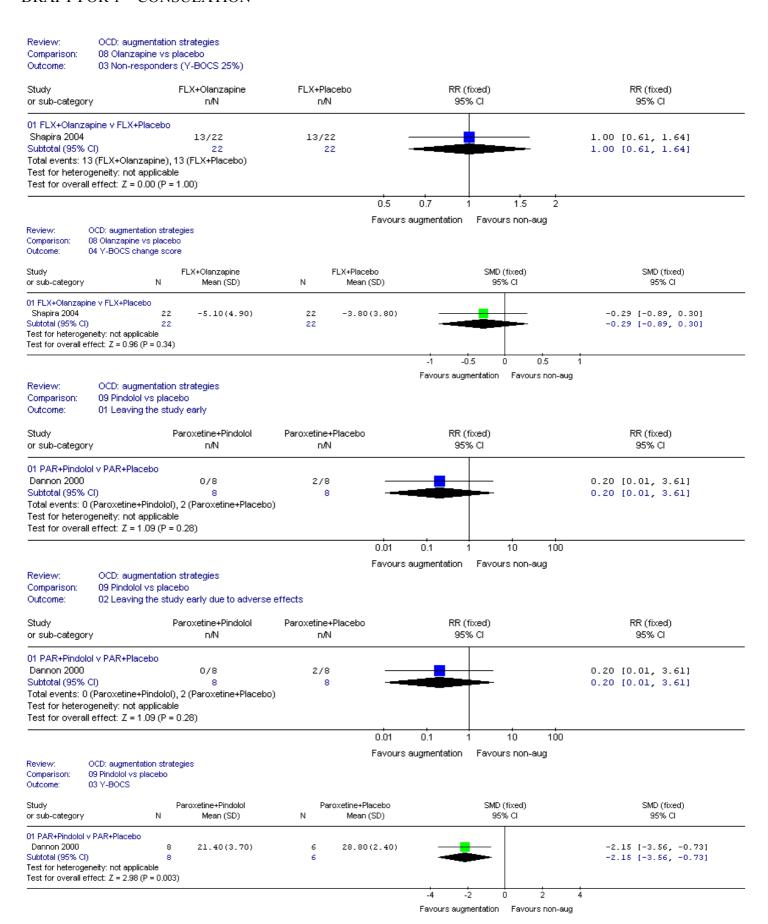


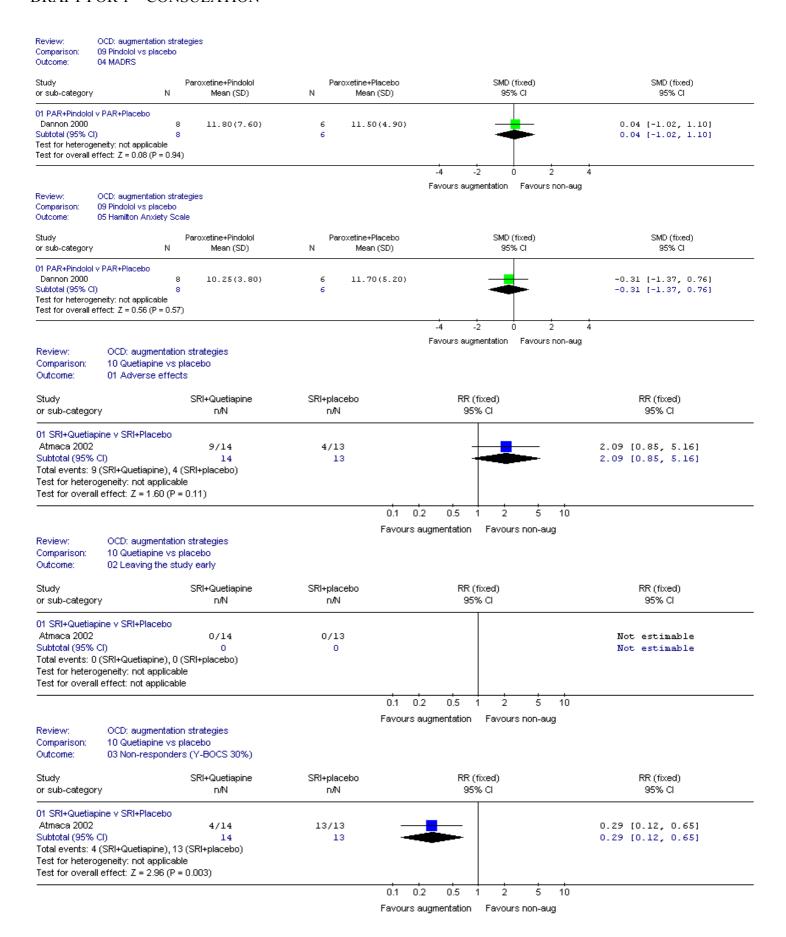


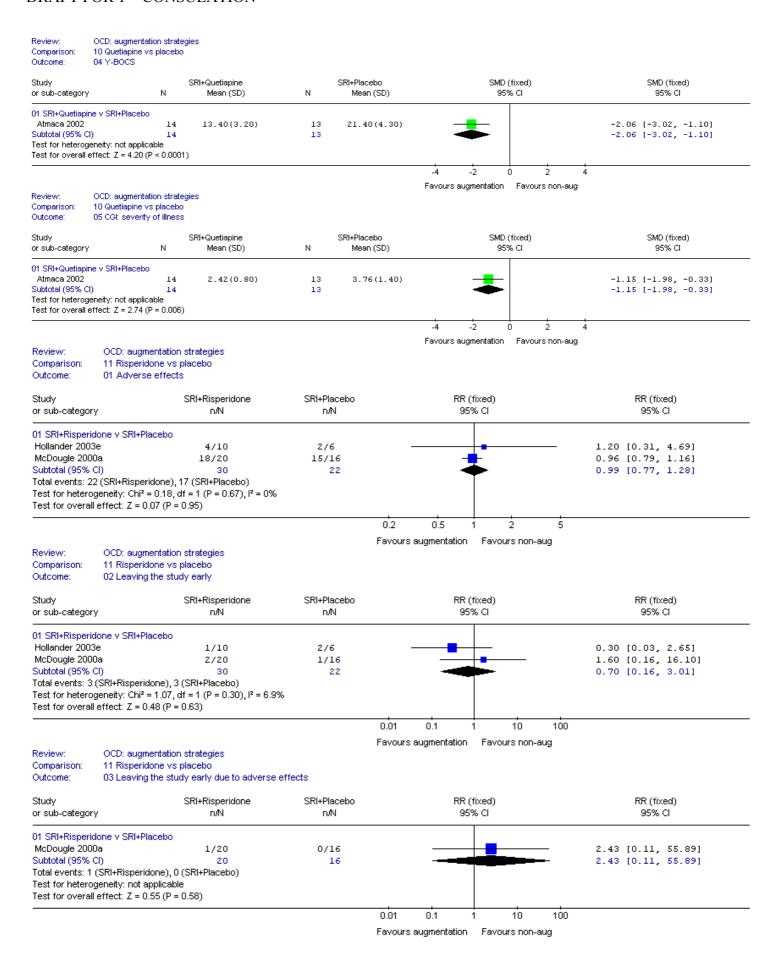
Review: OCD: augmentation strategies Comparison: 06 Lithium vs placebo Outcome: 01 Non-responders FLV+Lithium FLV+Placebo RR (fixed) RR (fixed) Study or sub-category n/N 95% CI 95% CI 01 FLV+Lithium v FLV+Placebo at 2 weeks McDougle 1991 (1) 9/11 9/9 0.82 [0.62, 1.08] Subtotal (95% CI) 9 0.82 [0.62, 1.08] Total events: 9 (FLV+Lithium), 9 (FLV+Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.41 (P = 0.16) 02 FLV+Lithium v FLV+Placebo at 4 weeks McDougle 1991 (2) 5/5 Not estimable Subtotal (95% CI) Not estimable Total events: 0 (FLV+Lithium), 0 (FLV+Placebo) Test for heterogeneity: not applicable Test for overall effect: not applicable Total (95% CI) 14 0.82 [0.62, 1.08] Total events: 14 (FLV+Lithium), 14 (FLV+Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.41 (P = 0.16) 0.5 0.7 1.5 Favours augmentation Favours non-aug OCD: augmentation strategies Review: 06 Lithium vs placebo Comparison: 02 Y-BOCS change score Outcome Study FLV+Lithium FLV+Placebo SMD (fixed) SMD (fixed) Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI or sub-category 01 FLV+Lithium v FLV+Placebo at 2 weeks McDougle 1991 (1) 11 -4.00(5.23) 1.22(5.24) -0.96 [-1.90, -0.01] Subtotal (95% CI) 11 -0.96 [-1.90, -0.01] Test for heterogeneity: not applicable Test for overall effect: Z = 1.99 (P = 0.05) 02 FLV+Lithium v FLV+Placebo at 4 weeks McDougle 1991 (2) 2.60(3.58) -1.40(2.07) 1.24 [-0.19, 2.66] Subtotal (95% CI) 1.24 [-0.19, 2.66] Test for heterogeneity: not applicable Test for overall effect: Z = 1.70 (P = 0.09) -0.29 [-1.07, 0.50] Test for heterogeneity: Chi² = 6.34, df = 1 (P = 0.01), l² = 84.2% Test for overall effect: Z = 0.72 (P = 0.47) Favours augmentation Favours non-aug OCD: augmentation strategies Review: Comparison: 06 Lithium vs placebo Outcome 03 Hamilton Depression Scale change score FLV+Placebo SMD (fixed) SMD (fixed) Study FLV+Lithium N 95% CI or sub-category Mean (SD) Mean (SD) 95% CI 01 FLV+Lithium v FLV+Placebo at 2 weeks McDougle 1991 (1) 1.1 -7.00(8.81) 0.00(9.06) -0.75 [-1.67, 0.17] Subtotal (95% CI) -0.75 [-1.67, 0.17] Test for heterogeneity: not applicable Test for overall effect: Z = 1.60 (P = 0.11) 02 FLV+Lithium v FLV+Placebo at 4 weeks McDougle 1991 (2) 4.60(6.15) -3.40(4.28) 1.36 [-0.09, 2.82] Subtotal (95% CI) 1.36 [-0.09, 2.82] Test for heterogeneity: not applicable Test for overall effect: Z = 1.83 (P = 0.07) Total (95% CI) -0.15 [-0.93, 0.63] Test for heterogeneity: $Chi^2 = 5.79$, df = 1 (P = 0.02), $I^2 = 82.7\%$ Test for overall effect: Z = 0.38 (P = 0.70)

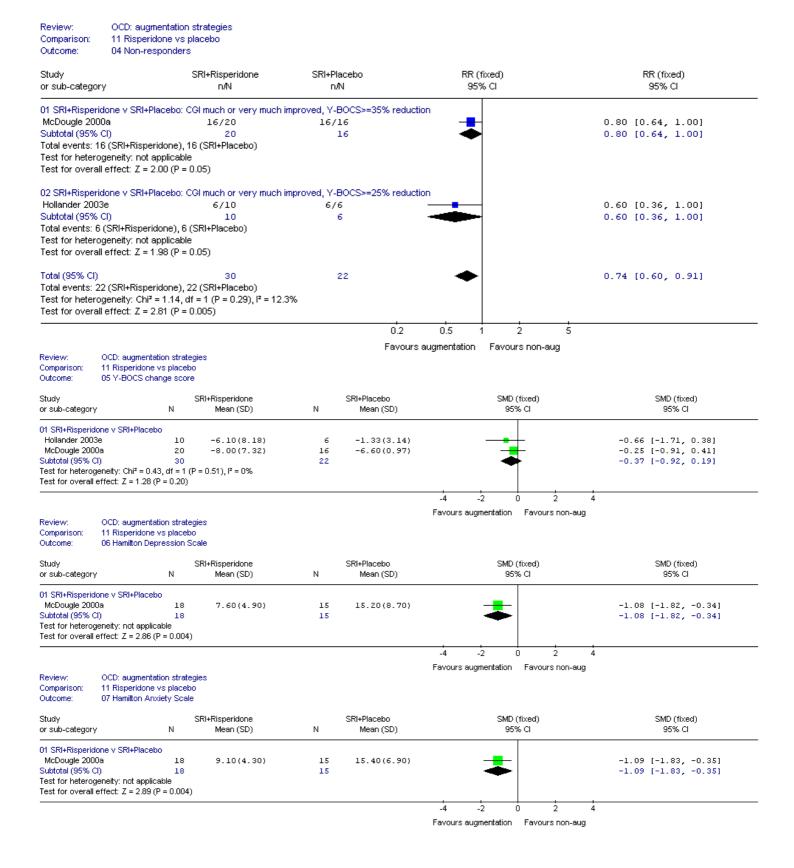
Favours augmentation Favours non-aug











Review: OCD: augmentation strategies Comparison: 12 All antipsychotics v placebo
Outcome: 01 Adverse effects

Outcome:

Study or sub-category	Augmentation n/N	non-augmentation n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 SRI+Quetiapine v SRI+Pla	acebo			
Atmaca 2002	9/14	4/13	 	2.09 [0.85, 5.16]
Subtotal (95% CI)	14	13		2.09 [0.85, 5.16]
Total events: 9 (Augmentati	ion), 4 (non-augmentation)			
Test for heterogeneity: not	applicable			
Test for overall effect: Z =	1.60 (P = 0.11)			
02 SRI+Risperidone v SRI+F	Placebo			
Hollander 2003e	4/10	2/6		1.20 [0.31, 4.69]
McDougle 2000a	18/20	15/16	-	0.96 [0.79, 1.16]
Subtotal (95% CI)	30	22	•	0.99 [0.77, 1.28]
Total events: 22 (Augments	ation), 17 (non-augmentation)			
Test for heterogeneity: Chi ²	$l^2 = 0.18$, df = 1 (P = 0.67), $l^2 = 0\%$,		
Test for overall effect: Z = I	0.07 (P = 0.95)			
Total (95% CI)	44	35	•	1.19 [0.89, 1.58]
Total events: 31 (Augments	ation), 21 (non-augmentation)			·
Test for heterogeneity: Chi ²	$l^2 = 6.13$, df = 2 (P = 0.05), $l^2 = 67$.	3%		
Test for overall effect: Z =				
			0.1 0.2 0.5 1 2 5	10
		F	avours augmentation Favours non-au	g

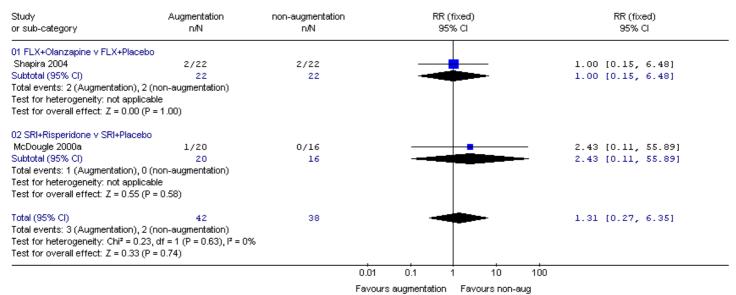
Review: OCD: augmentation strategies 12 All antipsychotics v placebo 02 Leaving the study early Comparison: Outcome:

Study or sub-category	Augmentation non- tegory n/N		RR (fixed) 95% Cl	RR (fixed) 95% Cl	
01 FLX+Olanzapine v FLX+Pl	laceho				
Shapira 2004	5/22	2/22		2.50 [0.54, 11.54]	
Subtotal (95% CI)	22	22		2.50 [0.54, 11.54]	
l'otal events: 5 (Augmentatio l'est for heterogeneity: not a	n), 2 (non-augmentation) pplicable			,,	
Test for overall effect: Z = 1.	.17 (P = 0.24)				
02 SRI+Quetiapine v SRI+Plac					
Atmaca 2002	0/14	0/13		Not estimable	
Subtotal (95% CI)	0	0		Not estimable	
otal events: 0 (Augmentatio					
est for heterogeneity: not a	• •				
Fest for overall effect: not ap	oplicable				
03 SRI+Risperidone v SRI+Pk	acebo				
Hollander 2003e	1/10	2/6		0.30 [0.03, 2.65]	
McDougle 2000a	2/20	1/16		1.60 [0.16, 16.10]	
ubtotal (95% CI)	30	22	-	0.70 [0.16, 3.01]	
otal events: 3 (Augmentatio	n), 3 (non-augmentation)				
est for heterogeneity: Chi² =	= 1.07, df = 1 (P = 0.30), l ² = 6.9%	•			
est for overall effect: Z = 0.	.48 (P = 0.63)				
otal (95% CI)	66	57	—	1.34 [0.49, 3.67]	
otal events: 8 (Augmentatio	n), 5 (non-augmentation)		Γ		
est for heterogeneity: Chi² =	$= 2.48$, df $= 2$ (P $= 0.29$), $I^2 = 19.3$	%			
est for overall effect: $Z = 0$.	.57 (P = 0.57)				
			0.1 1 10		

Favours augmentation Favours non-aug

Review: OCD: augmentation strategies Comparison: 12 All antipsychotics v placebo

Outcome: 03 Leaving the study early due to adverse effects

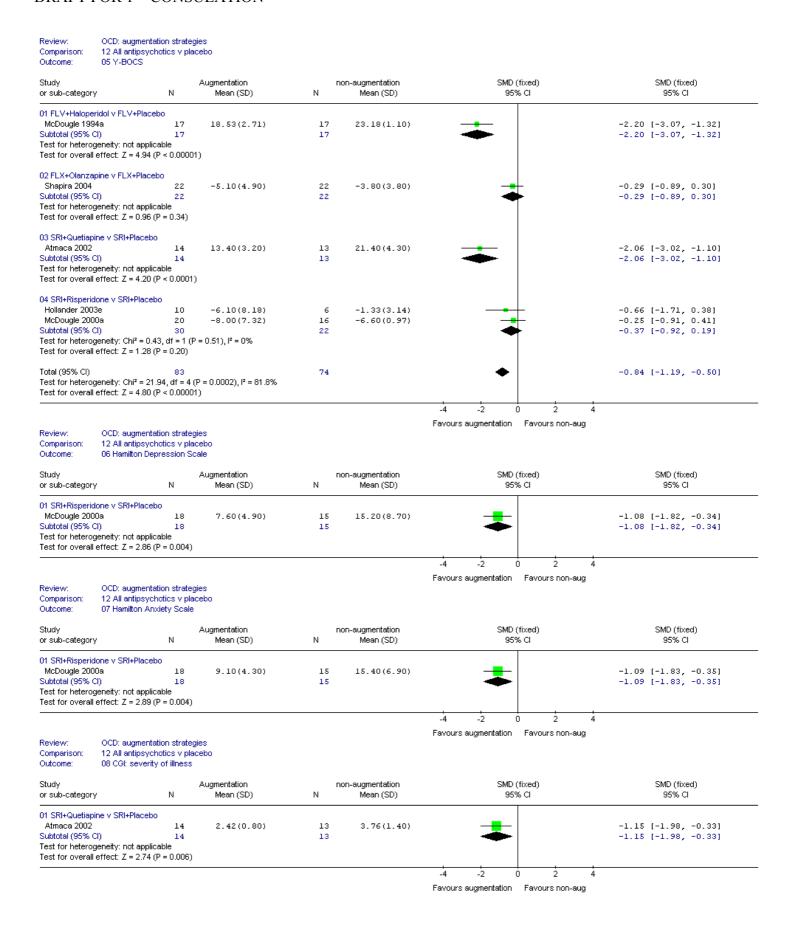


Review: OCD: augmentation strategies
Comparison: 12 All antipsychotics v placebo

Outcome: 04 Non-responders

Study or sub-category	Augmentation n/N	non-augmentation n <i>i</i> N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 FLV+Haloperidol v FLV+Plac	ebo			
McDougle 1994a	10/17	17/17		0.59 [0.40, 0.88]
Subtotal (95% CI)	17	17	◆	0.59 [0.40, 0.88]
Total events: 10 (Augmentation)	ı, 17 (non-augmentation)			
Test for heterogeneity: not appli				
Test for overall effect: $Z = 2.61$	(P = 0.009)			
02 FLX+Olanzapine v FLX+Place	ebo			
Shapira 2004	13/22	13/22		1.00 [0.61, 1.64]
Subtotal (95% CI)	22	22	-	1.00 [0.61, 1.64]
Total events: 13 (Augmentation)	ı, 13 (non-augmentation)		Ī	
Test for heterogeneity: not appli				
Test for overall effect: $Z = 0.00$	(P = 1.00)			
03 SRI+Quetiapine v SRI+Placeb	10			
Atmaca 2002	4/14	13/13 —		0.29 [0.12, 0.65]
Subtotal (95% CI)	14	13		0.29 [0.12, 0.65]
Total events: 4 (Augmentation),	, , ,			
Test for heterogeneity: not appli				
Test for overall effect: $Z = 2.96$	(P = 0.003)			
04 SRI+Risperidone v SRI+Place	bo			
Hollander 2003e	6/10	6/6		0.60 [0.36, 1.00]
McDougle 2000a	16/20	16/16	-	0.80 [0.64, 1.00]
Subtotal (95% CI)	30	22	◆	0.74 [0.60, 0.91]
Total events: 22 (Augmentation)				
Test for heterogeneity: Chi ² = 1.		3%		
Test for overall effect: $Z = 2.81$	(P = 0.005)			
Total (95% CI)	83	74	•	0.66 [0.54, 0.81]
Total events: 49 (Augmentation)	i, 65 (non-augmentation)		·	
Test for heterogeneity: Chi ² = 9.		9%		
Test for overall effect: $Z = 4.05$	(P < 0.0001)			
		0.1	0.2 0.5 1 2 5	10

Favours augmentation Favours non-aug



SSRIs (OCD, children) Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase)

Outcome: 01 Adverse events

Study	SSRI	Placebo	RR (fixed)	RR (fixed)
or sub-category	n/N	n/N	95% CI	95% CI
01 Fluoxetine				
Geller 2001	53/71	27/32		0.88 [0.72, 1.08]
Liebowitz 2002	21/21	19/22		1.16 [0.98, 1.37]
Subtotal (95% CI)	92	54	-	0.98 [0.85, 1.12]
Fotal events: 74 (SSRI), 46 (PI	lacebo)			
Test for heterogeneity: Chi² =	4.99 , $df = 1 (P = 0.03)$, $I^2 = 80$	1.0%		
Test for overall effect: $Z = 0.3$	34 (P = 0.73)			
02 Fluvoxamine				
Riddle 2001	48/57	48/63	 -	1.11 [0.93, 1.32]
Subtotal (95% CI)	57	63		1.11 [0.93, 1.32]
fotal events: 48 (SSRI), 48 (PI	lacebo)		-	·
Test for heterogeneity: not ap				
Test for overall effect: $Z = 1.1$	10 (P = 0.27)			
03 Paroxetine				
Geller 2004	83/98	77/105	——	1.15 [1.00, 1.33]
Subtotal (95% CI)	98	105	-	1.15 [1.00, 1.33]
fotal events: 83 (SSRI), 77 (PI	lacebo)			
Test for heterogeneity: not ap	plicable			
Test for overall effect: $Z = 1.9$	98 (P = 0.05)			
Fotal (95% CI)	247	222	•	1.09 [0.99, 1.19]
Total events: 205 (SSRI), 171	(Placebo)		•	•
Fest for heterogeneity: Chi² =	5.30, df = 3 (P = 0.15), I^2 = 43	3.4%		
Test for overall effect: $Z = 1.8$	30 (P = 0.07)			
		0.5	0.7 1 1.5	2
			Favours SSRI Favours Placeb	0

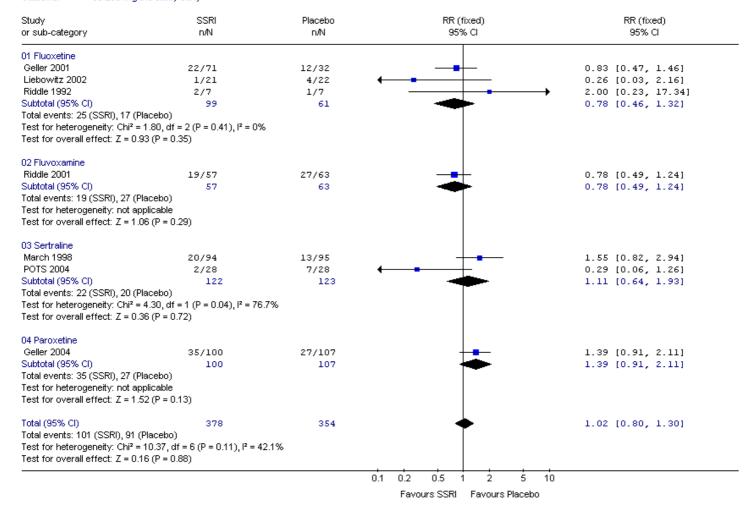
Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase)

Outcome: 02 Serious adverse events

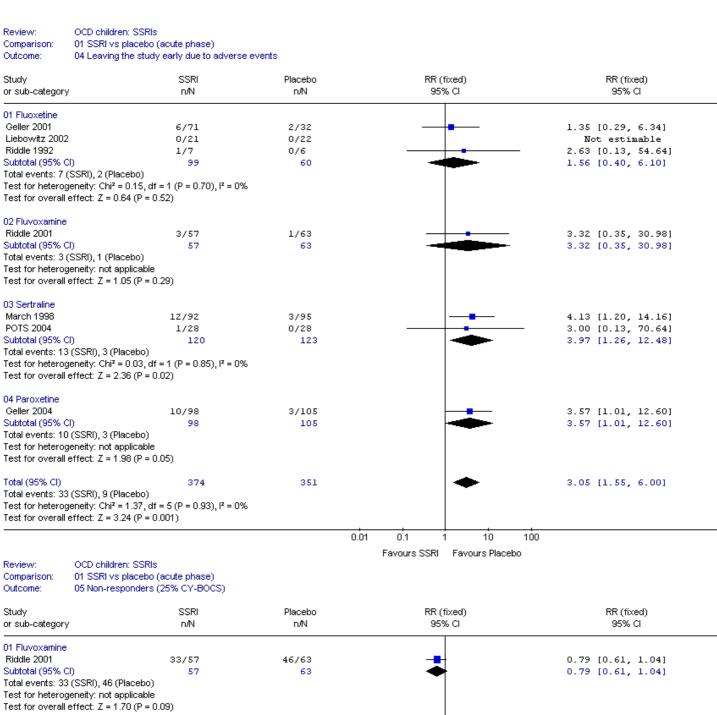
Study or sub-category			RR (fixed) 95% Cl	RR (fixed) 95% Cl	
01 Paroxetine					
Geller 2004	3/98	1/105		3.21 [0.34, 30.39]	
Subtotal (95% CI)	98	105	-	3.21 [0.34, 30.39]	
Total events: 3 (SSRI), 1 (Placebo)				•	
est for heterogeneity: not applicable					
est for overall effect: Z = 1.02 (P = 0.31)					
Fotal (95% CI)	98	105		3.21 [0.34, 30.39]	
otal events: 3 (SSRI), 1 (Placebo)					
est for heterogeneity; not applicable					
Fest for overall effect: Z = 1.02 (P = 0.31)					
		0.	01 0.1 1 10 1	00	
			Favours SSRI Favours Placebo		

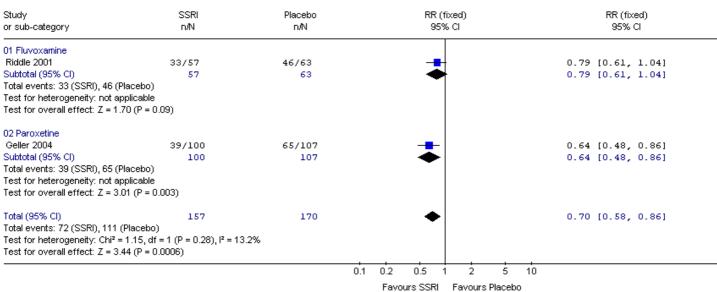
Review: OCD children: SSRIs

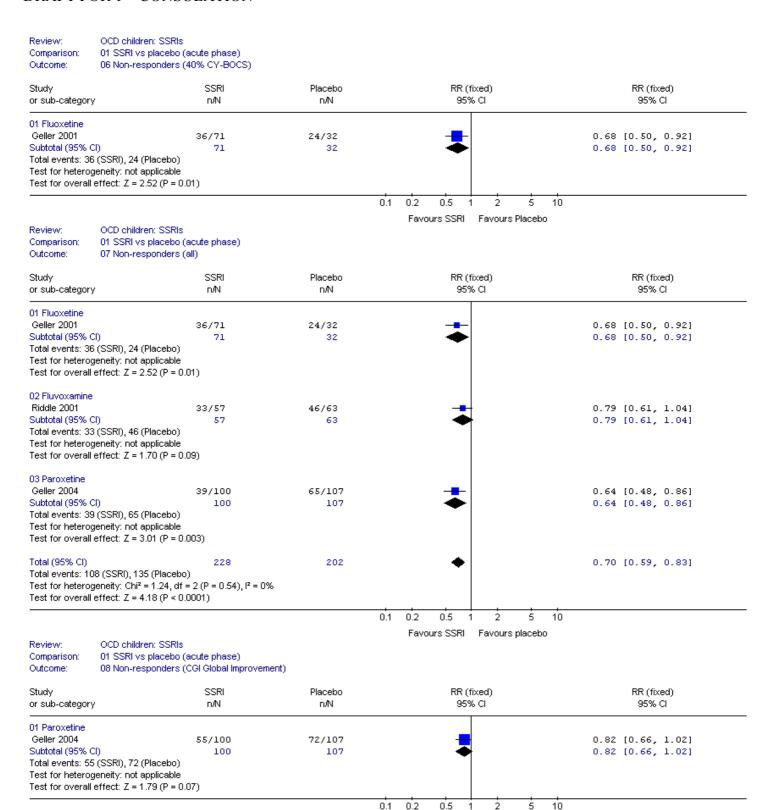
Comparison: 01 SSRI vs placebo (acute phase)
Outcome: 03 Leaving the study early



DRAFT FOR 1ST CONSULATION







Favours SSRI

Favours Placebo

Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) Outcome: 09 Remission (CY-BOCS < 11) Sertraline Placebo RR (fixed) RR (fixed) Study 95% CI or sub-category nΝ n/Ν 95% CI 01 Sertraline POTS 2004 22/28 27/28 0.81 [0.66, 1.00] Subtotal (95% CI) 28 28 0.81 [0.66, 1.00] Total events: 22 (Sertraline), 27 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.95 (P = 0.05) 0.1 0.2 0.5 2 5 Favours Sertraline Favours Placebo OCD children; SSRIs Review 01 SSRI vs placebo (acute phase) Comparison: 10 CY-BOCS Outcome: Study SSRI Placebo SMD (fixed) SMD (fixed) N Mean (SD) Ν or sub-category Mean (SD) 95% CI 95% CI 01 Fluoxetine Geller 2001 71 -9.50(9.20) 32 -5.20(7.40) -0.49 [-0.91, -0.07] Liebowitz 2002 21 14.71(8.73) 22 18.55(11.44) -0.37 [-0.97, 0.23] -0.18 [-1.27, 0.92] Riddle 1992 13.60(5.70) 6 14.80(7.00) Subtotal (95% CI) 99 60 -0.43 [-0.76, -0.10] Test for heterogeneity: $Chi^2 = 0.33$, df = 2 (P = 0.85), $I^2 = 0\%$ Test for overall effect: Z = 2.53 (P = 0.01) 02 Fluvoxamine Riddle 2001 57 18.20(8.60) 63 20.90(8.50) -0.31 [-0.67, 0.05] Subtotal (95% CD) 57 63 -0.31 [-0.67, 0.05] Test for heterogeneity: not applicable Test for overall effect: Z = 1.71 (P = 0.09) 03 Sertraline -0.41 [-0.70, -0.12] -0.66 [-1.20, -0.12] March 1998 92 -6.80(8.35) 95 -3.40(8.00) POTS 2004 28 16.50(9.10) 28 21.50(5.40) Subtotal (95% CI) 120 123 -0.47 [-0.72, -0.21] Test for heterogeneity: $Chi^2 = 0.61$, df = 1 (P = 0.43), $I^2 = 0\%$ Test for overall effect: Z = 3.60 (P = 0.0003) 04 Paroxetine Geller 2004 -8.78(7.65) 102 -5.34(7.78) -0.44 [-0.73, -0.16] Subtotal (95% CI) 94 102 -0.44 [-0.73, -0.16] Test for heterogeneity: not applicable Test for overall effect: Z = 3.07 (P = 0.002) Total (95% CI) 348 -0.43 [-0.58, -0.28] Test for heterogeneity: Chi² = 1.44, df = 6 (P = 0.96), l² = 0% Test for overall effect: Z = 5.59 (P < 0.00001) -0.5 0.5 Ó Favours SSRI Favours Placebo Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) 11 NIMH-OC Outcome

Study		SSRI		Placebo	SMD (fixed)	SMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% Cl	95% CI
01 Fluoxetine						
Geller 2001	71	-3.10(3.00)	32	-1.30(2.20)		-0.64 [-1.07, -0.22]
Liebowitz 2002	21	6.24(2.45)	22	7.18(2.75)		-0.35 [-0.96, 0.25]
Subtotal (95% CI)	92		54			-0.55 [-0.89, -0.20]
Test for heterogeneity: Ch	i ² = 0.59, df = 1 (P	= 0.44), I ² = 0%			_	
Test for overall effect: Z =	3.07 (P = 0.002)					
02 Fluvoxamine						
Riddle 2001	57	7.50(3.20)	63	8.30(2.60)		-0.27 [-0.63, 0.09]
Subtotal (95% CI)	57		63			-0.27 [-0.63, 0.09]
Test for heterogeneity: not	t applicable				_	
Test for overall effect: Z =	1.49 (P = 0.14)					
03 Sertraline						
March 1998	92	-2.20(2.78)	95	-1.30(2.63)		-0.33 [-0.62, -0.04]
Subtotal (95% CI)	92		95			-0.33 [-0.62, -0.04]
Test for heterogeneity: not	t applicable					
Test for overall effect: Z =	2.25 (P = 0.02)					
Total (95% CI)	241		212		•	-0.38 [-0.57, -0.19]
Test for heterogeneity: Ch	i ² = 1.91, df = 3 (P	= 0.59), I ² = 0%			-	·
Test for overall effect: Z =						
					-1 -0.5 0 0.5	+
					Favours SSRI Favours Pl	acebo

Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) Outcome 12 Child Obsessive Compulsive Impact Scale (Parent Version) SMD (fixed) SMD (fixed) Study Placebo or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine Liebowitz 2002 21 38.44(30.43) 22 53.95(41.97) -0.41 [-1.02, 0.19] Subtotal (95% CI) 21 22 -0.41 [-1.02, 0.19] Test for heterogeneity: not applicable Test for overall effect: Z = 1.34 (P = 0.18) ò Favours SSRI Favours Placebo OCD children; SSRIs Review: 01 SSRI vs placebo (acute phase) Comparison 13 Leyton Obsessional Inventory (Child Version): interference SMD (fixed) SMD (fixed) Study SSRI Placebo Mean (SD) or sub-category Ν Mean (SD) Ν 95% CI 95% CI 01 Fluoxetine Riddle 1992 20.60(19.40) 6 21.00(19.30) -0.02 [-1.11, 1.07] Subtotal (95% Ch -0.02 [-1.11, 1.07] Test for heterogeneity: not applicable Test for overall effect: Z = 0.03 (P = 0.97) Favours SSRI Favours Placebo Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) 14 Leyton Obsessional Inventory (Child Version): resistance Outcome Study SSRI Placebo SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine Riddle 1992 19.60(14.40) 22.00(23.10) -0.12 [-1.21, 0.97] Subtotal (95% CI) -0.12 [-1.21, 0.97] Test for heterogeneity; not applicable Test for overall effect: Z = 0.21 (P = 0.83) -4 -2 ń Favours SSRI Favours Placebo OCD children: SSRIs Review: Comparison: 01 SSRI vs placebo (acute phase) Outcome 15 Leyton Obsessional Inventory (Child Version): symptoms SSRI SMD (fixed) SMD (fixed) Study Placebo or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine 0.23 [-0.87, 1.32] Riddle 1992 16.30(8.40) 13.80(12.10) Subtotal (95% CI) 0.23 [-0.87, 1.32] Test for heterogeneity: not applicable Test for overall effect: Z = 0.41 (P = 0.68) Favours SSRI Favours Placebo OCD children; SSRIs Review: 01 SSRI vs placebo (acute phase) Comparison: Outcome 16 Children's Depression Rating Scale (Revised Version) SSRI SMD (fixed) SMD (fixed) Study Placebo Mean (SD) Ν Mean (SD) 95% CI 95% CI or sub-category Ν 01 Fluvoxamine Riddle 2001 57 27.40(8.00) 63 27.10(8.00) 0.04 [-0.32, 0.40] Subtotal (95% CI) 0.04 [-0.32, 0.40] 57 63 Test for heterogeneity: not applicable Test for overall effect: Z = 0.20 (P = 0.84) -0.5 0.5 0 Favours SSRI Favours Placebo Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) Outcome 17 Hamilton Rating Scale for Depression SSRI SMD (fixed) SMD (fixed) Study Placebo or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine Liebowitz 2002 21 9.14(6.56) 7.09(7.39) 0.29 [-0.31, 0.89] Subtotal (95% CI) 21 22 0.29 [-0.31, 0.89] Test for heterogeneity: not applicable Test for overall effect: Z = 0.94 (P = 0.35) -0.5 Ò 0.5

Favours SSRI Favours Placebo

Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) Outcome 18 Depression (CDRS; HRSD) SMD (fixed) SMD (fixed) Study Placebo or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine Liebowitz 2002 21 9.14(6.56) 22 7.09(7.39) 0.29 [-0.31, 0.89] Subtotal (95% CI) 21 22 0.29 [-0.31, 0.89] Test for heterogeneity: not applicable Test for overall effect: Z = 0.94 (P = 0.35) Riddle 2001 57 27.40(8.00) 63 27.10(8.00) 0.04 [-0.32, 0.40] Subtotal (95% CI) 57 63 0.04 [-0.32, 0.40] Test for heterogeneity; not applicable Test for overall effect: Z = 0.20 (P = 0.84) Total (95% CI) 85 0.10 [-0.20, 0.41] Test for heterogeneity: Chi² = 0.49, df = 1 (P = 0.48), l² = 0% Test for overall effect: Z = 0.65 (P = 0.51) -0.5 ń 0.5 Favours SSRI Favours placebo Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) Outcome 19 Multidimensional Anxiety Scale for Children SMD (fixed) SMD (fixed) Placebo or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine Geller 2001 71 -9.00(18.60) 32 -4.50(16.50) -0.25 [-0.67, 0.17] Subtotal (95% CI) -0.25 [-0.67, 0.17] Test for heterogeneity: not applicable Test for overall effect: Z = 1.16 (P = 0.24) -0.5 Ö 0.5 Favours SSRI Favours Placebo OCD children: SSRIs Review: 01 SSRI vs placebo (acute phase) Comparison: Outcome 20 Revised Children's Manifest Anxiety Scale SMD (fixed) SSRI SMD (fixed) Study Placebo Ν Mean (SD) N Mean (SD) 95% CI 95% CI or sub-category 01 Fluoxetine Riddle 1992 45.70(13.30) 40.20(16.90) 0.34 [-0.86, 1.53] Subtotal (95% CI) 0.34 [-0.86, 1.53] Test for heterogeneity: not applicable Test for overall effect: Z = 0.55 (P = 0.58) 0 Favours SSRI Favours Placebo Review: OCD children: SSRIs 01 SSRI vs placebo (acute phase) Comparison: 21 Anxiety (MASC; RCMAS) Outcome Study SSRI Placebo SMD (fixed) SMD (fixed) Mean (SD) Ν Mean (SD) or sub-category Ν 95% CI 95% CI 01 Fluoxetine Geller 2001 71 -9.00(18.60) 32 -4.50(16.50) -0.25 [-0.67, 0.17] 0.34 [-0.86, 1.53] -0.19 [-0.58, 0.21] Riddle 1992 6 45.70(13.30) 5 40.20(16.90) Subtotal (95% CI) 37 Test for heterogeneity: Chi² = 0.81, df = 1 (P = 0.37), l² = 0% Test for overall effect: Z = 0.92 (P = 0.36) -2 0 Favours SSRI Favours placebo Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) 22 Children's Global Assessment Scale Outcome Placebo SSRI SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Fluoxetine 70.40(13.20) 62.00(8.40) 0.69 [-0.44, 1.83] Subtotal (95% CI) 0.69 [-0.44, 1.83] Test for heterogeneity: not applicable Test for overall effect: Z = 1.20 (P = 0.23)

-2

Ò Favours SSRI Favours Placebo

Subtotal (95% CI)

Test for heterogeneity: not applicable Test for overall effect: Z = 0.55 (P = 0.58)

Review: OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) Outcome: 23 Systolic blood pressure - supine SMD (fixed) SMD (fixed) Study Placebo or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI 01 Sertraline v Placebo (at 1 week) March 1998 108.50(12.50) 95 107.60(10.60) 0.08 [-0.21, 0.36] Subtotal (95% CI) 95 0.08 [-0.21, 0.36] Test for heterogeneity: not applicable Test for overall effect: Z = 0.53 (P = 0.60) 02 Sertraline v Placebo (at 4 weeks) March 1998 92 108.10(12.10) 95 107.00(11.00) 0.09 [-0.19, 0.38] Subtotal (95% CI) 92 95 0.09 [-0.19, 0.38] Test for heterogeneity: not applicable Test for overall effect: Z = 0.65 (P = 0.52) 03 Sertraline v Placebo (at 12 weeks) March 1998 107.00(11.00) 92 95 107.40(10.60) -0.04 [-0.32, 0.25] Subtotal (95% CI) -0.04 [-0.32, 0.25] Test for heterogeneity: not applicable Test for overall effect: Z = 0.25 (P = 0.80) Favours sertraline Favours placebo OCD children: SSRIs. Review: 01 SSRI vs placebo (acute phase) Comparison: Outcome: 24 Systolic blood pressure - standing Study Sertraline Placebo SMD (fixed) SMD (fixed) Mean (SD) Mean (SD) Ν Ν or sub-category 95% CI 95% CI 01 Sertraline v Placebo (at 1 week) March 1998 92 108.40(11.00) 95 107.40(10.90) 0.09 [-0.20, 0.38] Subtotal (95% CI) 92 95 0.09 [-0.20, 0.38] Test for heterogeneity: not applicable Test for overall effect: Z = 0.62 (P = 0.53) 02 Sertraline v Placebo (at 4 weeks) March 1998 106.20(11.40) 107.20(11.70) -0.09 [-0.37, 0.20] 95 Subtotal (95% CI) -0.09 [-0.37, 0.20] Test for heterogeneity; not applicable Test for overall effect: Z = 0.59 (P = 0.56) 03 Sertraline v Placebo (at 12 weeks) March 1998 92 105.80(10.80) 95 107.10(10.90) -0.12 [-0.41, 0.17] -0.12 [-0.41, 0.17] Subtotal (95% Ch. 92 95 Test for heterogeneity: not applicable Test for overall effect: Z = 0.81 (P = 0.42) -10 -5 10 Ó Favours sertraline Favours placebo OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) 25 Diastolic blood pressure - supine Outcome: SMD (fixed) SMD (fixed) Placebo or sub-category Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Sertraline v Placebo (at 1 week) 64.80(8.50) 64.40(10.20) 0.04 [-0.24, 0.33] Subtotal (95% CI) 95 0.04 [-0.24, 0.33] Test for heterogeneity; not applicable Test for overall effect: Z = 0.29 (P = 0.77) 02 Sertraline v Placebo (at 4 weeks) March 1998 92 63.00(8.70) 95 63.80(9.40) -0.09 [-0.37, 0.20] Subtotal (95% CI) -0.09 [-0.37, 0.20] 92 95 Test for heterogeneity: not applicable Test for overall effect: Z = 0.60 (P = 0.55) 03 Sertraline v Placebo (at 12 weeks) March 1998 63.70(10.90) 64.50(8.80) -0.08 [-0.37, 0.21] 95

Favours sertraline Favours placebo

-0.08 [-0.37, 0.21]

03 Sertraline v Placebo (at 12 weeks)

Test for heterogeneity: not applicable Test for overall effect: Z = 0.54 (P = 0.59) 85.10(12.10)

March 1998

Subtotal (95% CI)

OCD children: SSRIs Review: Comparison: 01 SSRI vs placebo (acute phase) Outcome: 26 Diastolic blood pressure - standing SMD (fixed) SMD (fixed) Study Placebo or sub-category N Mean (SD) N Mean (SD) 95% CI 95% CI 01 Sertraline v Placebo (at 1 week) March 1998 67.60(9.40) 95 67.70(10.60) -0.01 [-0.30, 0.28] Subtotal (95% CI) 95 -0.01 [-0.30, 0.28] Test for heterogeneity: not applicable Test for overall effect: Z = 0.07 (P = 0.95) 02 Sertraline v Placebo (at 4 weeks) March 1998 92 67.20(10.60) 95 67.40(9.80) -0.02 [-0.31, 0.27] Subtotal (95% CI) 92 95 -0.02 [-0.31, 0.27] Test for heterogeneity: not applicable Test for overall effect: Z = 0.13 (P = 0.89) 03 Sertraline v Placebo (at 12 weeks) March 1998 -0.08 [-0.36, 0.21] 92 67.10(9.20) 95 67.80(8.90) Subtotal (95% CI) -0.08 [-0.36, 0.21] Test for heterogeneity: not applicable Test for overall effect: Z = 0.53 (P = 0.60) Favours sertraline Favours placebo OCD children: SSRIs. Review: 01 SSRI vs placebo (acute phase) Comparison: Outcome: 27 Heart rate - supine SMD (fixed) Study Sertraline Placebo SMD (fixed) Mean (SD) Mean (SD) Ν Ν or sub-category 95% CI 95% CI 01 Sertraline v Placebo (at 1 week) March 1998 92 75.40(12.70) 95 77.80(13.00) -0.19 [-0.47, 0.10] Subtotal (95% CI) 92 95 -0.19 [-0.47, 0.10] Test for heterogeneity: not applicable Test for overall effect: Z = 1.27 (P = 0.20) 02 Sertraline v Placebo (at 4 weeks) March 1998 76.90(11.50) 78.10(11.80) -0.10 [-0.39, 0.18] 95 Subtotal (95% CI) -0.10 [-0.39, 0.18] Test for heterogeneity; not applicable Test for overall effect: Z = 0.70 (P = 0.48)03 Sertraline v Placebo (at 12 weeks) March 1998 92 77.30(9.80) 95 78.40(13.00) -0.09 [-0.38, 0.19] -0.09 [-0.38, 0.19] Subtotal (95% Ch. 92 95 Test for heterogeneity: not applicable Test for overall effect: Z = 0.65 (P = 0.52) -10 -5 10 Ò Favours sertraline Favours placebo OCD children: SSRIs Comparison: 01 SSRI vs placebo (acute phase) 28 Heart rate - standing Outcome: Sertraline SMD (fixed) SMD (fixed) Study Placebo or sub-category Mean (SD) Ν Mean (SD) 95% CI 95% CI 01 Sertraline v Placebo (at 1 week) 81.40(13.90) 86.10(13.30) -0.34 [-0.63, -0.06] Subtotal (95% CI) 95 -0.34 [-0.63, -0.06] Test for heterogeneity: not applicable Test for overall effect: Z = 2.34 (P = 0.02) 02 Sertraline v Placebo (at 4 weeks) March 1998 92 83.90(13.80) 95 84.50(12.00) -0.05 [-0.33, 0.24] -0.05 [-0.33, 0.24] Subtotal (95% CI) 92 95 Test for heterogeneity: not applicable Test for overall effect: Z = 0.32 (P = 0.75)

Favours sertraline Favours placebo

86.20(15.30)

95

-0.08 [-0.37, 0.21]

-0.08 [-0.37, 0.21]

Review: OCD children: SSRIs

01 SSRI vs placebo (acute phase) Comparison:

29 Suicidality (Columbia reclassification - "Outcome 3: definitive suicidal behaviour/ideation") Outcome:

Study or sub-category	Treatment n/N	Control n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Fluoxetine				
Geller 2001	1/71	0/32		1.38 [0.06, 32.87]
Subtotal (95% CI)	71	32		1.38 [0.06, 32.87]
Total events: 1 (Treatment), 0 (Contro				
Test for heterogeneity: not applicable Test for overall effect: Z = 0.20 (P = 0				
rest for overall effect. Z = 0.20 (F = 0	1.04)			
02 Fluvoxamine				
Riddle 2001	2/57	0/63	-	5.52 [0.27, 112.55]
Subtotal (95% CI)	57	63		- 5.52 [0.27, 112.55]
Total events: 2 (Treatment), 0 (Contro				
Test for heterogeneity: not applicable				
Test for overall effect: $Z = 1.11$ (P = 0	1.27)			
03 Paroxetine				
Geller 2004	1/99	0/107	-	3.24 [0.13, 78.62]
Subtotal (95% CI)	99	107		3.24 [0.13, 78.62]
Fotal events: 1 (Treatment), 0 (Contro				
Test for heterogeneity: not applicable				
Test for overall effect: $Z = 0.72$ (P = 0	1.47)			
04 Sertraline				
March 1998	0/92	1/95	-	0.34 [0.01, 8.34]
Subtotal (95% CI)	92	95		0.34 [0.01, 8.34]
Fotal events: 0 (Treatment), 1 (Contro	,			
est for heterogeneity: not applicable				
est for overall effect: Z = 0.66 (P = 0).51)			
Fotal (95% CI)	319	297		1.81 [0.46, 7.13]
Total events: 4 (Treatment), 1 (Contro	l)		-	•
Test for heterogeneity: Chi² = 1.72, df	$I = 3 (P = 0.63), I^2 = 0\%$			
Test for overall effect: $Z = 0.84$ (P = 0	0.40)			
		0.0	1 0.1 1 10 1	00
			Favours treatment Favours control	

OCD children: SSRIs

Comparison: 02 SSRI vs placebo (continuation phase)

Outcome: 01 Adverse events

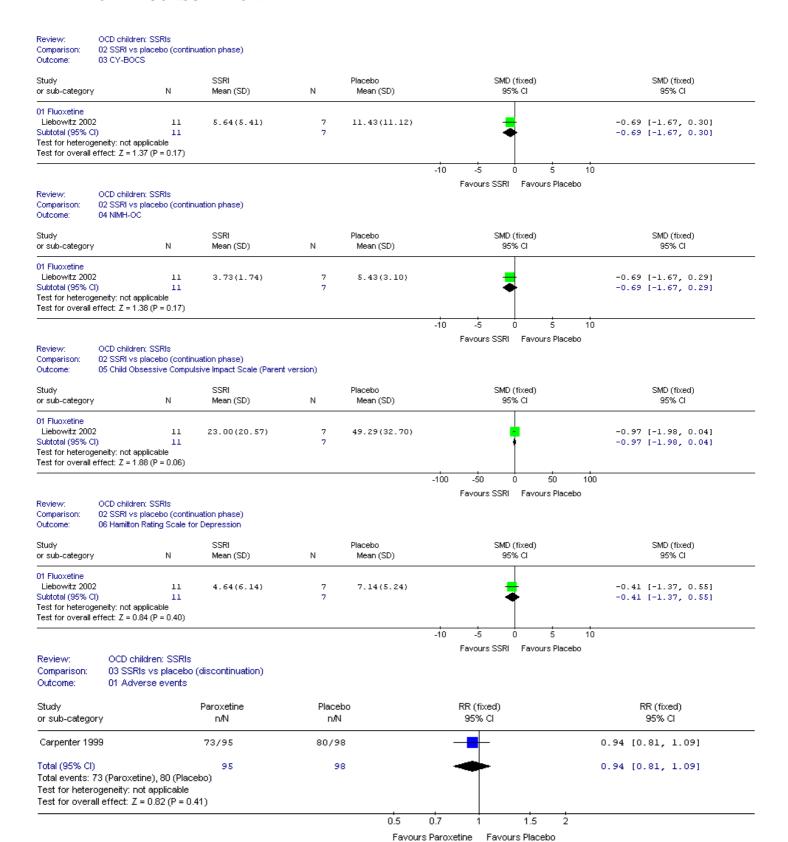
Study or sub-category	SSRI n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Fluoxetine				
Liebowitz 2002	3/11	0/7		4.67 [0.28, 78.68]
Subtotal (95% CI)	11	7		4.67 [0.28, 78.68]
Total events: 3 (SSRI), 0 (Plac	ebo)			
Test for heterogeneity: not ap	plicable			
Test for overall effect: $Z = 1.0$	07 (P = 0.29)			
		(0.01 0.1 1 10 100	
			Favours SSRI Favours Placebo	

OCD children: SSRIs Review:

Comparison: 02 SSRI vs placebo (continuation phase)

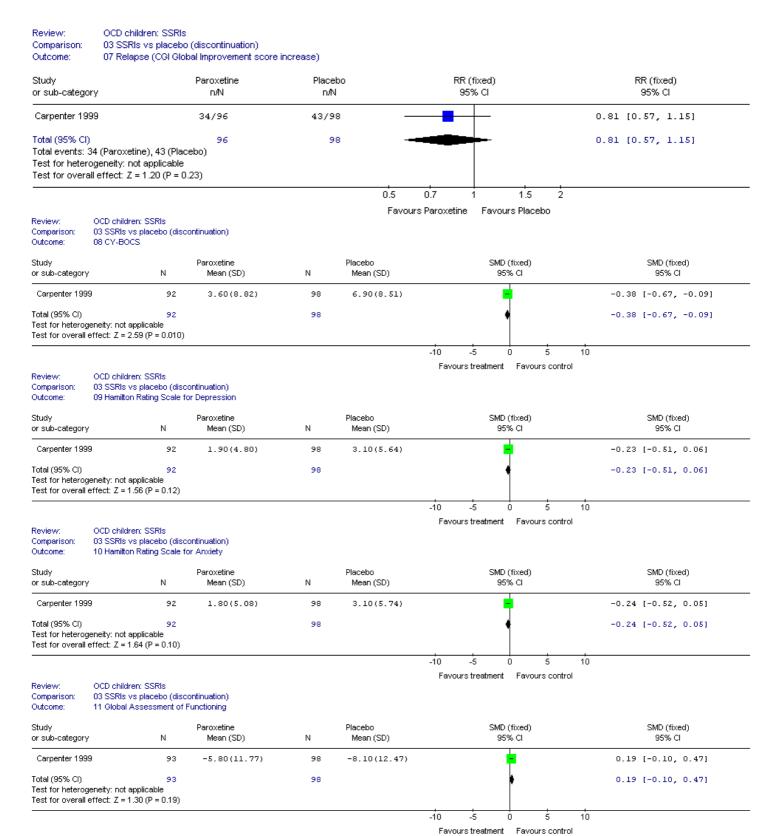
Outcome: 02 Leaving study early

Study or sub-category	SSRI n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
01 Fluoxetine				
Liebowitz 2002	1/12	0/7		1.85 [0.09, 40.05]
Subtotal (95% CI)	1/12	0/7		1.85 [0.09, 40.05]
Test for heterogeneity: not as	oplicable		T	
Test for overall effect: $Z = 0$.	39 (P = 0.70)			
		(0.01 0.1 1 10 100	1
			Favours SSRI Favours Placebo	



Review: OCD children: SSRIs Comparison: 03 SSRIs vs placebo (discontinuation) Outcome: 02 Serious adverse events Paroxetine Placebo RR (fixed) RR (fixed) Study 95% CI 95% CI or sub-category n/Ν nΝ Carpenter 1999 2/95 2/98 1.03 [0.15, 7.18] Total (95% CI) 95 98 1.03 [0.15, 7.18] Total events: 2 (Paroxetine), 2 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.03 (P = 0.97) 0.2 0.5 Favours Paroxetine Favours Placebo Review: OCD children: SSRIs 03 SSRIs vs placebo (discontinuation) Comparison: 03 Leaving the study early Outcome: Study Paroxetine RR (fixed) RR (fixed) Placebo or sub-category n/Ν n/N 95% CI 95% CI Carpenter 1999 54/96 65/98 0.85 [0.68, 1.06] Total (95% CI) 96 98 0.85 [0.68, 1.06] Total events: 54 (Paroxetine), 65 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 1.43 (P = 0.15) 0.5 0.7 1.5 ż Favours Paroxetine Favours Placebo Review: OCD children: SSRIs. Comparison: 03 SSRIs vs placebo (discontinuation) Outcome: 04 Leaving the study early due to adverse events RR (fixed) RR (fixed) Study Paroxetine Placebo 95% CI 95% CI or sub-category nΝ n/N Carpenter 1999 8/95 11/98 0.75 [0.32, 1.78] Total (95% CI) 98 0.75 [0.32, 1.78] Total events: 8 (Paroxetine), 11 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 0.65 (P = 0.52) 0.2 0.5 ż 5 10 Favours Paroxetine Favours Placebo OCD children: SSRIs Review: Comparison: 03 SSRIs vs placebo (discontinuation) Outcome: 05 Non-responders (25% CY-BOCS) Study Paroxetine Placebo RR (fixed) RR (fixed) or sub-category n/Ν n/Ν 95% CI 95% CI Carpenter 1999 72/96 85/98 0.86 [0.75, 0.99] Total (95% CI) 96 98 0.86 [0.75, 0.99] Total events: 72 (Paroxetine), 85 (Placebo) Test for heterogeneity: not applicable Test for overall effect: Z = 2.05 (P = 0.04) Favours Paroxetine Favours Placebo Review: OCD children: SSRIs Comparison: 03 SSRIs vs placebo (discontinuation) Outcome: 06 Non-responders (CGI Global Improvement < "much improved")

Study or sub-category	Paroxetine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
Carpenter 1999	42/96	55/98	-	0.78 [0.59, 1.04]
Total (95% CI) Total events: 42 (Paroxetine) Test for heterogeneity: not al Test for overall effect: Z = 1.	oplicable	98		0.78 [0.59, 1.04]
			.5 0.7 1 1.5 Favours Paroxetine Favours Placeb	2



Clomipramine (OCD, children)

OCD children: Clomipramine Review: 01 Clomipramine vs placebo Comparison: Outcome: 01 Leaving study early

Study or sub-category	Clomipramine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
DeVeaugh-Geiss 1992	4/31	2/29		1.87 [0.37, 9.46]
March 1990	2/8	0/8	-	— 5.00 [0.28, 90.18]
Total (95% CI) Total events: 6 (Clomipramine),		37	-	2.48 [0.62, 9.93]
Test for heterogeneity: $Chi^2 = 0$ Test for overall effect: $Z = 1.28$, , , , ,			
		0.	01 0.1 1 10	100

Favours Clomipramine Favours Placebo

Favours Clomipramine Favours Placebo

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OCD children: Clomipramine Comparison: 01 Clomipramine vs placebo

Outcome: 02 Leaving study early due to adverse effects

Study or sub-category	Clomipramine n/N	Placebo n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl
DeVeaugh-Geiss 1992	2/31	0/29		- 4.69 [0.23, 93.70]
March 1990	1/8	0/8		3.00 [0.14, 64.26]
Total (95% CI)	39	37		3.86 [0.45, 32.80]
Total events: 3 (Clomipramine),	0 (Placebo)			
Test for heterogeneity: Chi ² = 0	0.04 , df = 1 (P = 0.84), I^2 = 0%			
Test for overall effect: $Z = 1.24$	4 (P = 0.22)			

OCD children: Clomipramine Review: Comparison: 01 Clomipramine vs placebo

03 Y-BOCS

Study or sub-category	N	Clomipramine Mean (SD)	N	Placebo Mean (SD)			ID (fixed) 95% CI			D (fixed) 95% Cl
March 1990	8	19.30(8.60)	8	25.60(2.40)		-	+		-0.94 [-1	.99, 0.11]
Total (95% CI) Test for heterogeneity: not ap Test for overall effect: Z = 1.7			8		,	~			-0.94 [-1	.99, 0.11]
					-4	-2	Ó	2	4	

OCD children: Clomipramine 01 Clomipramine vs placebo 04 NIMH-OC

Comparison: Outcome:

Study or sub-category	N	Clomipramine Mean (SD)	N	Placebo Mean (SD)		SMD (fixed 95% CI)	SMD (fixed) 95% Cl
March 1990	8	7.20(2.70)	8	9.50(1.90)		-		-0.93 [-1.98, 0.12]
Total (95% CI) Test for heterogeneity: not a Test for overall effect: Z = 1			8		,			-0.93 [-1.98, 0.12]
					-4	-2 0	2	4

Review: OCD children: Clomipramine

Comparison: 02 Clomipramine continuation vs Desipramine substitution

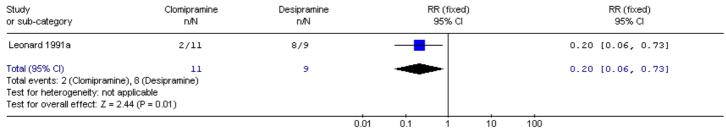
01 Leaving study early Outcome:

Study or sub-category	Clomipramine n <i>i</i> N	Desipramine n/N	RR (fixed) 95% Cl	RR (fixed) 95% Cl		
Leonard 1991a	0/11	1/10		0.31 [0.01, 6.74]		
Total (95% CI) Total events: 0 (Clomipramin Test for heterogeneity: not a Test for overall effect: Z = 0	applicable	10		0.31 [0.01, 6.74]		
			0.01 0.1 1 10 Favours Clomipramine Favours Desipran	100		

Review: OCD children: Clomipramine

Comparison: 02 Clomipramine continuation vs Desipramine substitution

Outcome: 02 Relapse (Physician's Relapse Scale)



Favours Clomipramine Favours Desipramine

Review: OCD children: Clomipramine

Comparison: 02 Clomipramine continuation vs Desipramine substitution

Outcome: 03 Comprehensive Psychopathological Rating Scale: obsessive-compulsive

Study or sub-category	N	Clomipramine Mean (SD)	N	Desipramine Mean (SD)			(fixed) % Cl		SMD (fixed) 95% Cl
Leonard 1991a	11	5.20(4.00)	9	6.30(3.30)					-0.28 [-1.17, 0.60]
Total (95% CI) Test for heterogeneity: not a Test for overall effect: Z = 0			9		,	•	-	,	-0.28 [-1.17, 0.60]
					-4	-2	O :	2 4	1

Favours Clomipramine Favours Desipramine

Review: OCD children: Clomipramine

Comparison: 02 Clomipramine continuation vs Desipramine substitution

Outcome: 04 NIMH-OC

Study or sub-category	N	Clomipramine Mean (SD)	N	Desipramine Mean (SD)			D (fixed) 95% Cl			SMD (fixed) 95% Cl
Leonard 1991a	11	5.00(2.30)	9	5.80(0.40)		-	-			-0.44 [-1.34, 0.45]
Total (95% CI) Test for heterogeneity: not	11		9			-				-0.44 [-1.34, 0.45]
Test for overall effect: Z =										
					-4	-2	ó	2	4	

Pharmacological (BDD) Review: BDD: pharmacological interventions Comparison: 01 Fluoxetine vs placebo Outcome: 01 Adverse effects Study Fluoxetine Placebo RR (fixed) RR (fixed) or sub-category nNn/N 95% CI 95% CI Phillips 2002b 28/34 21/33 1.29 [0.96, 1.75] Total (95% CI) 28/34 21/33 1.29 [0.96, 1.75] Test for heterogeneity: not applicable Test for overall effect: Z = 1.68 (P = 0.09) 0.5 0.7 1.5 Favours Fluoxetine Favours Placebo BDD: pharmacological interventions Review: Comparison: 01 Fluoxetine vs placebo Outcome: 02 Leaving study early Study Fluoxetine Placebo RR (fixed) RR (fixed) 95% CI 95% CI n/N n/N or sub-category Phillips 2002b 3/34 5/33 0.58 [0.15, 2.24] Total (95% CI) 3/34 5/33 0.58 [0.15, 2.24] Test for heterogeneity: not applicable Test for overall effect: Z = 0.79 (P = 0.43) 5 0.2 0.5 10 Favours Fluoxetine Favours Placebo BDD: pharmacological interventions Review: Comparison: 01 Fluoxetine vs placebo 03 Leaving study early due to adverse effects Outcome: RR (fixed) Study Fluoxetine Placebo RR (fixed) or sub-category n/N n/N 95% CI 95% CI Phillips 2002b 0/34 0/33 Not estimable Total (95% CI) 0/0 0/0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 0.1 0.2 0.5 ż 5 10 Favours Fluoxetine Favours Placebo Review: BDD: pharmacological interventions Comparison: 01 Fluoxetine vs placebo Outcome: 04 Non-responders Study Fluoxetine Placebo RR (fixed) RR (fixed) 95% CI 95% CI or sub-category n/Ν n/N Phillips 2002b 16/34 27/33 0.58 [0.39, 0.85] Total (95% CI) 27/33 0.58 [0.39, 0.85] 16/34 Test for heterogeneity: not applicable Test for overall effect: Z = 2.77 (P = 0.006) 0.2 0.5 Favours Fluoxetine Favours Placebo BDD: pharmacological interventions Review 01 Fluoxetine vs placebo Comparison: 05 BDD-YBOCS Outcome: Study Fluoxetine Placebo SMD (fixed) SMD (fixed) Ν Ν Mean (SD) Mean (SD) 95% CI 95% CI or sub-category Phillips 2002b 21.00(9.80) 33 26.90(9.50) -0.60 [-1.09, -0.11] -0.60 [-1.09, -0.11] Total (95% CI) 33 Test for heterogeneity: not applicable Test for overall effect: Z = 2.41 (P = 0.02)

Favours Fluoxetine

Favours Placebo

Review: BDD: pharmacological interventions Comparison 01 Fluoxetine vs placebo Outcome 06 BDD-NIMH SMD (fixed) Study Fluoxetine Placebo SMD (fixed) or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI Phillips 2002b 6.60(3.00) 33 7.90(2.20) -0.49 [-0.97, 0.00] 34 Total (95% CI) 33 -0.49 [-0.97, 0.00] Test for heterogeneity: not applicable Test for overall effect; Z = 1.96 (P = 0.05) -0.5 ò 0.5 Favours Fluoxetine Favours Placebo BDD: pharmacological interventions Review: Comparison 01 Fluoxetine vs placebo 07 Hamilton Rating Scale for Depression Outcome SMD (fixed) SMD (fixed) Study Fluoxetine Placebo 95% CI or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI Phillips 2002b 12.50(10.10) 33 19.50(10.50) -0.67 [-1.16, -0.18] Total (95% CI) 33 -0.67 [-1.16] -0.181 Test for heterogeneity: not applicable Test for overall effect: Z = 2.67 (P = 0.008) -2 0 Favours Fluoxetine Favours Placebo Review: BDD: pharmacological interventions Comparison: 01 Fluoxetine vs placebo Outcome 08 Global Assessment of Functioning Scale Study Fluoxetine Placebo SMD (fixed) SMD (fixed) or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI Phillips 2002b -68.90(15.70) 33 -57.00(12.30) -0.83 [-1.33, -0.33] Total (95% CI) 33 -0.83 [-1.33, -0.33] Test for heterogeneity; not applicable Test for overall effect: Z = 3.26 (P = 0.001) -2 ń Favours Placebo Favours Fluoxetine BDD: pharmacological interventions Review: Comparison: 01 Fluoxetine vs placebo Outcome 09 Social & Occupational Functioning Scale Fluoxetine SMD (fixed) SMD (fixed) Study Placebo or sub-category Ν Mean (SD) Ν Mean (SD) 95% CI 95% CI Phillips 2002b -0.68 [-1.17, -0.19] 34 -71.10(17.80) 33 -59.90(14.60) Total (95% CI) 33 -0.68 [-1.17, -0.19] Test for heterogeneity: not applicable Test for overall effect: Z = 2.70 (P = 0.007)Favours Fluoxetine Favours Placebo BDD: pharmacological interventions Review: 02 Clomipramine v Desipramine Comparison 01 BDD-YBOCS at 8 weeks Outcome SMD (fixed) SMD (fixed) Study Clomipramine Desipramine Ν 95% CI or sub-category Ν Mean (SD) Mean (SD) 95% CI Hollander 1999 12 17.41(6.85) 11 23.14(7.86) -0.75 [-1.60, 0.10] Total (95% CI) 11 -0.75 [-1.60. 0.10] Test for heterogeneity: not applicable Test for overall effect: Z = 1.73 (P = 0.08) -4 0 Favours CMI Favours DMI Review: BDD: pharmacological interventions Comparison: 02 Clomipramine v Desipramine 02 NIMH-BDD at 8 weeks Outcome Clomipramine Desipramine SMD (fixed) SMD (fixed) Study or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI Hollander 1999 5.92(1.83) 9.09(2.35) -1.46 [-2.40, -0.52] 12 11 Total (95% CI) 11 -1.46 [-2.40, -0.52] Test for heterogeneity: not applicable Test for overall effect: Z = 3.04 (P = 0.002) -4 -2 Ò ż 4

Favours CMI Favours DMI

BDD: pharmacological interventions Review: Comparison: 02 Clomipramine v Desipramine Outcome: 03 HAM-D at 8 weeks

SMD (fixed) SMD (fixed) Study Clomipramine Desipramine or sub-category N Mean (SD) Ν Mean (SD) 95% CI 95% CI 9.42(7.89) Hollander 1999 12 11 14.64(5.61) -0.73 [-1.58, 0.12] Total (95% CI) 11 -0.73 [-1.58, 0.12] Test for heterogeneity: not applicable Test for overall effect: Z = 1.68 (P = 0.09)Ó

Favours CMI Favours DMI

Favours Placebo

Favours Placebo

Favours Pimozide Favours Placebo

Review: BDD: pharmacological interventions

Comparison: 03 Pimozide v Placebo

Outcome: 01 Non-responders (Y-BOCS 30%)

Study or sub-category	Pimozide n/N	Placebo n/N		(fixed) 5% Cl		RR (fixed) 95% Cl
Phillips_in press	9/11	14/17	_	+	(0.99 [0.70, 1.42]
Total (95% CI) Test for heterogeneity: not ap Test for overall effect: Z = 0.0	•	14/17		+		0.99 [0.70, 1.42]
		0.2	0.5	1 2	5	

Favours Pimozide

Favours Pimozide

Review: BDD: pharmacological interventions

03 Pimozide v Placebo Comparison: 02 Leaving the study early Outcome:

RR (fixed) RR (fixed) Study Pimozide Placebo or sub-category $n /\!\! N$ n/N 95% CI 95% CI Phillips_in press 6/11 13/17 0.71 [0.39, 1.30] Total (95% CI) 6/11 13/17 0.71 [0.39, 1.30] Test for heterogeneity: not applicable Test for overall effect: Z = 1.10 (P = 0.27)0.2 0.5 5

Review: BDD: pharmacological interventions

Comparison: 03 Pimozide v Placebo

Outcome 03 Y-BOCS

Study or sub-category	N	Pimozide Mean (SD)	N	Placebo Mean (SD)			D (random 95% Cl)		VVMD (random) 95% Cl
Phillips_in press	11	23.90(6.60)	17	28.00(7.80)		-	+			-4.10 [-9.48, 1.28]
Total (95% CI) Test for heterogeneity: not Test for overall effect: Z =			17				-			-4.10 [-9.48, 1.28]
					-10	-5	0	5	10	

BDD: pharmacological interventions 03 Pimozide v Placebo Review:

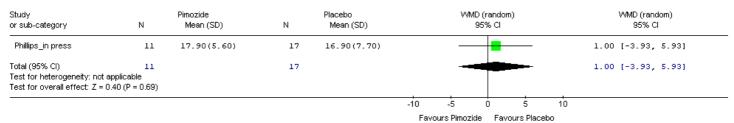
Comparison:

Outcome 04 Brown Assessment of Beliefs Scale

Study or sub-category	N	Pimozide Mean (SD)	N	Placebo Mean (SD)	WMD (random) 95% Cl	WMD (random) 95% Cl
Phillips_in press	11	13.50(7.30)	17	17.20(6.00)		-3.70 [-8.87, 1.47]
Total (95% CI) Test for heterogeneity: not Test for overall effect: Z =	• •		17			-3.70 [-8.87, 1.47]
					-10 -5 0 5 Favours Pimozide Favours Placebo	10

Review: BDD: pharmacological interventions Comparison: 03 Pimozide v Placebo

05 Hamilton Depression Rating Scale Outcome:



BDD: pharmacological interventions 03 Pimozide v Placebo Review:

Comparison: Outcome 06 Brief Psychiatric Rating Scale

