Author(s): Rachel Burbeck
Date: 2008-07-18
Question: Should duloxetine vs placebo be used for MDD (acute phase)?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	duloxetine	placebo	Relative (95% CI)	Absolute	Quality	
Mean change scores at endpoint - data for doses above licensed dose (60 mg) - Sensitivity analysis: 60 mg (measured with: HAMD-17; range of scores: 0-52; Better indicated by lower values)												
4	randomised trials	no serious limitations	no serious inconsistency	serious[1]	no serious imprecision	none	729	511	-	MD 1.85 lower (2.71 to 0.98 lower)	⊕⊕⊕O MODERATE	
Mean change scores at endpoint - data for doses above licensed dose (60 mg) - 80 mg (Better indicated by lower values)												
4	randomised trials	no serious limitations	no serious inconsistency	serious[2]	no serious imprecision	none	353	369	-	MD 1.97 lower (2.83 to 1.11 lower)	⊕⊕⊕O MODERATE	
Mean change scores at endpoint - data for doses above licensed dose (60 mg) - 120 mg (Better indicated by lower values)												
3	randomised trials	no serious limitations	no serious inconsistency	serious[3]	no serious imprecision	none	261	260	-	MD 2.57 lower (3.77 to 1.37 lower)	⊕⊕⊕O MODERATE	
Mean change scores at endpoint - data for doses above licensed dose (60 mg) - 40 mg - 120 mg (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[4]	very serious[5]	none	81	72	-	MD 0.9 lower (3.08 lower to 1.28 higher)	⊕OOO VERY LOW	
Mean change scores at endpoint - overall (Better indicated by lower values)												
10	randomised trials	no serious limitations	no serious inconsistency	serious[6]	no serious imprecision	none	1229	1020	-	MD 1.9 lower (2.44 to 1.35 lower)	⊕⊕⊕O MODERATE	
Non-response - data for doses above licensed dose (60 mg) - 60 mg (HAMD < 50% reduction)												
6	randomised trials	no serious limitations	no serious inconsistency	serious[7]	no serious imprecision	none	589/1034 (57%)	565/808 (69.9%)	RR 0.8 (0.73 to 0.88)	14 fewer per 100 (from 8 fewer to 19 fewer)	⊕⊕⊕O MODERATE	
Non-response - data for doses above licensed dose (60 mg) - 80 mg (HAMD < 50% reduction)												
4	randomised trials	no serious limitations	no serious inconsistency	serious[8]	serious[9]	none	235/566 (41.5%)	228/371 (61.5%)	RR 0.74 (0.6 to 0.9)	16 fewer per 100 (from 6 fewer to 25 fewer)	⊕⊕OO LOW	
Non-response - data for doses above licensed dose (60 mg) - 120 mg (HAMD < 50% reduction)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[10]	very serious[11]	none	38/70 (54.3%)	45/70 (64.3%)	RR 0.84 (0.64 to 1.11)	10 fewer per 100 (from 23 fewer to 7 more)	⊕OOO VERY LOW	
Non-response - data for doses above licensed dose (60 mg) - 40 mg - 120 mg (HAMD < 50% reduction)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[12]	very serious[13]	none	42/82 (51.2%)	54/77 (70.1%)	RR 0.73 (0.57 to 0.94)	19 fewer per 100 (from 4 fewer to 30 fewer)	⊕OOO VERY LOW	
Non-response - overall (HAMD < 50% reduction)												
12	randomised trials	no serious limitations	serious[14]	serious[15]	no serious imprecision	none	904/1752 (51.6%)	892/1326 (67.3%)	RR 0.78 (0.74 to 0.83)	15 fewer per 100 (from 11 fewer to 17 fewer)	⊕⊕OO LOW	
Non-remission - data for doses above licensed dose (60 mg) - Sensitivity analysis: 60 mg												
5	randomised trials	no serious limitations	no serious inconsistency	serious[16]	no serious imprecision	none	583/893 (65.3%)	519/667 (77.8%)	RR 0.83 (0.78 to 0.89)	13 fewer per 100 (from 9 fewer to 17 fewer)	⊕⊕⊕O MODERATE	
Non-remission - data for doses above licensed dose (60 mg) - 80 mg												
4	randomised trials	no serious limitations	no serious inconsistency	serious[17]	no serious imprecision	none	213/363 (58.7%)	266/371 (71.7%)	RR 0.82 (0.74 to 0.91)	13 fewer per 100 (from 6 fewer to 19 fewer)	⊕⊕⊕O MODERATE	
Non-remission - data for doses above licensed dose (60 mg) - 40 mg - 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[18]	very serious[19]	none	50/82 (61%)	54/77 (70.1%)	RR 0.87 (0.69 to 1.09)	9 fewer per 100 (from 22 fewer to 6 more)	⊕OOO VERY LOW	
Non-remission - data for doses above licensed dose (60 mg) - 120 mg												
3	randomised trials	no serious limitations	no serious inconsistency	serious[20]	no serious imprecision	none	149/266 (56%)	183/262 (69.8%)	RR 0.8 (0.7 to 0.92)	14 fewer per 100 (from 6 fewer to 21 fewer)	⊕⊕⊕O MODERATE	
Non-remission - overall												
11	randomised trials	no serious limitations	no serious inconsistency	serious[21]	no serious imprecision	none	995/1604 (62%)	891/1185 (75.2%)	RR 0.83 (0.79 to 0.87)	13 fewer per 100 (from 10 fewer to 16 fewer)	⊕⊕⊕O MODERATE	
Depression-related pain: BPI item 5 average pain (measured with: BP item 5 average pain in last 24 hrs; range of scores: 1-11; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[22]	no serious imprecision	none	288	295	-	MD 0.74 lower (1.13 to 0.34 lower)	⊕⊕⊕O MODERATE	

[1] Selective outpatients from multiple sites
[2] As 1

[3] As 1
[4] As 1
[5] Single study; inconclusive effect size
[6] As 1
[7] As 1
[8] As 1
[9] Significant heterogeneity (> 50%) random effects model used
[10] As 1
[11] Single study; inconclusive effect size
[12] As `
[13] As 5
[14] As 9
[15] As 1
[16] As 1
[17] As 1
[18] As 1
[19] As 11
[20] As 1
[21] As 1
[22] As 1

Author(s): Rachel Burbeck
Date: 2009-07-13
Question: Should duloxetine vs placebo - acceptability and tolerability be used for MDD (acute phase)?
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Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	duloxetine	placebo - acceptability and tolerability	Relative (95% CI)	Absolute	Quality	Importance
Leaving treatment early - any reason (data by doses above licensed dose 60mg) - 60 mg												
6	randomised trials	no serious limitations	no serious inconsistency	serious[1]	no serious imprecision	none	318/1034 (30.8%)	227/808 (28.1%)	RR 1.13 (0.98 to 1.3)	4 more per 100 (from 1 fewer to 8 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - any reason (data by doses above licensed dose 60mg) - Sensitivity analysis: 80 mg												
3	randomised trials	no serious limitations	no serious inconsistency	serious[2]	very serious[3]	none	60/279 (21.5%)	68/281 (24.2%)	RR 0.88 (0.66 to 1.17)	3 fewer per 100 (from 8 fewer to 4 more)	⊕OOO VERY LOW	
Leaving treatment early - any reason (data by doses above licensed dose 60mg) - 120 mg												
3	randomised trials	no serious limitations	no serious inconsistency	serious[4]	very serious[5]	none	44/266 (16.5%)	55/262 (21%)	RR 0.79 (0.56 to 1.12)	4 fewer per 100 (from 9 fewer to 3 more)	⊕OOO VERY LOW	
Leaving treatment early - any reason (data by doses above licensed dose 60mg) - 40 mg - 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[6]	very serious[7]	none	25/82 (30.5%)	31/75 (41.3%)	RR 0.74 (0.48 to 1.13)	11 fewer per 100 (from 21 fewer to 5 more)	⊕OOO VERY LOW	
Leaving treatment early - any reason (overall)												
11	randomised trials	no serious limitations	no serious inconsistency	serious[8]	serious[9]	none	447/1661 (26.9%)	350/1234 (28.4%)	RR 1.02 (0.91 to 1.15)[10]	1 more per 100 (from 3 fewer to 4 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions (data by doses above licensed dose 60 mg) - 60 mg												
6	randomised trials	no serious limitations	serious[11]	serious[12]	no serious imprecision	none	110/1034 (10.6%)	38/808 (4.7%)	RR 2.29 (1.31 to 4)	6 more per 100 (from 1 more to 14 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions (data by doses above licensed dose 60 mg) - 80 mg												
4	randomised trials	no serious limitations	no serious inconsistency	serious[13]	no serious imprecision	none	35/363 (9.6%)	16/371 (4.3%)	RR 2.11 (1.18 to 3.76)	5 more per 100 (from 1 more to 12 more)		
Leaving treatment early - adverse reactions (data by doses above licensed dose 60 mg) - 120 mg												
3	randomised trials	no serious limitations	no serious inconsistency	serious[14]	serious[15]	none	14/266 (5.3%)	8/262 (3.1%)	RR 1.72 (0.72 to 4.07)	2 more per 100 (from 1 fewer to 9 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions (overall)												
11	randomised trials	no serious limitations	no serious inconsistency[16]	serious[17]	no serious imprecision	none	159/1663 (9.6%)	57/1249 (4.6%)	RR 2.22 (1.66 to 2.95)	6 more per 100 (from 3 more to 9 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - lack of efficacy (data by doses above licensed dose 60 mg) - 60 mg (sensitivity analysis)												
4	randomised trials	no serious limitations	no serious inconsistency	serious[18]	no serious imprecision	none	38/911 (4.2%)	60/686 (8.7%)	RR 0.30 (0.18 to 0.51)	6 fewer per 100 (from 4 fewer to 7 fewer)	⊕⊕⊕O MODERATE	
Leaving treatment early - lack of efficacy (data by doses above licensed dose 60 mg) - 80 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[19]	very serious[20]	none	6/188 (3.2%)	11/192 (5.7%)	RR 0.55 (0.21 to	3 fewer per 100 (from 5	⊕OOO VERY LOW	

									1.46)	fewer to 3 more)		
Leaving treatment early - lack of efficacy (data by doses above licensed dose 60 mg) - 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[21]	very serious[22]	none	4/196 (2%)	11/192 (5.7%)	RR 0.36 (0.12 to 1.1)	4 fewer per 100 (from 5 fewer to 1 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy (overall): sensitivity analysis												
6	randomised trials	no serious limitations	no serious inconsistency	serious[23]	no serious imprecision	none	48/1295 (3.7%)	71/878 (8.1%)	RR 0.34 (0.22 to 0.54)	5 fewer per 100 (from 4 fewer to 6 fewer)	⊕⊕⊕O MODERATE	
Number reporting side-effects (data by doses above licensed dose 60 mg) - 60 mg												
5	randomised trials	no serious limitations	serious[24]	serious[25]	no serious imprecision	none	705/893 (78.9%)	455/667 (68.2%)	RR 1.14 (1.06 to 1.23)	10 more per 100 (from 4 more to 16 more)	⊕⊕OO LOW	
Number reporting side-effects (data by doses above licensed dose 60 mg) - 120 mg												
3	randomised trials	no serious limitations	no serious inconsistency	serious[26]	no serious imprecision	none	143/266 (53.8%)	122/262 (46.6%)	RR 1.12 (0.97 to 1.28)	6 more per 100 (from 1 fewer to 13 more)	⊕⊕⊕O MODERATE	
Number reporting side-effects (data by doses above licensed dose 60 mg) - 40 mg - 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[27]	serious[28]	none	73/82 (89%)	55/75 (73.3%)	RR 1.21 (1.04 to 1.42)	15 more per 100 (from 3 more to 31 more)	⊕⊕OO LOW	
Number reporting side-effects (data by doses above licensed dose 60 mg) - 80 mg												
4	randomised trials	no serious limitations	no serious inconsistency	serious[29]	no serious imprecision	none	239/363 (65.8%)	188/371 (50.7%)	RR 1.27 (1.15 to 1.41)	14 more per 100 (from 8 more to 21 more)	⊕⊕⊕O MODERATE	
Number reporting side-effects (overall)												
10	randomised trials	no serious limitations	no serious inconsistency	serious[30]	no serious imprecision	none	1098/1534 (71.6%)	698/1113 (62.7%)	RR 1.18 (1.12 to 1.24)	11 more per 100 (from 8 more to 15 more)	⊕⊕⊕O MODERATE	
Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 60 mg (measured with: kg; Better indicated by lower values)												
3	randomised trials	no serious limitations	serious[31]	serious[32]	no serious imprecision	none	479	364	-	MD 0.49 lower (1.04 lower to 0.05 higher)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 80 mg (measured with: kg; Better indicated by lower values)												
3	randomised trials	no serious limitations	serious[33]	serious[34]	no serious imprecision	none	265	271	-	MD 0.70 lower (1.28 to 0.12 lower)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 120 mg (measured with: kg; Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[35]	serious[36]	serious[37]	none	158	159	-	MD 0.61 lower (1.72 lower to 0.49 higher)	⊕OOO VERY LOW	
Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 40 mg - 120 mg (measured with: kg; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[38]	serious[39]	none	81	72	-	MD 1.09 lower (1.71 to 0.47 lower)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint (overall) (measured with: kg ; Better indicated by lower values)												
8	randomised trials	no serious limitations	serious[40]	serious[41]	no serious imprecision	none	890	773	-	MD 0.69 lower (1 to 0.38 lower)	⊕⊕OO LOW	

[1] Selected outpatients from multiple sites
[2] As 1
[3] Inconclusive effect size
[4] As 1
[5] As 3
[6] As 1
[7] Inconsistent effect size; single study
[8] As 1
[9] Wide range of control group risks in individual studies (13% to 42%)
[10] Unlikely to be a difference
[11] Significant heterogeneity; random effects model used
[12] As 1
[13] As 1
[14] As 1
[15] Inconclusive effect size
[16]
[17] As 1
[18] As
[19] As 1
[20] As 3
[21] As 1
[22] As 3

[23] As 1
[24] As 12
[25] As 1
[26] As 1
[27] As 1
[28] Single study
[29] As 1
[30] As 1
[31] As 12
[32] As 1
[33] As 12
[34] As 1
[35] As 12
[36] As 1
[37] As 3
[38] As 1
[39] As 30
[40] As 12
[41] As 1

Author(s): Rachel Burbeck
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Question: Should duloxetine at different doses be used for MDD (acute phase)?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	duloxetine at different doses	control	Relative (95% CI)	Absolute	Quality	Importance
Mean change scores at endpoint - 30 mg vs 60 mg (measured with: HAMD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[1]	very serious[2]	none	202	198	-	MD 0.83 higher (0.43 lower to 2.09 higher)	⊕OOO VERY LOW	
Mean change scores at endpoint - 40 mg vs 80 mg (measured with: HAMD; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[3]	very serious[4]	none	174	167	-	MD 0.58 higher (0.87 lower to 2.03 higher)	⊕OOO VERY LOW	
Mean change scores at endpoint - 80 mg vs 120 mg (measured with: HAMD; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[5]	very serious[6]	none	186	195	-	MD 0.7 higher (0.28 lower to 1.68 higher)	⊕OOO VERY LOW	
Non-response - 30 mg vs 60 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[7]	no serious imprecision[8]	none	136/219 (62.1%)	278/428 (65%)	RR 0.96 (0.84 to 1.08)	3 fewer per 100 (from 10 fewer to 5 more)	⊕⊕⊕O MODERATE	
Non-response - 40 mg vs 80 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[9]	serious[10]	none	110/177 (62.1%)	103/175 (58.9%)	RR 1.05 (0.89 to 1.24)	3 more per 100 (from 6 fewer to 14 more)	⊕⊕OO LOW	
Non-response - 80 mg vs 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[11]	serious[12]	none	66/188 (35.1%)	61/196 (31.1%)	RR 1.13 (0.85 to 1.5)	4 more per 100 (from 5 fewer to 16 more)	⊕⊕OO LOW	
Non-remission - 40 mg vs 80 mg												
2	randomised trials	no serious limitations	serious[13]	serious[14]	serious[15]	none	128/177 (72.3%)	109/175 (62.3%)	RR 1.15 (0.92 to 1.44)	9 more per 100 (from 5 fewer to 27 more)	⊕OOO VERY LOW	
Non-remission - 30 mg vs 60 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[16]	no serious imprecision[17]	none	125/219 (57.1%)	252/428 (58.9%)	RR 0.97 (0.84 to 1.11)	2 fewer per 100 (from 9 fewer to 6 more)	⊕⊕⊕O MODERATE	
Non-remission - 80 mg vs 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[18]	serious[19]	none	104/188 (55.3%)	107/196 (54.6%)	RR 1.01 (0.83 to 1.23)	1 more per 100 (from 9 fewer to 13 more)	⊕⊕OO LOW	

[1] As 1
[2] As 2
[3] As 1
[4] As 2
[5] As 1
[6] Inconclusive effect size
[7] As 1
[8] As 10
[9] As 1
[10] As 8
[11] As 1
[12] As 8
[13] Significant heterogeneity; random effects model used
[14] As 1

[15] As 8
[16] As 1
[17] As 10
[18] As 1
[19] As 10

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should duloxetine at different doses - acceptability and tolerability be used for MDD (acute phase)?
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Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	duloxetine at different doses - acceptability and tolerability	control	Relative (95% CI)	Absolute	Quality	Importance
Leaving treatment early - any reason - 30 mg vs 60 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[1]	very serious[2]	none	54/219 (24.7%)	129/428 (30.1%)	RR 0.82 (0.62 to 1.07)	5 fewer per 100 (from 11 fewer to 2 more)	⊕OOO VERY LOW	
Leaving treatment early - any reason - 40 mg vs 80 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[3]		none	31/86 (36%)	41.8%	RR 0.86 (0.6 to 1.25)	59 fewer per 1000 (from 167 fewer to 104 more)		
Leaving treatment early - any reason - 80 mg vs 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[4]	serious[5]	none	22/188 (11.7%)	20/196 (10.2%)	RR 1.15 (0.65 to 2.03)	2 more per 100 (from 4 fewer to 11 more)	⊕⊕OO LOW	
Leaving treatment early - due to adverse reaction - 30 mg vs 60 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[6]	serious[7]	none	10/219 (4.6%)	42/428 (9.8%)	RR 0.47 (0.24 to 0.91)	5 fewer per 100 (from 1 fewer to 7 fewer)	⊕⊕OO LOW	
Leaving treatment early - due to adverse reaction - 40 mg vs 80 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[8]	very serious[9]	none	21/177 (11.9%)	27/175 (15.4%)	RR 0.77 (0.45 to 1.31)	4 fewer per 100 (from 8 fewer to 5 more)	⊕OOO VERY LOW	
Leaving treatment early - due to adverse reaction - 80 mg vs 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[10]	very serious[11]	none	8/188 (4.3%)	7/196 (3.6%)	RR 1.2 (0.44 to 3.24)	1 more per 100 (from 2 fewer to 8 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy - 30 mg vs 60 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[12]	very serious[13]	none	3/219 (1.4%)	6/428 (1.4%)	RR 0.98 (0.25 to 3.87)	0 fewer per 100 (from 1 fewer to 4 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy - 80 mg vs 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[14]	very serious[15]	none	6/188 (3.2%)	2.1%	RR 1.56 (0.45 to 5.44)	12 more per 1000 (from 12 fewer to 93 more)	⊕OOO VERY LOW	
No reporting side effects - 30 mg vs 60 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[16]	serious[17]	none	160/219 (73.1%)	315/428 (73.6%)	RR 0.99 (0.9 to 1.1)	1 fewer per 100 (from 7 fewer to 7 more)	⊕⊕OO LOW	
No reporting side effects - 40 mg vs 80 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[18]	no serious imprecision[19]	none	151/177 (85.3%)	151/175 (86.3%)	RR 0.99 (0.91 to 1.07)	9 fewer per 1000 (from 78 fewer to 60 more)	⊕⊕⊕O MODERATE	
No reporting side effects - 80 mg vs 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[15]	serious[20]	none	88/188 (46.8%)	81/196 (41.3%)	RR 1.12 (0.9 to 1.4)	5 more per 100 (from 4 fewer to 17 more)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint - 30 mg vs 60 mg (measured with: kg; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[21]	serious[22]	none	168	155	-	MD 0.35 lower (1 lower to 0.3 higher)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint - 40 mg vs 80 mg (measured with: kg; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[23]	serious[24]	none	158	167	-	MD 0.19 lower (0.69 lower to 0.31 higher)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint - 80 mg vs 120 mg (measured with: kg; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[25]	serious[26]	none	93	93	-	MD 0.08 lower (0.69 lower to 0.53 higher)	⊕⊕OO LOW	

[1] As 1

[2] Inconclusive effect size; single study
[3] As 1
[4] As 1
[5] Inconclusive effect size
[6] As 1
[7] Single study
[8] As 1
[9] As 7
[10] As 1
[11] As 7
[12] As 1
[13] As 4
[14] As 1
[15] As 1
[16] As 1
[17] As 11
[18] As 1
[19] Unlikely to be a difference
[20] As 7
[21] As 1
[22] As 11
[23] As 1
[24] As 7
[25] As 1
[26] As 7

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should duloxetine vs other antidepressants be used for MDD (acute phase) ?
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Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	duloxetine	other antidepressants	Relative (95% CI)	Absolute	Quality	
Mean change scores at endpoint (all data) (measured with: HAMD; Better indicated by lower values)												
12	randomised trials	no serious limitations	serious[1]	serious[2]	no serious imprecision[3]	none	1601	1544	-	MD 0.19 higher (0.44 lower to 0.81 higher)	⊕⊕OO LOW	
Mean change scores at endpoint - paroxetine (measured with: HAMD; Better indicated by lower values)												
5	randomised trials	no serious limitations	serious[4]	serious[5]	no serious imprecision	none	591	593	-	MD 0.2 lower (1.14 lower to 0.74 higher)	⊕⊕OO LOW	
Mean change scores at endpoint - fluoxetine (measured with: HAMD; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[6]	very serious[7]	none	147	70	-	MD 1.1 lower (3.03 lower to 0.83 higher)	⊕OOO VERY LOW	
Mean change scores at endpoint - escitalopram (measured with: HAMD; Better indicated by lower values)												
3	randomised trials	no serious limitations	serious[8]	serious[9]	no serious imprecision	none	545	551	-	MD 0.66 higher (0.61 lower to 1.93 higher)	⊕⊕OO LOW	
Mean change scores at endpoint - venlafaxine (measured with: HAMD; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[10]	no serious imprecision	none	318	330	-	MD 1.06 higher (0.02 lower to 2.14 higher)	⊕⊕⊕O MODERATE	
Non-response (all data)												
12	randomised trials	no serious limitations	serious[11]	serious[12]	no serious imprecision	none	805/1645 (48.9%)	718/1563 (45.9%)	RR 1.05 (0.95 to 1.17)	2 more per 100 (from 2 fewer to 8 more)	⊕⊕OO LOW	
Non-response - paroxetine												
5	randomised trials	no serious limitations	serious[13]	serious[14]	no serious imprecision[15]	none	263/601 (43.8%)	257/599 (42.9%)	RR 1.01 (0.81 to 1.26)	0 more per 100 (from 8 fewer to 11 more)	⊕⊕OO LOW	
Non-response - fluoxetine												
2	randomised trials	no serious limitations	no serious inconsistency	serious[16]	serious[17]	none	80/152 (52.6%)	37/70 (52.9%)	RR 0.99 (0.72 to 1.36)	1 fewer per 100 (from 15 fewer to 19 more)	⊕⊕OO LOW	
Non-response - escitalopram												

3	randomised trials	no serious limitations	no serious inconsistency	serious[18]	no serious imprecision	none	331/562 (58.9%)	315/557 (56.6%)	RR 1.04 (0.94 to 1.16)	2 more per 100 (from 3 fewer to 9 more)	⊕⊕⊕O MODERATE	
Non-response - venlafaxine												
2	randomised trials	no serious limitations	serious[19]	serious[20]	serious[21]	none	131/330 (39.7%)	109/337 (32.3%)	RR 1.23 (0.92 to 1.64)	7 more per 100 (from 3 fewer to 21 more)	⊕OOO VERY LOW	
Non-remission (all data)												
12	randomised trials	no serious limitations	serious[22]	serious[23]	no serious imprecision	none	948/1645 (57.6%)	879/1563 (56.2%)	RR 1.02 (0.94 to 1.11)	1 more per 100 (from 3 fewer to 6 more)	⊕⊕OO LOW	
Non-remission - paroxetine												
5	randomised trials	no serious limitations	no serious inconsistency[24]	serious[25]	no serious imprecision[26]	none	334/601 (55.6%)	337/599 (56.3%)	RR 0.99 (0.9 to 1.1)	1 fewer per 100 (from 6 fewer to 6 more)	⊕⊕⊕O MODERATE	
Non-remission - fluoxetine												
2	randomised trials	no serious limitations	very serious[27]	serious[28]	very serious[29]	none	92/152 (60.5%)	51.8%	RR 1.21 (0.56 to 2.61)	109 more per 1000 (from 228 fewer to 834 more)	⊕OOO VERY LOW	
Non-remission - escitalopram												
3	randomised trials	no serious limitations	serious[30]	serious[31]	no serious imprecision	none	345/562 (61.4%)	334/557 (60%)	RR 1.06 (0.89 to 1.26)	4 more per 100 (from 7 fewer to 16 more)	⊕⊕OO LOW	
Non-remission - venlafaxine												
2	randomised trials	no serious limitations	serious[32]	serious[33]	no serious imprecision	none	177/330 (53.6%)	171/337 (50.7%)	RR 1.06 (0.88 to 1.27)	3 more per 100 (from 6 fewer to 14 more)	⊕⊕OO LOW	

[1] Significant heterogenity; random effects model used
[2] Selected outpatients from multiple sites
[3] Unlikely to be a difference
[4] As 1
[5] As 2
[6] As 2
[7] Inconclusive effect size
[8] As 1
[9] As 2
[10] As 2
[11] As 1
[12] As 2
[13] As 1
[14] As 27
[15]
[16] As 2
[17] As 7
[18] As 2
[19] As 1
[20] As 2
[21] As 7
[22] As 1
[23] As 2
[24]
[25] As 2
[26]
[27] As 1 - studies are not compatible as so much heterogeneity
[28] As 2
[29] As 7
[30] As 1
[31] As 2
[32] As 1
[33] As 2

Author(s): Rachel Burbeck
Date: 2009-07-13
Question: Should duloxetine vs other antidepressants - acceptability and tolerability be used for MDD (acute phase) ?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**duloxetine**	**other antidepressants - acceptability and tolerability**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Leaving treatment early - any reason												
11	randomised	no serious	serious[1]	serious[2]	no serious	none				7 more		

	trials	limitations			imprecision		472/1494 (31.6%)	344/1420 (24.2%)	RR 1.27 (1.10 to 1.47)	per 100 (from 2 more to 11 more)	⊕⊕OO LOW	
Leaving treatment early - any reason - paroxetine												
5	randomised trials	no serious limitations	no serious inconsistency[3]	serious[4]	no serious imprecision	none	176/601 (29.3%)	145/599 (24.2%)	RR 1.21 (1.01 to 1.45)	5 more per 100 (from 0 more to 11 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - any reason - fluoxetine												
2	randomised trials	no serious limitations	no serious inconsistency	serious[5]	very serious[6]	none	49/152 (32.2%)	26/70 (37.1%)	RR 0.87 (0.59 to 1.27)	5 fewer per 100 (from 15 fewer to 10 more)	⊕OOO VERY LOW	
Leaving treatment early - any reason - escitalopram												
2	randomised trials	no serious limitations	serious[7]	serious[8]	no serious imprecision	none	131/411 (31.9%)	87/414 (21%)	RR 1.64 (0.97 to 2.78)	13 more per 100 (from 1 fewer to 37 more)	⊕⊕OO LOW	
Leaving treatment early - any reason - venlafaxine												
2	randomised trials	no serious limitations	no serious inconsistency	serious[9]	no serious imprecision	none	116/330 (35.2%)	86/337 (25.5%)	RR 1.37 (1.09 to 1.72)	9 more per 100 (from 2 more to 18 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - adverse reactions												
10	randomised trials	no serious limitations	no serious inconsistency	serious[10]	no serious imprecision	none	147/1412 (10.4%)	91/1383 (6.6%)	RR 1.54 (1.2 to 1.99)	4 more per 100 (from 1 more to 7 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - adverse reactions - paroxetine												
5	randomised trials	no serious limitations	no serious inconsistency	serious[11]	serious[12]	none	55/601 (9.2%)	42/599 (7%)	RR 1.32 (0.9 to 1.93)	2 more per 100 (from 1 fewer to 7 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions - fluoxetine												
1	randomised trials	no serious limitations	no serious inconsistency	serious[13]	very serious[14]	none	7/70 (10%)	1/33 (3%)	RR 3.3 (0.42 to 25.74)	7 more per 100 (from 2 fewer to 75 more)	⊕OOO VERY LOW	
Leaving treatment early - adverse reactions - escitalopram												
2	randomised trials	no serious limitations	serious[15]	serious[16]	serious[17]	none	37/411 (9%)	17/414 (4.1%)	RR 2.62 (0.67 to 10.3)	7 more per 100 (from 1 fewer to 38 more)	⊕OOO VERY LOW	
Leaving treatment early - adverse reactions - venlafaxine												
2	randomised trials	no serious limitations	no serious inconsistency	serious[18]	no serious imprecision	none	48/330 (14.5%)	31/337 (9.2%)	RR 1.58 (1.04 to 2.42)	5 more per 100 (from 0 more to 13 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - lack of efficacy												
7	randomised trials	no serious limitations	no serious inconsistency	serious[19]	no serious imprecision	none	40/1167 (3.4%)	37/1174 (3.2%)	RR 1.09 (0.7 to 1.68)	0 more per 100 (from 1 fewer to 2 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - lack of efficacy - paroxetine												
3	randomised trials	no serious limitations	no serious inconsistency	serious[20]	very serious[21]	none	7/426 (1.6%)	3/423 (0.7%)	RR 2.29 (0.6 to 8.78)	1 more per 100 (from 0 fewer to 6 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy - fluoxetine - no data												
0	no evidence available					none	0/0 (0%)	0%	not pooled	not pooled		
Leaving treatment early - lack of efficacy - escitalopram												
2	randomised trials	no serious limitations	no serious inconsistency	serious[22]	very serious[23]	none	22/411 (5.4%)	25/414 (6%)	RR 0.88 (0.51 to 1.53)	1 fewer per 100 (from 3 fewer to 3 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy - venlafaxine												
2	randomised trials	no serious limitations	no serious inconsistency	serious[24]	very serious[25]	none	11/330 (3.3%)	9/337 (2.7%)	RR 1.24 (0.52 to 2.95)	1 more per 100 (from 1 fewer to 5 more)	⊕OOO VERY LOW	
No reporting side effects												
9	randomised trials	no serious limitations	no serious inconsistency	serious[26]	no serious imprecision	none	1010/1274 (79.3%)	949/1243 (76.3%)	RR 1.02 (0.98 to 1.07)	2 more per 100 (from 2 fewer to 5 more)	⊕⊕⊕O MODERATE	
No reporting side effects - paroxetine												
5	randomised trials	no serious limitations	no serious inconsistency	serious[27]	no serious imprecision	none			RR 1.07	5 more per 100		

							424/601 (70.5%)	389/599 (64.9%)	(0.99 to 1.15)	(from 1 fewer to 10 more)	⊕⊕⊕O MODERATE	
No reporting side effects - fluoxetine												
1	randomised trials	no serious limitations	no serious inconsistency	serious[28]	serious[29]	none	62/70 (88.6%)	30/33 (90.9%)	RR 0.97 (0.85 to 1.12)	3 fewer per 100 (from 14 fewer to 11 more)	⊕⊕OO LOW	
No reporting side effects - escitalopram												
1	randomised trials	no serious limitations	no serious inconsistency	serious[30]	serious[31]	none	241/273 (88.3%)	237/274 (86.5%)	RR 1.02 (0.96 to 1.09)	2 more per 100 (from 3 fewer to 8 more)	⊕⊕OO LOW	
No reporting side effects - venlafaxine												
2	randomised trials	no serious limitations	serious[32]	serious[33]	no serious imprecision	none	283/330 (85.8%)	293/337 (86.9%)	RR 0.99 (0.88 to 1.11)	1 fewer per 100 (from 10 fewer to 10 more)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint (sensitivity analysis) (measured with: kg; Better indicated by lower values)												
7	randomised trials	no serious limitations	no serious inconsistency	serious[34]	no serious imprecision	none	1042	1016	-	MD 0 higher (0.03 lower to 0.03 higher)	⊕⊕⊕O MODERATE	
Mean weight change (kg) at endpoint - paroxetine (measured with: kg; Better indicated by lower values)												
3	randomised trials	no serious limitations	no serious inconsistency	serious[35]	no serious imprecision	none	422	412	-	MD 0 higher (0.03 lower to 0.03 higher)	⊕⊕⊕O MODERATE	
Mean weight change (kg) at endpoint - fluoxetine (measured with: kg; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[36]	serious[37]	none	65	33	-	MD 0.01 lower (0.74 lower to 0.72 higher)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint - escitalopram (measured with: kg; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[38]	serious[39]	none	273	274	-	MD 0.06 higher (1.08 lower to 1.2 higher)	⊕⊕OO LOW	
Mean weight change (kg) at endpoint - venlafaxine (measured with: kg; Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[40]	no serious imprecision	none	282	297	-	MD 0.39 higher (0.09 lower to 0.86 higher)	⊕⊕⊕O MODERATE	

[1] Significant heterogenity; random effects model used
[2] Selected outpatients from multiple sites
[3]
[4] As 2
[5] As 2
[6] Inconsistent effect size
[7] As 1
[8] As 2
[9] As 2
[10] As 2
[11] As 2
[12] As 6
[13] As 2
[14] Inconsistent effect size; single study
[15] As 1
[16] As 2
[17] As 6
[18] As 2
[19] As 2
[20] As 2
[21] As 6
[22] As 2
[23] As 6
[24] As 2
[25] As 6
[26] As 2
[27] As 2
[28] As 2
[29] Single study
[30] As 2
[31] As 30
[32] As 1 (studies not compatible)
[33] As 2
[34] As 2

[35] As 2
[36] As 2
[37] As 30
[38] As 2
[39] As 30
[40] As 2

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine vs placebo be used for MDD?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine	placebo	Relative (95% CI)	Absolute	Quality	
Mean change scores from end of acute phase - 80 mg (measured with: HAMD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency[1]	serious[2]	serious[3]	none	70	70	-	MD 1 lower (2.5 lower to 0.5 higher)	⊕⊕OO LOW	
Mean change scores from end of acute phase - 120 mg (measured with: HAMD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[4]	serious[5]	none	80	70	-	MD 0.2 lower (1.78 lower to 1.38 higher)	⊕⊕OO LOW	
Leaving treatment early - for any reason - 80 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[6]	serious[7]	none	58/71 (81.7%)	62/71 (87.3%)	RR 0.94 (0.81 to 1.08)	5 fewer per 100 (from 17 fewer to 7 more)	⊕⊕OO LOW	
Leaving treatment early - for any reason - 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency[8]	serious[9]	serious[10]	none	62/81 (76.5%)	62/71 (87.3%)	RR 0.88 (0.75 to 1.02)	10 fewer per 100 (from 22 fewer to 2 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions - 80 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[11]	no serious imprecision	none	7/146 (4.8%)	6/129 (4.7%)	RR 0.96 (0.34 to 2.73)	0 fewer per 100 (from 3 fewer to 8 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - adverse reactions - 120 mg												
2	randomised trials	no serious limitations	no serious inconsistency	serious[12]	no serious imprecision	none	6/151 (4%)	6/129 (4.7%)	RR 0.84 (0.28 to 2.54)	1 fewer per 100 (from 3 fewer to 7 more)	⊕⊕⊕O MODERATE	
Leaving treatment early - lack of efficacy - 80 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[13]	serious[3]	none	1/71 (1.4%)	1/71 (1.4%)	RR 1 (0.06 to 15.68)	0 fewer per 100 (from 1 fewer to 21 more)	⊕⊕OO LOW	
Leaving treatment early - lack of efficacy - 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[14]	serious[15]	none	4/81 (4.9%)	1/71 (1.4%)	RR 3.51 (0.4 to 30.65)	4 more per 100 (from 1 fewer to 42 more)	⊕⊕OO LOW	

[1]
[2] Single study
[3] As 3
[4] As 2
[5] As 3
[6] As 2
[7] As 3
[8]
[9] As 2
[10] As 3
[11] As 2
[12] As 2
[13] As 2
[14] As 2
[15] As 3

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine at different doses be used for MDD?
Settings:
Bibliography:

Quality assessment	Summary of findings	

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine at different doses	control	Relative (95% CI)	Absolute		
Mean change scores from end of acute phase - 80 mg vs 120 mg (measured with: HAMD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[1]	serious[2]	none	70	80	-	MD 0.8 lower (2.18 lower to 0.58 higher)	⊕⊕OO LOW	
Leaving treatment early - for any reason - 80 mg vs 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[3]	serious[4]	none	58/71 (81.7%)	62/81 (76.5%)	RR 1.07 (0.91 to 1.26)	5 more per 100 (from 7 fewer to 20 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions - 80 mg vs 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[5]	very serious[6]	none	2/71 (2.8%)	3/81 (3.7%)	RR 0.76 (0.13 to 4.42)	1 fewer per 100 (from 3 fewer to 13 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy - 80 mg vs 120 mg												
1	randomised trials	no serious limitations	no serious inconsistency	serious[7]	very serious[8]	none	1/71 (1.4%)	4/81 (4.9%)	RR 0.29 (0.03 to 2.49)	4 fewer per 100 (from 5 fewer to 7 more)	⊕OOO VERY LOW	

[1] Selected patients from multiple sites
[2] Single study
[3] As 1
[4] As 2
[5] As 1
[6] As 2 + inconsistent effect size
[7] As 1
[8] As 6

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine vs other drugs be used for MDD?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine	other drugs	Relative (95% CI)	Absolute		
Mean change scores from end of acute phase - 80 mg vs paroxetine (measured with: HAMD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[1]	serious[2]	none	70	70	-	MD 0.3 higher (1.06 lower to 1.66 higher)	⊕⊕OO LOW	
Leaving treatment early - for any reason - paroxetine												
1	randomised trials	no serious limitations	no serious inconsistency	serious[3]	serious[4]	none	58/71 (81.7%)	61/70 (87.1%)	RR 0.94 (0.81 to 1.08)	5 fewer per 100 (from 17 fewer to 7 more)	⊕⊕OO LOW	
Leaving treatment early - adverse reactions - paroxetine												
2	randomised trials	no serious limitations	no serious inconsistency	serious[5]	very serious[6]	none	7/146 (4.8%)	2/140 (1.4%)	RR 2.84 (0.7 to 11.6)	3 more per 100 (from 0 fewer to 15 more)	⊕OOO VERY LOW	
Leaving treatment early - lack of efficacy - paroxetine												
1	randomised trials	no serious limitations	no serious inconsistency	serious[7]	very serious[8]	none	1/71 (1.4%)	2/70 (2.9%)	RR 0.49 (0.05 to 5.31)	1 fewer per 100 (from 3 fewer to 12 more)	⊕OOO VERY LOW	

[1] Single study
[2] No explanation was provided
[3] As 1
[4] As 2
[5] As 1
[6] Inconsistent effect size
[7] As 1
[8] As 2 + inconsistent effect size

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should Continuation phase for those achieving remission: duloxetine vs placebo - acceptability/tolerability data only be used for MDD?
Settings:
Bibliography:

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Should Continuation phase no entry criteria: duloxetine vs other drugs be used for MDD?
Settings:
Bibliography:

	Summary of findings	

Quality assessment							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Continuation phase no entry criteria: duloxetine	other drugs	Relative (95% CI)	Absolute	Quality	Importance
Mean scores at endpoint - escitalopram (measured with: HAMD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious[1]	serious[2]	none	146	141	-	MD 1.34 higher (0.25 lower to 2.93 higher)	⊕⊕OO LOW	
Non-response - escitalopram												
1	randomised trials	no serious limitations	no serious inconsistency	serious[3]	very serious[4]	none	49/151 (32.5%)	40/143 (28%)	RR 1.16 (0.82 to 1.65)	4 more per 100 (from 5 fewer to 18 more)	⊕OOO VERY LOW	
Non-remission - escitalopram												
1	randomised trials	no serious limitations	no serious inconsistency	serious[5]	serious[6]	none	39/151 (25.8%)	28/143 (19.6%)	RR 1.32 (0.86 to 2.02)	6 more per 100 (from 3 fewer to 20 more)	⊕⊕OO LOW	
Leaving treatment early - any reason - escitalopram												
1	randomised trials	no serious limitations	no serious inconsistency	serious[7]	very serious[8]	none	37/151 (24.5%)	31/143 (21.7%)	RR 1.13 (0.74 to 1.72)	3 more per 100 (from 6 fewer to 16 more)	⊕OOO VERY LOW	
Leaving treatment early - adverse reactions - escitalopram												
1	randomised trials	no serious limitations	no serious inconsistency	serious[9]	serious[10]	none	26/151 (17.2%)	13/143 (9.1%)	RR 1.89 (1.01 to 3.54)	8 more per 100 (from 0 more to 23 more)	⊕⊕OO LOW	
Leaving treatment early - lack of efficacy - escitalopram												
1	randomised trials	no serious limitations	no serious inconsistency[11]	serious[12]	very serious[13]	none	2/151 (1.3%)	7/143 (4.9%)	RR 0.27 (0.06 to 1.28)	4 fewer per 100 (from 5 fewer to 1 more)	⊕OOO VERY LOW	

[1] Selected patients from multiple sites
[2] Single study
[3] As 1
[4] Single study + inconistent effect size
[5] As 1
[6] As 2
[7] As 1
[8] As 4
[9] As 1
[10] As 2
[11]
[12] No explanation was provided
[13] As 4

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Relapse prevention: duloxetine vs placebo for
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Relapse prevention: duloxetine	placebo	Relative (95% CI)	Absolute	Quality	Importance
Relapse												
1	no methodology chosen					none	62/136 (45.6%)	66.9%	RR 0.68 (0.55 to 0.85)	214 fewer per 1000 (from 100 fewer to 301 fewer)		
Relapse - 60 mg												
1	no methodology chosen					none	62/136 (45.6%)	66.9%	RR 0.68 (0.55 to 0.85)	214 fewer per 1000 (from 100 fewer to 301 fewer)		
Leaving treatment early - any reason												
1	no methodology chosen					none	33/136 (24.3%)	26.1%	RR 0.93 (0.62 to 1.4)	18 fewer per 1000 (from 99 fewer to 104 more)		
Leaving treatment early - any reason - 60 mg												
1	no methodology chosen					none	33/136 (24.3%)	26.1%	RR 0.93 (0.62 to 1.4)	18 fewer per 1000 (from 99 fewer to 104 more)		
Leaving treatment early - due to adverse reactions												
1	no methodology chosen					none	5/136 (3.7%)	3.5%	RR 1.04 (0.31 to 3.53)	1 more per 1000 (from 24 fewer to 89 more)		
Leaving treatment early - due to adverse reactions - 60 mg												
1	no methodology chosen					none	5/136 (3.7%)	3.5%	RR 1.04 (0.31 to 3.53)	1 more per 1000 (from 24 fewer to 89 more)		
Leaving treatment early - lack of efficacy												
1	no					none				15 more per		

	methodology chosen						3/136 (2.2%)	0.7%	RR 3.13 (0.33 to 29.75)	1000 (from 5 fewer to 201 more)		
Leaving treatment early - lack of efficacy - 60 mg												
1	no methodology chosen					none	3/136 (2.2%)	0.7%	RR 3.13 (0.33 to 29.75)	15 more per 1000 (from 5 fewer to 201 more)		
No reporting adverse reactions												
1	no methodology chosen					none	82/136 (60.3%)	69%	RR 0.87 (0.73 to 1.04)	90 fewer per 1000 (from 186 fewer to 28 more)		
No reporting adverse reactions - 60 mg												
1	no methodology chosen					none	82/136 (60.3%)	69%	RR 0.87 (0.73 to 1.04)	90 fewer per 1000 (from 186 fewer to 28 more)		
Mean weight change (kg) (Better indicated by lower values)												
1	no methodology chosen					none	97	99	-	MD 0.08 higher (0.82 lower to 0.98 higher)		
Mean weight change (kg) - 60 mg (Better indicated by lower values)												
1	no methodology chosen					none	97	99	-	MD 0.08 higher (0.82 lower to 0.98 higher)		

Author(s): Rachel Burbeck
Date: 2008-07-14
Question: Acute-phase non-responders: duloxetine 60 mg vs duloxetine 120 mg for
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Acute-phase non-responders: duloxetine 60 mg**	**duloxetine 120 mg**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Efficacy - no data (Better indicated by lower values)												
0	no evidence available					none	0	0	-	not pooled		
Leaving treatment early - any reason												
1	no methodology chosen					none	26/131 (19.8%)	27.4%	RR 0.72 (0.46 to 1.13)	77 fewer per 1000 (from 148 fewer to 36 more)		
Leaving treatment early - any reason - 60 mg vs 120 mg												
1	no methodology chosen					none	26/131 (19.8%)	27.4%	RR 0.72 (0.46 to 1.13)	77 fewer per 1000 (from 148 fewer to 36 more)		
Leaving treatment early - adverse reactions												
1	no methodology chosen					none	6/131 (4.6%)	5.7%	RR 0.81 (0.28 to 2.35)	11 fewer per 1000 (from 41 fewer to 77 more)		
Leaving treatment early - adverse reactions - 60 mg vs 120 mg												
1	no methodology chosen					none	6/131 (4.6%)	5.7%	RR 0.81 (0.28 to 2.35)	11 fewer per 1000 (from 41 fewer to 77 more)		
Leaving treatment early - lack of efficacy												
1	no methodology chosen					none	5/131 (3.8%)	8.1%	RR 0.47 (0.17 to 1.35)	43 fewer per 1000 (from 67 fewer to 28 more)		
Leaving treatment early - lack of efficacy - 60 mg vs 120 mg												
1	no methodology chosen					none	5/131 (3.8%)	8.1%	RR 0.47 (0.17 to 1.35)	43 fewer per 1000 (from 67 fewer to 28 more)		

Author(s): NCCMH
Date: 2009-07-13
Question: Should Bright light vs waitlist be used for SAD?
Settings: Range, including community, primary care and outpatients
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	waitlist	Relative (95% CI)	Absolute	Quality	
Leaving study early for any reason (overall) (total number not completing study)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	3/42 (7.1%)	3/40 (7.5%) 8.7%	RR 0.95 (0.21 to 4.32)	0 fewer per 100 (from 6 fewer to 25 more) 0 fewer per 100 (from 7 fewer to 29 more)	⊕⊕OO LOW	
Leaving study early due to side effects - Light box vs waitlist control												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	0/16 (0%)	0/15 (0%) 0%	not pooled	not pooled not pooled	⊕⊕⊕O MODERATE	
Leaving study early - Light room vs waitlist control												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	1/26 (3.8%)	1/25 (4%) 0%	RR 0.96 (0.06 to 14.55)	0 fewer per 100 (from 4 fewer to 54 more) 0 fewer per 100 (from 0 fewer to 0 more)	⊕⊕⊕O MODERATE	
Mean self rated SAD depression scores (SIGH-SAD-SR) at endpoint - Light room vs waitlist control (measured with: SIGH-SAD-SR; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	24	24	-	MD 12.8 lower (18.52 to 7.08 lower)	⊕⊕⊕O MODERATE	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Light box vs waitlist control (measured with: SIGH-SAD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[5]	none	16	15	-	MD 10.4 lower (15.99 to 4.81 lower)	⊕⊕⊕O MODERATE	
Mean clinician rated typical depression scores (HRSD-21) at endpoint - Light box vs waitlist control (measured with: HRSD; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	16	15	-	MD 6.3 lower (10.34 to 2.26 lower)	⊕⊕⊕⊕ HIGH	
Mean self-rated depression score - overall (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision[6]	none	40	39	-	MD 1.15 lower (1.63 to 0.67 lower)	⊕⊕⊕⊕ HIGH	
Mean self rated depression scores at endpoint - Light room vs waitlist control (HRSD-21-SR) (measured with: HRSD-21-SR; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[7]	none	24	24	-	MD 7.7 lower (11.58 to 3.82 lower)	⊕⊕⊕O MODERATE	
Mean self rated depression scores at endpoint - Light box vs waitlist control (BDI) (measured with: BDI; Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[8]	none	16	15	-	MD 10.9 lower (16.99 to 4.81 lower)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Light box vs waitlist control (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[9]	none	16	15	-	MD 4 lower (6.73 to 1.27 lower)	⊕⊕⊕O MODERATE	
Mean self rated atypical depression scores (SAD-SRsubscale) at endpoint - Light room vs waitlist control (measured with: SAD-SR subscale (of SIGH-SAD); Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[10]	none	24	24	-	MD 5.2 lower (7.39 to 3.01 lower)	⊕⊕⊕O MODERATE	
Non remission (SIGHSAD-SR) (overall)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/42 (47.6%)	36/40 (90%) 88%	RR 0.53 (0.38 to 0.74)	42 fewer per 100 (from 23 fewer to 56 fewer) 41 fewer per 100 (from 23 fewer to 55 fewer)	⊕⊕⊕⊕ HIGH	
Non remission (SIGHSAD-SR) - Light room vs waitlist control												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[11]	none	12/26 (46.2%)	24/25 (96%) 96%	RR 0.48 (0.31 to 0.73)	50 fewer per 100 (from 26 fewer to 66 fewer) 50 fewer per 100 (from 26 fewer to 66 fewer)	⊕⊕⊕O MODERATE	
Non remission (SIGHSAD-SR) - Light box vs waitlist control												

1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[12]	none	8/16 (50%)	12/15 (80%) 80%	RR 0.62 (0.36 to 1.08)	30 fewer per 100 (from 51 fewer to 6 more) 30 fewer per 100 (from 51 fewer to 6 more)	⊕⊕⊕O MODERATE	
Non response (SIGHSAD) - Light room vs waitlist control												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[13]	none	13/26 (50%)	25/25 (100%) 100%	RR 0.50 (0.34 to 0.73)	50 fewer per 100 (from 27 fewer to 66 fewer) 50 fewer per 100 (from 27 fewer to 66 fewer)	⊕⊕⊕O MODERATE	

[1] Inconclusive effect size
[2] Single study
[3] As 3
[4] As 3
[5] As 3
[6]
[7] As 3
[8] As 3
[9] As 3
[10] As 3
[11] As 3
[12] As 3
[13] As 3

Author(s): NCCMH
Date: 2009-07-13
Question: Bright light vs attentional control for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	attentional control	Relative (95% CI)	Absolute		
Leaving study early for any reason (overall)												
5	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	18/134 (13.4%)	18/124 (14.5%) 13.1%	RR 0.92 (0.51 to 1.64)	1 fewer per 100 (from 7 fewer to 9 more) 1 fewer per 100 (from 6 fewer to 8 more)	⊕⊕OO LOW	
Leaving study early for any reason - Light box vs deactivated negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	8/41 (19.5%)	9/40 (22.5%) 22.5%	RR 0.87 (0.37 to 2.02)	3 fewer per 100 (from 14 fewer to 23 more) 3 fewer per 100 (from 14 fewer to 23 more)	⊕⊕OO LOW	
Leaving study early for any reason - Low dose (<5000luxhrs/day) LED light vs negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[3]	none	1/15 (6.7%)	2/11 (18.2%) 18.2%	RR 0.37 (0.04 to 3.55)	11 fewer per 100 (from 17 fewer to 46 more) 11 fewer per 100 (from 17 fewer to 46 more)	⊕⊕OO LOW	
Leaving study early for any reason - Light box vs high dose (>300lux) dim red light box												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[4]	none	6/33 (18.2%)	5/26 (19.2%) 19.2%	RR 0.95 (0.32 to 2.76)	1 fewer per 100 (from 13 fewer to 34 more) 1 fewer per 100 (from 13 fewer to 34 more)	⊕⊕OO LOW	
Leaving study early for any reason - Light box vs low-density ionisation												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	2/23 (8.7%)	2/25 (8%) 8%	RR 1.09 (0.17 to 7.1)	1 more per 100 (from 7 fewer to 49 more) 1 more per 100 (from 7 fewer to 49 more)	⊕⊕OO LOW	
Leaving study early for any reason - Low dose (<5000luxhrs/day) light box vs no light box												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none		0/12 (0%)		0 more per 100 (from 0		

							1/10 (10%)	0%	RR 3.55 (0.16 to 78.56)	fewer to 0 more) 0 more per 100 (from 0 fewer to 0 more)	⊕⊕OO LOW	
Leaving study early for any reason - Low dose (<5000luxhrs/day) light visor vs no light visor												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[7]	none	0/12 (0%)	0/10 (0%) 0%	not pooled	not pooled not pooled	⊕⊕⊕O MODERATE	
Leaving study early due to lack of efficacy - Low dose (<5000luxhrs/day) LED light vs negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[8]	none	0/15 (0%)	1/11 (9.1%) 9.1%	RR 0.25 (0.01 to 5.62)	7 fewer per 100 (from 9 fewer to 42 more) 7 fewer per 100 (from 9 fewer to 42 more)	⊕⊕OO LOW	
Reported side effects (overall)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[9]	none	25/45 (55.6%)	21/36 (58.3%) 44.6%	RR 0.98 (0.73 to 1.32)	1 fewer per 100 (from 16 fewer to 19 more) 1 fewer per 100 (from 12 fewer to 14 more)	⊕⊕OO LOW	
Reported side effects - Low dose (<5000luxhrs/day) LED light vs negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[10]	none	2/15 (13.3%)	1/11 (9.1%) 9.1%	RR 1.47 (0.15 to 14.21)	4 more per 100 (from 8 fewer to 120 more) 4 more per 100 (from 8 fewer to 120 more)	⊕⊕⊕O MODERATE	
Reported side effects - Light visor vs dim light visor												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[11]	none	23/30 (76.7%)	20/25 (80%) 80%	RR 0.96 (0.73 to 1.27)	3 fewer per 100 (from 22 fewer to 22 more) 3 fewer per 100 (from 22 fewer to 22 more)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint (overall) (Better indicated by lower values)												
6	randomised trials	no serious limitations	serious[12]	no serious indirectness	serious[13]	none	139	131	-	MD 2.78 lower (6.81 lower to 1.26 higher)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Low dose (<5000luxhrs/day) LED light vs negative ion generator (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[14]	none	14	9	-	MD 4.7 lower (10.34 lower to 0.94 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Light visor vs dim light visor (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[15]	no serious indirectness	serious[16]	none	64	58	-	MD 0.86 higher (7.56 lower to 9.29 higher)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Light box vs low-density ionisation (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[17]	no serious indirectness	no serious imprecision	none	40	42	-	MD 8.56 lower (14.73 to 2.39 lower)	⊕⊕⊕O MODERATE	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Low dose (<5000luxhrs/day) light box vs no light box (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[18]	none	9	12	-	MD 1.4 higher (4.93 lower to 7.73 higher)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Low dose (<5000luxhrs/day) light visor vs no light visor (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[19]	none	12	10	-	MD 0.2 lower (6.22 lower to 5.82 higher)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint (overall) (Better indicated by lower values)												
5	randomised trials	no serious limitations	serious[20]	no serious indirectness	serious[21]	none	106	103	-	SMD 0.07 lower (0.51 lower to 0.37 higher)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Light visor vs dim light visor (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[22]	no serious indirectness	serious[23]	none	64	58	-	SMD 0.05 higher (0.52 lower to 0.63 higher)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Light box vs low-density ionisation (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[24]	none	21	23	-	SMD 0.81 lower (1.43 to 0.19 lower)	⊕⊕⊕O MODERATE	

Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Low dose (<5000luxhrs/day) light box vs no light box (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[25]	none	9	12	-	SMD 0.26 higher (0.61 lower to 1.13 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Low dose (<5000luxhrs/day) light visor vs no light visor (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[26]	none	12	10	-	SMD 0.2 higher (0.64 lower to 1.04 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint (overall) (Better indicated by lower values)												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	55	55	-	MD 1.25 lower (2.77 lower to 0.27 higher)	⊕⊕⊕⊕ HIGH	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Light visor vs dim light visor (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[27]	none	34	33	-	MD 2.1 lower (4.31 lower to 0.11 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Low dose (<5000luxhrs/day) light box vs no light box (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[28]	none	9	12	-	MD 1.2 higher (2.48 lower to 4.88 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Low dose (<5000luxhrs/day) light visor vs no light visor (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[29]	none	12	10	-	MD 1.3 lower (3.84 lower to 1.24 higher)	⊕⊕⊕O MODERATE	
Mean self rated depression scores (BDI) at endpoint - Light box vs deactivated negative ion generator (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[30]	none	33	31	-	MD 2.6 lower (6.72 lower to 1.52 higher)	⊕⊕⊕O MODERATE	
Non remission (SIGHSAD or SIGHSAD-SR or HDRS) (overall)												
6	randomised trials	no serious limitations	serious[31]	no serious indirectness	serious[32]	none	99/176 (56.3%)	98/160 (61.3%) 70.5%	RR 0.89 (0.66 to 1.2)	7 fewer per 100 (from 21 fewer to 12 more) 8 fewer per 100 (from 24 fewer to 14 more)	⊕⊕OO LOW	
Non remission (SIGHSAD or SIGHSAD-SR or HDRS) - Low dose (<5000luxhrs/day) LED light vs negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[33]	none	7/15 (46.7%)	10/11 (90.9%) 90.9%	RR 0.51 (0.29 to 0.91)	45 fewer per 100 (from 8 fewer to 65 fewer) 45 fewer per 100 (from 8 fewer to 65 fewer)	⊕⊕⊕O MODERATE	
Non remission (SIGHSAD or SIGHSAD-SR or HDRS) - Light box vs deactivated negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[34]	none	21/41 (51.2%)	30/40 (75%) 75%	RR 0.68 (0.48 to 0.97)	24 fewer per 100 (from 2 fewer to 39 fewer) 24 fewer per 100 (from 2 fewer to 39 fewer)	⊕⊕⊕O MODERATE	
Non remission (SIGHSAD or SIGHSAD-SR or HDRS) - Light visor vs dim light visor												
2	randomised trials	no serious limitations	serious[35]	no serious indirectness	serious[36]	none	33/64 (51.6%)	22/58 (37.9%) 38.7%	RR 1.34 (0.79 to 2.27)	13 more per 100 (from 8 fewer to 48 more) 13 more per 100 (from 8 fewer to 49 more)	⊕⊕OO LOW	
Non remission (SIGHSAD or SIGHSAD-SR or HDRS) - Light box vs high dose (>300lux) dim red light box												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[37]	none	25/33 (75.8%)	19/26 (73.1%) 73.1%	RR 1.04 (0.77 to 1.4)	3 more per 100 (from 17 fewer to 29 more) 3 more per 100 (from 17 fewer to 29 more)	⊕⊕OO LOW	
Non remission (SIGHSAD or SIGHSAD-SR or HDRS) - Light box vs low-density ionisation												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[38]	none		17/25 (68%)	RR 0.83	12 fewer per 100 (from 32 fewer to 20 more)		

							13/23 (56.5%)	68%	(0.53 to 1.3)	12 fewer per 100 (from 32 fewer to 20 more)	⊕⊕OO LOW	
Non response (SIGHSAD) (overall)												
7	randomised trials	no serious limitations	serious[39]	no serious indirectness	serious[40]	none	83/183 (45.4%)	92/171 (53.8%) 58.3%	RR 0.86 (0.64 to 1.15)	8 fewer per 100 (from 19 fewer to 8 more) 8 fewer per 100 (from 21 fewer to 9 more)	⊕⊕OO LOW	
Non response (SIGHSAD) - Light box vs deactivated negative ion generator												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[41]	none	19/41 (46.3%)	25/40 (62.5%) 62.5%	RR 0.74 (0.49 to 1.11)	16 fewer per 100 (from 32 fewer to 7 more) 16 fewer per 100 (from 32 fewer to 7 more)	⊕⊕⊕O MODERATE	
Non response (SIGHSAD) - Light visor vs dim light visor												
2	randomised trials	no serious limitations	serious[42]	no serious indirectness	serious[43]	none	30/64 (46.9%)	22/58 (37.9%) 37.2%	RR 1.24 (0.56 to 2.75)	9 more per 100 (from 17 fewer to 66 more) 9 more per 100 (from 16 fewer to 65 more)	⊕⊕OO LOW	
Non response (SIGHSAD) - Light box vs high dose (>300lux) dim red light box												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[44]	none	13/33 (39.4%)	14/26 (53.8%) 53.9%	RR 0.73 (0.42 to 1.27)	15 fewer per 100 (from 31 fewer to 15 more) 15 fewer per 100 (from 31 fewer to 15 more)	⊕⊕⊕O MODERATE	
Non response (SIGHSAD) - Light box vs low-density ionisation												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[45]	none	9/23 (39.1%)	18/25 (72%) 72%	RR 0.54 (0.31 to 0.96)	33 fewer per 100 (from 3 fewer to 50 fewer) 33 fewer per 100 (from 3 fewer to 50 fewer)	⊕⊕⊕O MODERATE	
Non response (SIGHSAD) - Low dose (<5000luxhrs/day) light box vs no light box												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[46]	none	7/10 (70%)	7/12 (58.3%) 58.3%	RR 1.2 (0.64 to 2.25)	12 more per 100 (from 21 fewer to 73 more) 12 more per 100 (from 21 fewer to 73 more)	⊕⊕⊕O MODERATE	
Non response (SIGHSAD) - Low dose (<5000luxhrs/day) light visor vs no light visor												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[47]	none	5/12 (41.7%)	6/10 (60%) 60%	RR 0.69 (0.3 to 1.61)	19 fewer per 100 (from 42 fewer to 37 more) 19 fewer per 100 (from 42 fewer to 37 more)	⊕⊕⊕O MODERATE	

[1] Inconclusive effect size
[2] Single study; inconclusive effect size
[3] As 2
[4] As 2
[5] As 2
[6] As 2
[7] As 2
[8] As 2
[9] As 2
[10] As 2
[11] Inconclusive effect size
[12] Significant heterogeneity; random effects model used
[13] As 1
[14] As 15
[15] As 1
[16] As 15

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[39] As 15
[40] As 1
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[46] As 17
[47] As 17

Author(s): NCCMH
Date: 2008-11-25
Question: Bright light vs active treatment control for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	active treatment control	Relative (95% CI)	Absolute	Quality	
Leaving study early for any reason - Light box vs group CBT												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	2/25 (8%)	4/24 (16.7%) 17.8%	RR 0.53 (0.12 to 2.31)	8 fewer per 100 (from 15 fewer to 22 more) 8 fewer per 100 (from 16 fewer to 23 more)	⊕⊕⊕O MODERATE	
Leaving study early for any reason - Light box + placebo pill vs dim light box + fluoxetine												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	12/68 (17.6%)	8/68 (11.8%) 9.8%	RR 1.5 (0.65 to 3.44)	6 more per 100 (from 4 fewer to 29 more) 5 more per 100 (from 3 fewer to 24 more)	⊕⊕⊕O MODERATE	
Leaving study early for any reason - Light box + hypericum vs dim light + hypericum												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/10 (0%)	0/10 (0%) 0%	not pooled	not pooled not pooled	⊕⊕⊕⊕ HIGH	
Leaving study early due to side effects - Light box + placebo pill vs dim light box + fluoxetine												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[3]	none	1/48 (2.1%)	2/48 (4.2%) 4.2%	RR 0.5 (0.05 to 5.33)	2 fewer per 100 (from 4 fewer to 18 more) 2 fewer per 100 (from 4 fewer to 18 more)	⊕⊕OO LOW	
Leaving study early due to side effects - Light box vs group CBT												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	0/16 (0%)	0/15 (0%) 0%	not pooled	not pooled not pooled	⊕⊕⊕O MODERATE	
Leaving study early due to lack of efficacy - Light box + placebo pill vs dim light box + fluoxetine												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	2/43 (4.7%)	0/48 (0%) 0%	RR 5.57 (0.27 to 112.85)	0 more per 100 (from 0 fewer to 0 more) 0 more per 100 (from 0 fewer to 0 more)		
Reported side effects - Light box + placebo pill vs dim light box + fluoxetine												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[6]	none	37/48		RR 1.03	22 more per 1000 (from		

							(77.1%)	75%	(0.82 to 1.29)	135 fewer to 217 more)		
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Light box vs group CBT (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	16	15	-	MD 0.2 lower (6.5 lower to 6.1 higher)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Light box + placebo pill vs dim light box + fluoxetine (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	68	68	-	MD 0.49 lower (3.72 lower to 2.74 higher)	⊕⊕⊕⊕ HIGH	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Light box vs group CBT (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[8]	none	16	15	-	SMD 0.13 lower (0.83 lower to 0.58 higher)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Light box + placebo pill vs dim light box + fluoxetine (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	68	68	-	SMD 0.04 lower (0.38 lower to 0.29 higher)	⊕⊕⊕⊕ HIGH	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Light box + hypericum vs dim light + hypericum (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness[9]	very serious[10]	none	10	10	-	SMD 0.32 lower (1.2 lower to 0.57 higher)	⊕⊕OO LOW	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Light box vs group CBT (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[11]	none	16	15	-	MD 0.4 higher (2.68 lower to 3.48 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Light box + placebo pill vs dim light box + fluoxetine (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[12]	none	68	68	-	MD 0.3 lower (1.75 lower to 1.15 higher)	⊕⊕OO LOW	
Mean self rated depression scores (BDI) at endpoint - Light box vs group CBT (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[13]	none	16	15	-	MD 0.7 lower (7.16 lower to 5.76 higher)		
Mean self rated depression scores (BDI) at endpoint - Light box + placebo pill vs dim light box + fluoxetine (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[14]	none	48	48	-	MD 1.6 lower (5.68 lower to 2.48 higher)	⊕⊕OO LOW	
Non remission - Light box + placebo pill vs dim light box + fluoxetine												
2	randomised trials	no serious limitations	serious[15]	no serious indirectness	serious[16]	none	34/68 (50%)	37/68 (54.4%) 60.4%	RR 0.92 (0.67 to 1.27)	4 fewer per 100 (from 18 fewer to 15 more) 5 fewer per 100 (from 20 fewer to 16 more)	⊕⊕OO LOW	
Non remission - Light box vs group CBT												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/25 (48%)	15/24 (62.5%) 63.3%	RR 0.77 (0.46 to 1.28)	14 fewer per 100 (from 34 fewer to 17 more) 15 fewer per 100 (from 34 fewer to 18 more)	⊕⊕⊕⊕ HIGH	
Non response - Light box + placebo pill vs dim light box + fluoxetine												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[17]	none	22/68 (32.4%)	23/68 (33.8%) 34.2%	RR 0.96 (0.59 to 1.54)	1 fewer per 100 (from 14 fewer to 18 more) 1 fewer per 100 (from 14 fewer to 18 more)	⊕⊕OO LOW	

[1] Inconclusive effect size
[2] As 1
[3] Inconclusive effect size/single study
[4] Single study
[5] As 3
[6] As 4
[7] As 3
[8] As 3
[9]
[10] As 3
[11] As 4
[12] As 1
[13] As 3

[14] As 3
[15] Significant heterogeneity; random effects model used
[16] As 1
[17] As 1

Author(s): NCCMH
Date: 2008-11-25
Question: Bright light vs light + CBT combo for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	light + CBT combo	Relative (95% CI)	Absolute	Quality	
Leaving study early for any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	2/25 (8%)	2/23 (8.7%) 9.6%	RR 0.92 (0.17 to 4.91)	1 fewer per 100 (from 7 fewer to 34 more) 1 fewer per 100 (from 8 fewer to 38 more)	⊕⊕⊕O MODERATE	
Leaving study early due to side effects												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	0/16 (0%)	1/15 (6.7%) 6.7%	RR 0.31 (0.01 to 7.15)	5 fewer per 100 (from 7 fewer to 41 more) 5 fewer per 100 (from 7 fewer to 41 more)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	16	15	-	MD 4.2 higher (0.52 lower to 8.92 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	16	15	-	SMD 0.46 higher (0.26 lower to 1.17 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[5]	none	16	15	-	MD 2 higher (0.12 lower to 4.12 higher)	⊕⊕⊕O MODERATE	
Mean self rated depression scores (BDI) at endpoint (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	16	15	-	MD 2.3 higher (2.47 lower to 7.07 higher)	⊕⊕OO LOW	
Non remission (SIGHSAD)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/25 (48%)	5/23 (21.7%) 19.6%	RR 2.22 (0.92 to 5.32)	27 more per 100 (from 2 fewer to 94 more) 24 more per 100 (from 2 fewer to 85 more)	⊕⊕⊕⊕ HIGH	

[1] Inconclusive effect size
[2] Inconclusive effect size; single study
[3] Single study
[4] As 2
[5] As 4
[6] As 2

Author(s): NCCMH
Date: 2009-07-13
Question: Morning vs afternoon/evening bright light box for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Morning	afternoon/evening bright light box	Relative (95% CI)	Absolute	Quality	
Leaving study early for any reason (overall)												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	8/66 (12.1%)	8/64 (12.5%) 0%	RR 0.98 (0.41 to 2.35)	0 fewer per 100 (from 7 fewer to 17 more) 0 fewer per 100 (from 0 fewer to 0 more)	⊕⊕⊕O MODERATE	

Leaving study early for any reason - SAD												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	8/50 (16%)	8/49 (16.3%) 10%	RR 0.98 (0.41 to 2.35)	0 fewer per 100 (from 10 fewer to 22 more) 0 fewer per 100 (from 6 fewer to 13 more)	⊕⊕⊕O MODERATE	
Leaving study early for any reason - Subsyndromal SAD												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	0/16 (0%)	0/15 (0%) 0%	not pooled	not pooled not pooled	⊕⊕⊕O MODERATE	
Leaving study early due to side effects - Subsyndromal SAD												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	0/16 (0%)	0/15 (0%) 0%	not pooled	not pooled not pooled	⊕⊕⊕O MODERATE	
Reported side effects - Subsyndromal SAD												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	1/16 (6.3%)	2/15 (13.3%) 13.3%	RR 0.47 (0.05 to 4.65)	7 fewer per 100 (from 13 fewer to 49 more) 7 fewer per 100 (from 13 fewer to 49 more)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint (overall) (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	35	33	-	MD 1.38 lower (5.49 lower to 2.73 higher)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - Subsyndromal SAD (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	16	14	-	MD 0.6 higher (3.89 lower to 5.09 higher)	⊕⊕OO LOW	
Mean clinician rated SAD depression scores (SIGH-SAD) at endpoint - SAD (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[8]	none	19	19	-	MD 3.6 lower (8.5 lower to 1.3 higher)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-31) at endpoint (overall) (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[9]	none	25	22	-	SMD 0.05 lower (0.63 lower to 0.52 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - Subsyndromal SAD (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[10]	none	16	14	-	SMD 0.15 lower (0.87 lower to 0.57 higher)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint - SAD (HRSD-31) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[11]	none	9	8	-	SMD 0.12 higher (0.83 lower to 1.07 higher)	⊕⊕OO LOW	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint - Subsyndromal SAD (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[12]	none	16	14	-	MD 1 higher (1.72 lower to 3.72 higher)	⊕⊕OO LOW	
Mean self rated depression scores (BDI) at endpoint - SAD (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[13]	none	33	32	-	MD 0.9 lower (4.66 lower to 2.86 higher)	⊕⊕OO LOW	
Non remission - SAD												
2	randomised trials	no serious limitations	serious[14]	no serious indirectness	serious[15]	none				0 fewer per 100		

							27/50 (54%)	26/48 (54.2%) 42.5%	RR 1.00 (0.69 to 1.45)	(from 17 fewer to 24 more) 0 fewer per 100 (from 13 fewer to 19 more)	⊕⊕OO LOW	
Non response (overall)												
3	randomised trials	no serious limitations	serious[16]	no serious indirectness	serious[17]	none	29/66 (43.9%)	27/63 (42.9%) 40%	RR 1 (0.51 to 1.98)	0 fewer per 100 (from 21 fewer to 42 more) 0 fewer per 100 (from 20 fewer to 39 more)	⊕⊕OO LOW	
Non response - SAD												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[18]	none	24/50 (48%)	18/48 (37.5%) 32.5%	RR 1.26 (0.78 to 2.01)	10 more per 100 (from 8 fewer to 38 more) 8 more per 100 (from 7 fewer to 33 more)	⊕⊕⊕O MODERATE	
Non response - Subsyndromal SAD												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[19]	none	5/16 (31.3%)	9/15 (60%) 60%	RR 0.52 (0.23 to 1.2)	29 fewer per 100 (from 46 fewer to 12 more) 29 fewer per 100 (from 46 fewer to 12 more)	⊕⊕⊕O MODERATE	

[1] Inconclusive effect size
[2] As 1
[3] Single study
[4] As 3
[5] Inconclusive effect size; single study
[6] As 1
[7] As 5
[8] As 5
[9] As 1
[10] As 5
[11] As 5
[12] As 5
[13] As 5
[14] Significant heterogeneity; random effects model used
[15] As 1
[16] As 15
[17] As 1
[18] As 1
[19] As 5

Author(s): NCCMH
Date: 2009-07-13
Question: Dawn simulation vs attentional control for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Dawn simulation**	**attentional control**	**Relative (95% CI)**	**Absolute**	**Quality**	
Leaving study early for any reason												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	2/70 (2.9%)	10/71 (14.1%) 19.4%	RR 0.33 (0.05 to 2.22)	9 fewer per 100 (from 13 fewer to 17 more) 13 fewer per 100 (from 18 fewer to 24 more)	⊕⊕OO LOW	
Leaving study early due to side effects												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	0/31 (0%)	1/31 (3.2%) 3.2%	RR 0.33 (0.01 to 7.88)	2 fewer per 100 (from 3 fewer to 22 more) 2 fewer per 100 (from 3 fewer to 22 more)	⊕⊕OO LOW	
Leaving study early due to lack of efficacy												

2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3,4]	none	0/45 (0%)	6/44 (13.6%) 11.9%	RR 0.14 (0.02 to 1.1)	12 fewer per 100 (from 13 fewer to 1 more) 10 fewer per 100 (from 12 fewer to 1 more)	⊕⊕⊕O MODERATE	
Reported side effects												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	6/14 (42.9%)	1/13 (7.7%) 7.7%	RR 5.57 (0.77 to 40.26)	35 more per 100 (from 2 fewer to 302 more) 35 more per 100 (from 2 fewer to 302 more)	⊕⊕OO LOW	
Mean clinician rated typical depression scores (HAMD-17/HRSD-21) at endpoint (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[6]	no serious indirectness	no serious imprecision	none	37	36	-	SMD 0.53 lower (1.62 lower to 0.15 higher)	⊕⊕⊕O MODERATE	
Mean clinician rated atypical depression scores (SADsubscale) at endpoint (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[7]	no serious indirectness	very serious[8]	none	37	36	-	MD 2.20 lower (7.52 lower to 3.11 higher)	⊕OOO VERY LOW	
Non remission (SIGHSAD)												
2	randomised trials	no serious limitations	serious[9]	no serious indirectness	serious[10]	none	25/56 (44.6%)	29/58 (50%) 49.9%	RR 0.9 (0.46 to 1.78)	5 fewer per 100 (from 27 fewer to 39 more) 5 fewer per 100 (from 27 fewer to 39 more)	⊕⊕OO LOW	
Non response (SIGHSAD)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[11]	none	14/56 (25%)	21/58 (36.2%) 36.3%	RR 0.71 (034 to 1.48)	11 fewer per 100 (from 17 more to 1195 more) 11 fewer per 100 (from 17 more to 1198 more)	⊕⊕⊕O MODERATE	

[1] Inconclusive effect size
[2] Inconclusive effect size; single study
[3] No explanation was provided
[4] As 1
[5] As 3
[6] Significant heterogeneity; random effects model used
[7] As 6
[8] As 2
[9] As 6
[10] As 2
[11] As 2

Author(s): NCCMH
Date: 2008-11-25
Question: Bright light box vs dawn simulation for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light box	dawn simulation	Relative (95% CI)	Absolute	Quality	
Leaving study early for any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	5/56 (8.9%)	1/56 (1.8%) 2%	RR 3.72 (0.62 to 22.22)	5 more per 100 (from 1 fewer to 38 more) 5 more per 100 (from 1 fewer to 42 more)	⊕⊕⊕O MODERATE	
Leaving study early due to side effects												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	2/33 (6.1%)	0%	RR 4.71 (0.23 to 94.31)	0 more per 1000 (from 0 fewer to 0 more)		
Leaving study early due to lack of efficacy												
1	randomised	no serious	no serious	no serious	no serious	none	0/31	0/31 (0%)	not	not pooled	⊕⊕⊕⊕	

	trials	limitations	inconsistency	indirectness	imprecision		(0%)	0%	pooled	not pooled	HIGH	
Non remission (SIGHSAD)												
2	randomised trials	no serious limitations	serious[3]	no serious indirectness	very serious[4]	none	30/56 (53.6%)	25/56 (44.6%) 46.1%	RR 1.19 (0.7 to 2)	8 more per 100 (from 13 fewer to 45 more) 9 more per 100 (from 14 fewer to 46 more)	⊕OOO VERY LOW	
Non response (SIGHSAD)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[5]	none	20/56 (35.7%)	14/56 (25%) 26.1%	RR 1.45 (0.82 to 2.58)	11 more per 100 (from 5 fewer to 39 more) 12 more per 100 (from 5 fewer to 41 more)	⊕⊕⊕O MODERATE	
Depression: mean endpoint scores (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	21	24	-	MD 0.9 lower (4 lower to 2.2 higher)	⊕⊕OO LOW	
SAD: mean endpoint scores (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	21	24	-	MD 1.8 lower (6.98 lower to 3.38 higher)	⊕⊕OO LOW	

[1] Inconclusive effect size
[2] Inconclusive effect size; single study
[3] Significant effect size - random effects model used
[4] As 1
[5] Inconclusive effect size
[6] As 2
[7] As 2

Author(s): NCCMH
Date: 2008-11-25
Question: Relapse Prevention for
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Relapse Prevention	control	Relative (95% CI)	Absolute		
Leaving study early for any reason - Bright white light visor vs no treatment control												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	4/18 (22.2%)	1/10 (10%) 10%	RR 2.22 (0.29 to 17.27)	12 more per 100 (from 7 fewer to 163 more) 12 more per 100 (from 7 fewer to 163 more)	⊕⊕OO LOW	
Leaving study early for any reason - Bright white light visor vs dim red light visor												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	4/18 (22.2%)	3/18 (16.7%) 16.7%	RR 1.33 (0.35 to 5.13)	6 more per 100 (from 11 fewer to 69 more) 6 more per 100 (from 11 fewer to 69 more)	⊕⊕OO LOW	
Relapse during course of study (BDI>=13 for 2 consec wks) - Bright white light visor vs no treatment control												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	9/18 (50%)	8/10 (80%) 80%	RR 0.63 (0.36 to 1.09)	30 fewer per 100 (from 51 fewer to 7 more) 30 fewer per 100 (from 51 fewer to 7 more)	⊕⊕⊕O MODERATE	
Relapse during course of study (BDI>=13 for 2 consec wks) - Bright white light visor vs dim red light visor												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	9/18 (50%)	4/18 (22.2%) 22.2%	RR 2.25 (0.84 to 5.99)	28 more per 100 (from 4 fewer to 111 more) 28 more per 100 (from 4 fewer to 111 more)	⊕⊕⊕O MODERATE	

[1] Inconclusive effect size; single study
[2] As 1
[3] Single study
[4] As 3

Author(s):
Date: 2009-01-23
Question: Should Acute phase treatment: antidepressants v placebo - efficacy data be used for ?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Acute phase treatment: antidepressants v placebo - efficacy data	control	Relative (95% CI)	Absolute	Quality	Importance
Number not acheiving =/> 50% reduction in SIGH-SAD score at endpoint (overall)												
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	57/129 (44.2%)	68/126 (54%) 57.8%	RR 0.82 (0.63 to 1.05)	10 fewer per 100 (from 20 fewer to 3 more) 10 fewer per 100	⊕⊕⊕⊕HIGH	
Number not acheiving =/> 50% reduction SIGH-SAD score												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	41/93 (44.1%)	47/94 (50%) 50%	RR 0.88 (0.65 to 1.2)	6 fewer per 100 (from 18 fewer to 10 more) 6 fewer per 100	⊕⊕OOLOW	
Number not acheiving =/> 50% reduction in outcome score at endpoint - Fluoxetine v Placebo												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	16/36 (44.4%)	21/32 (65.6%) 65.6%	RR 0.68 (0.43 to 1.05)	21 fewer per 100 (from 37 fewer to 3 more) 20 fewer per 100	⊕⊕OOLOW	
Mean endpoint SIGH-SAD (clinician rated) (antidepressants) (range of scores: -; Better indicated by less)												
2	randomised trial	no serious limitations	serious[3]	no serious indirectness	serious[4]	none	52	47	-	SMD -0.11 (-0.65 to 0.42)	⊕⊕OOLOW	
Mean endpoint (clinician rated) (antidepressants) - Moclobemide v Placebo (range of scores: -; Better indicated by less)												

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	16	15	-	SMD 0.23 (-0.48 to 0.94)	⊕⊕OOLOW
Mean endpoint (clinician rated) (antidepressants) - Fluoxetine v Placebo (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	36	32	-	SMD -0.33 (-0.81 to 0.15)	⊕⊕OOLOW
Mean endpoint BDI (self rated) - Fluoxetine v Placebo (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	36	32	-	MD -1.7 (-6.53 to 3.13)	⊕⊕OOLOW
Mean change (clinician rated) - Sertraline v Placebo (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[8]	none	93	93	-	MD -4.51 (-8.23 to -0.79)	⊕⊕⊕OMODERATE

[1] Single study; inconclusive effect size[2] As 1[3] Significant heterogeneity - random effects model used[4] Inconclusive effect size[5] As 1[6] As 1[7] As 1[8] Single study

Author(s):
Date: 2009-01-23
Question: Should Acute phase treatment: antidepressants v placebo - acceptibility and tolerability be used for ?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Acute phase treatment: antidepressants v placebo - acceptibility and tolerability	control	Relative (95% CI)	Absolute	Quality	Importance
Number leaving the study early for any reason (overall)												
2	randomised trial	no serious limitations	serious[1]	no serious indirectness	very serious[2]	none	20/109 (18.3%)	23/112 (20.5%) 19%	RR 0.7 (0.16 to 3.05)	6 fewer per 100 (from 17 fewer to 42 more) 5 fewer per 100	⊕OOOVERY LOW	
Number leaving the study early for any reason - Sertraline v Placebo												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[3]	none	20/93 (21.5%)	20/94 (21.3%) 21.3%	RR 1.01 (0.58 to 1.75)	0 more per 100 (from -9 fewer to 16 more) 0 more per 100	⊕⊕OOLOW	
Number leaving the study early for any reason - Moclobemide v Placebo												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[4]	none	0/16 (0%)	3/18 (16.7%) 16.7%	RR 0.16 (0.01 to 2.87)	14 fewer per 100 (from 17 fewer to 31 more) 14 fewer per 100	⊕⊕OOLOW	
Number leaving the study early due to side effects												
3	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	12/145 (8.3%)	8/144 (5.6%)	RR 1.48 (0.63 to	3 more per 100 (from -2 fewer to 14 more)	⊕⊕OOLOW	

								5.3%	3.47)	2 more per 100	
Number leaving the study early due to side effects - Sertraline v Placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	10/93 (10.8%)	5/94 (5.3%) 5.3%	RR 2.02 (0.72 to 5.69)	5 more per 100 (from -1 fewer to 25 more) 5 more per 100	⊕⊕OOLOW
Number leaving the study early due to side effects - Moclobemide v Placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	0/16 (0%)	2/18 (11.1%) 11.1%	RR 0.22 (0.01 to 4.34)	9 fewer per 100 (from 11 fewer to 37 more) 8 fewer per 100	⊕⊕OOLOW
Number leaving the study early due to side effects - Fluoxetine v Placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness[8]	very serious	none	2/36 (5.6%)	1/32 (3.1%) 3.1%	RR 1.78 (0.17 to 18.69)	2 more per 100 (from -3 fewer to 55 more) 2 more per 100	⊕⊕OOLOW
Number reporting side effects - Sertraline v Placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[9]	none	76/93 (81.7%)	47/94 (50%) 50%	RR 1.63 (1.31 to 2.04)	31 more per 100 (from 15 more to 52 more) 31 more per 100	⊕⊕⊕OMODERATE
Number reporting side effects - Fluoxetine v Placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[10]	none	35/36 (97.2%)	29/32 (90.6%) 90.6%	RR 1.07 (0.95 to 1.21)	6 more per 100 (from -5 fewer to 19 more) 6 more per 100	⊕⊕⊕OMODERATE

[1] Significant heterogeneity - random effects model used [2] Inconclusive effect size [3] Single study, inconclusive effect size [4] As 3 [5] As 2 [6] As 2 [7] As 3 [8] As 3 [9] Single study [10] As 9

Author(s):
Date: 2009-01-23
Question: Should Acute-phase treatment: antidepressants v active control be used for ?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Acute-phase treatment: antidepressants v active control	control	Relative (95% CI)	Absolute	Quality	
Mean endpoint SIGH-SAD (clinician rated) - Moclobemide v Fluoxetine (range of scores: -; Better indicated by less)												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	11	18	-	MD -1.6 (-7.01 to 3.81)	⊕⊕OOLOW	

[1] No explanation was provided

Author(s):
Date: 2009-01-23
Question: Should Acute-phase treatment: other interventions be used for ?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Acute-phase treatment: other interventions	control	Relative (95% CI)	Absolute		
Number not acheiving =/> 50% reduction in SIGH-SAD score at endpoint - High ion density v Low ion density												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	5/12 (41.7%)	11/13 (84.6%)	RR 0.49 (0.24 to 1)	43 fewer per 100 (from 64 fewer to 0 more)	⊕⊕⊕OMODERATE	
								84.6%		43 fewer per 100		

Author(s):
Date: 2009-01-24
Question: Should Continuation treatment be used for SAD?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Continuation treatment	control	Relative (95% CI)	Absolute	Quality	
Mean endpoint HAMD-21 (clinician-rated) - Propanolol v Placebo (range of scores: -; Better indicated by less)												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	12	11	-	MD -7 (-11.24 to -2.76)	⊕⊕⊕OMODERATE	
Number leaving the study early for any reason - Propanolol v Placebo												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious	none	1/13 (7.7%)	0/11 (0%) 0%	RR 2.57 (0.12 to 57.44)	0 more per 100 (from 0 fewer to 0 more) 0 more per 100	⊕⊕OOLOW	

Author(s):
Date: 2009-01-24
Question: Should Prevention of further episodes be used for SAD?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Prevention of further episodes	control	Relative (95% CI)	Absolute		
Relapse Prevention - Number of patients expriencing a recurrence												
3	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	92/542 (17%)	153/519 (29.5%)	RR 0.58 (0.46 to 0.72)	12 fewer per 100 (from 8 fewer to - 16 fewer)	⊕⊕⊕⊕HIGH	
								31.9%		13 fewer per 100		

Author(s):
Date: 2009-01-15
Question: Should Dose escalation be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Dose escalation	control	Relative (95% CI)	Absolute	Quality	
Mean depression scores (overall) (range of scores: -; Better indicated by less)												
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	228	215	-	SMD -0.11 (-0.29 to 0.08)	⊕⊕⊕⊕HIGH	
Mean depression scores - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg (range of scores: -; Better indicated by less)												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	130	118	-	SMD -0.01 (-0.26 to 0.24)	⊕⊕⊕OMODERATE	
Mean depression scores - Same-dose sertraline (100mg) vs high-dose sertraline (200mg) (range of scores: -; Better indicated by less)												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	98	97	-	SMD -0.22 (-0.51 to 0.06)	⊕⊕⊕OMODERATE	
Number not achieving remission (overall)												
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	154/230 (67%)	158/222 (71.2%) 71.2%	RR 0.94 (0.83 to 1.06)	4 fewer per 100 (from 12 fewer to 4 more) 4 fewer per 100	⊕⊕⊕⊕HIGH	
Number not achieving remission - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	92/131 (70.2%)	88/124 (71%) 71%	RR 0.99 (0.84 to 1.16)	1 fewer per 100 (from 11 fewer to 11 more) 0 fewer per 100	⊕⊕⊕OMODERATE	

Number not achieving remission - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	62/99 (62.6%)	70/98 (71.4%) 71.4%	RR 0.88 (0.72 to 1.07)	9 fewer per 100 (from 20 fewer to 5 more) 8 fewer per 100	⊕⊕⊕OMODERATE
Number not achieving response (overall)											
2	randomised trial	no serious limitations	serious[5]	no serious indirectness	serious[6]	none	103/230 (44.8%)	121/222 (54.5%) 53.6%	RR 0.8 (0.59 to 1.1)	11 fewer per 100 (from 22 fewer to 5 more) 10 fewer per 100	⊕⊕OOLOW
Number not achieving response - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	73/131 (55.7%)	76/124 (61.3%) 61.3%	RR 0.91 (0.74 to 1.12)	6 fewer per 100 (from 16 fewer to 7 more) 5 fewer per 100	⊕⊕OOLOW
Number not achieving response - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[8]	none	30/99 (30.3%)	45/98 (45.9%) 45.9%	RR 0.66 (0.46 to 0.95)	16 fewer per 100 (from 2 fewer to -25 fewer) 15 fewer per 100	⊕⊕⊕OMODERATE
Leaving treatment early for any reason (overall)											
2	randomised trial	no serious limitations	no serious inconsistency[9]	no serious indirectness	serious[10]	none	36/230 (15.7%)	49/222 (22.1%) 21.4%	RR 0.7 (0.48 to 1.04)	7 fewer per 100 (from 11 fewer to 1 more) 6 fewer per 100	⊕⊕⊕OMODERATE
Leaving treatment early for any reason - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[11]	none	26/131 (19.8%)	34/124 (27.4%) 27.4%	RR 0.72 (0.46 to 1.13)	8 fewer per 100 (from 15 fewer to 4 more) 7 fewer per 100	⊕⊕⊕OMODERATE
Leaving treatment early for any reason - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness[12]	very serious[13]	none	10/99 (10.1%)	15/98 (15.3%) 15.3%	RR 0.66 (0.31 to 1.4)	5 fewer per 100 (from 11 fewer to 6 more) 5 fewer per 100	⊕⊕OOLOW
Leaving treatment early due to side effects (overall)											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[14]	none	12/230 (5.2%)	12/223 (5.4%) 5.4%	RR 0.97 (0.45 to 2.11)	0 fewer per 100 (from 3 fewer to 6 more) 0 fewer per 100	⊕⊕OOLOW
Leaving treatment early due to side effects - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[15]	none	6/131 (4.6%)	7/124 (5.6%) 5.7%	RR 0.81 (0.28 to 2.35)	1 fewer per 100 (from 4 fewer to 8 more) 1 fewer per 100	⊕⊕OOLOW
Leaving treatment early due to side effects - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[16]	none	6/99 (6.1%)	5/99 (5.1%) 5.1%	RR 1.2 (0.38 to 3.8)	1 more per 100 (from -3 fewer to 14 more) 1 more per 100	⊕⊕OOLOW
Leaving treatment early due to lack of efficacy - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[17]	none	5/131 (3.8%)	10/124 (8.1%) 8.1%	RR 0.47 (0.17 to 1.35)	4 fewer per 100 (from 7 fewer to 3 more) 4 fewer per 100	⊕⊕OOLOW
Number reporting side effects - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[18]	none	45/99 (45.5%)	54/98 (55.1%) 55.1%	RR 0.82 (0.62 to 1.09)	10 fewer per 100 (from 21 fewer to 5 more) 9 fewer per 100	⊕⊕OOLOW

[1] As 1[2] As 1[3] As 1[4] Significant heterogeneity - random effects model used[5] Inconclusive effect size[6] Single study; inconclusive effect size[7] As 1[8] As 5[9] [Added in error not needed][10] As 7[11] As 7[12] As 7 [13] As 6[14] As 7[15] As 7[16] As 7[17] As 7[18] No explanation was provided

Author(s):
Date: 2009-01-15
Question: Should Switching: continuing AD vs switching be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Switching: continuing AD	switching	Relative (95% CI)	Absolute	Quality	Importance
Number not achieving response - Nortripytline vs fluoxetine												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	21/68 (30.9%)	41/142 (28.9%) 28.9%	RR 1.07 (0.69 to 1.66)	2 more per 100 (from -9 fewer to 19 more) 2 more per 100	⊕⊕OOLOW	
Number not achieving response - Fluoxetine vs mianserin												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	24/38 (63.2%)	18/34 (52.9%) 52.9%	RR 1.19 (0.8 to 1.78)	10 more per 100 (from -11 fewer to 41 more) 10 more per 100	⊕⊕OOLOW	
Number not achieving response - Venlafaxine versus fluoxetine												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	46/59 (78%)	50/60 (83.3%) 83.3%	RR 0.94 (0.78 to 1.12)	5 fewer per 100 (from 18 fewer to 10 more) 4 fewer per 100	⊕⊕⊕OMODERATE	
Number not achieving remission - Nortripytline vs fluoxetine												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[4]	none	12/68 (17.6%)	19/142 (13.4%)	RR 1.32 (0.68 to 2.56)	4 more per 100 (from -4 fewer to 21 more)	⊕⊕OOLOW	

								13.4%		4 more per 100	
Number not achieving remission - Fluoxetine vs mianserin											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	31/38 (81.6%)	22/34 (64.7%) 64.7%	RR 1.26 (0.94 to 1.69)	17 more per 100 (from -4 fewer to 45 more) 16 more per 100	⊕⊕OOLOW
Number not achieving remission - Venlafaxine versus fluoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[6]	none	30/59 (50.8%)	41/60 (68.3%) 68.3%	RR 0.74 (0.55 to 1.01)	18 fewer per 100 (from 31 fewer to 1 more) 17 fewer per 100	⊕⊕⊕OMODERATE
Other comparisons: mean endpoint scores (self-rated) - Nortriptyline vs fluoxetine (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[7]	none	68	142	-	MD 1.05 (-1.31 to 3.41)	⊕⊕⊕OMODERATE
Other comparisons: mean endpoint scores (self-rated) - Fluoxetine vs mianserin (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[8]	none	38	33	-	MD 1.8 (-1.63 to 5.23)	⊕⊕OOLOW
Other comparisons: mean endpoint scores (self-rated) - Venlafaxine versus fluoxetine (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[9]	none	59	60	-	MD -2.03 (-5.22 to 1.16)	⊕⊕OOLOW
Other comparisons: number leaving treatment early for any reason - Nortripytline vs fluoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness[10]	very serious	none	8/68 (11.8%)	28/142 (19.7%) 19.7%	RR 0.6 (0.29 to 1.24)	8 fewer per 100 (from 14 fewer to 5 more) 7 fewer per 100	⊕⊕OOLOW
Other comparisons: number leaving treatment early for any reason - Venlafaxine versus fluoxetine											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[11]	none	15/59 (25.4%)	12/60 (20%) 20%	RR 1.27 (0.65 to 2.48)	5 more per 100 (from -7 fewer to 30 more) 5 more per 100	⊕⊕OOLOW
Other comparisons: number leaving treatment early because of side effects - Nortripytline vs fluoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[12]	none	2/68 (2.9%)	4/142 (2.8%) 2.9%	RR 1.04 (0.2 to 5.56)	0 more per 100 (from -2 fewer to 13 more) 0 more per 100	⊕⊕OOLOW
Other comparisons: number leaving treatment early because of side effects - Fluoxetine continuation vs mianserin											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[13]	none	7/38 (18.4%)	12/34 (35.3%) 35.3%	RR 0.52 (0.23 to 1.17)	17 fewer per 100 (from 27 fewer to 6 more) 16 fewer per 100	⊕⊕OOLOW
Other comparisons: number leaving treatment early because of side effects - Venlafaxine versus fluoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[14]	none	1/59 (1.7%)	3/60 (5%) 5%	RR 0.34 (0.04 to 3.17)	3 fewer per 100 (from 5 fewer to 11 more) 3 fewer per 100	⊕⊕OOLOW
Other comparisons: number reporting side effects - Nortripytline vs fluoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[15]	none	58/68 (85.3%)	119/142 (83.8%) 85.3%	RR 0.98 (0.87 to 1.11)	2 fewer per 100 (from 11 fewer to 9 more) 1 fewer per 100	⊕⊕⊕OMODERATE

[1] As 1[2] Single study[3] As 1[4] As 1[5] No explanation was provided[6] As 3[7] As 3[8] As 1[9] As 1[10] As 1[11] As 1[12] As 1[13] As 1[14] As 1[15] As 3

Author(s):
Date: 2009-01-15
Question: Should Switching: switching to single or combination drugs be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Switching: switching to single or combination drugs	control	Relative (95% CI)	Absolute	Quality	
Switch to venlafaxine vs swich to another antidepressant (efficacy) - Non-response												
2	randomised trial	no serious limitations	serious[1]	no serious indirectness	serious[2]	none	157/255 (61.6%)	173/264 (65.5%) 67.4%	RR 0.91 (0.73 to 1.14)	6 fewer per 100 (from 18 fewer to 9 more) 6 fewer per 100	⊕⊕OOLOW	
Switch to venlafaxine vs swich to another antidepressant (efficacy) - Non-remission												
2	randomised trial	no serious limitations	serious[3]	no serious indirectness	serious[4]	none	133/255 (52.2%)	144/264 (54.5%) 64.2%	RR 0.91 (0.67 to 1.24)	5 fewer per 100 (from 18 fewer to 13 more) 5 fewer per 100	⊕⊕OOLOW	
Switch to venlafaxine vs swich to another antidepressant (efficacy) - versus SSRI (range of scores: -; Better indicated by less)												
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[5]	194	202	-	MD -0.5 (-2.09 to 1.09)	⊕⊕⊕OMODERATE	
Switch to venlafaxine vs swich to another antidepressant (acceptability/tolerability) - Number reporting side effects												
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	157/260 (60.4%)	169/266 (63.5%) 63.7%	RR 0.95 (0.83 to 1.09)	3 fewer per 100 (from 11 fewer to 6 more) 3 fewer per 100	⊕⊕⊕⊕HIGH	
Switch to venlafaxine vs swich to another antidepressant (acceptability/tolerability) - Leaving treatment early for any reason												

2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	58/261 (22.2%)	50/268 (18.7%) 16.1%	RR 1.19 (0.85 to 1.67)	4 more per 100 (from -3 fewer to 13 more) 3 more per 100	⊕⊕OOLOW
Switch to venlafaxine vs swich to another antidepressant (acceptability/tolerability) - Leaving treatment early due to side effects											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	16/261 (6.1%)	14/268 (5.2%) 5.1%	RR 1.17 (0.58 to 2.36)	1 more per 100 (from -2 fewer to 7 more) 0 more per 100	⊕⊕OOLOW
Switch to augmentation strategy vs switch to single drug: efficacy outcomes - Fluoxetine + olanzapine vs fluoxetine - non-response											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[8]	183/389 (47%)	82/202 (40.6%) 48.6%	RR 0.88 (0.74 to 1.05)	5 fewer per 100 (from 11 fewer to 2 more) 5 fewer per 100	⊕⊕⊕OMODERATE
Switch to augmentation strategy vs switch to single drug: efficacy outcomes - Fluoxetine + olanzapine vs fluoxetine - non-remission											
2	randomised trial	no serious limitations	serious[9]	no serious indirectness	very serious[10]	none	209/389 (53.7%)	69/202 (34.2%) 48.4%	RR 1 (0.69 to 1.47)	0 fewer per 100 (from 11 fewer to 16 more) 0 fewer per 100	⊕OOOVERY LOW
Switch to augmentation strategy vs switch to single drug: efficacy outcomes - Fluoxetine + olanzapine vs fluoxetine (range of scores: -; Better indicated by less)											
2	randomised trial	no serious limitations	serious[11]	no serious indirectness	serious[12]	none	389	202	-	MD -1.13 (-3.22 to 0.97)	⊕⊕OOLOW
Switch to augmentation strategy vs switch to single drug: acceptability/tolerability - Fluoxetine + olanzapine vs fluoxetine - leaving treatment early for any reason											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[13]	none	90/389 (23.1%)	40/202 (19.8%) 19.9%	RR 1.12 (0.79 to 1.59)	2 more per 100 (from -4 fewer to 12 more) 2 more per 100	⊕⊕OOLOW

Switch to augmentation strategy vs switch to single drug: acceptability/tolerability - Fluoxetine + olanzapine vs fluoxetine - leaving treatment early due to side effects											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	39/389 (10%)	7/202 (3.5%) 3.9%	RR 2.41 (1.07 to 5.43)	5 more per 100 (from 0 more to 16 more) 5 more per 100	⊕⊕⊕⊕HIGH
Switch to augmentation strategy vs switch to single drug: acceptability/tolerability - Fluoxetine + olanzapine vs fluoxetine - number reporting side effects											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[14]	none	129/146 (88.4%)	119/142 (83.8%) 83.8%	RR 1.05 (0.96 to 1.16)	4 more per 100 (from -3 fewer to 13 more) 4 more per 100	⊕⊕⊕OMODERATE

[1] Significant heterogeneity - random effects model used[2] Inconclusive effect size[3] As 1[4] As 2[5] As 2[6] As 2[7] As 2[8] As 2[9] As 1[10] As 2[11] As 1[12] As 2[13] As 2[14] As 5

Author(s):
Date: 2009-01-15
Question: Should Switching: switching to single drug (randomised first-step drug) be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Switching: switching to single drug (randomised first-step drug)	control	Relative (95% CI)	Absolute	Quality	
Switching strategies: Number of people not achieving at least 50% reduction in depression score - Sertrline to imipramine v imipramine to sertraline												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	65/117 (55.6%)	21/51 (41.2%)	RR 1.35 (0.94 to 1.95)	14 more per 100 (from -2 fewer to 39 more)	⊕⊕OOLOW	
								41.2%		14 more per 100		
Switching strategies: Mean endpoint scores - Sertrline to imipramine v imipramine to sertraline (range of scores: -; Better indicated by less)												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	117	50	-	MD 2.5 (-0.38 to 5.38)	⊕⊕OOLOW	
Switching strategies: Leaving the study early - Sertrline to imipramine v imipramine to sertraline												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	29/117 (24.8%)	5/51 (9.8%)	RR 2.53 (1.04 to 6.16)	15 more per 100 (from 0 more to 51 more)	⊕⊕⊕OMODERATE	
								9.8%		14 more per 100		

[1] Single study; inconclusive effect size[2] As 1[3] Single study

Author(s):
Date: 2009-01-15
Question: Should Switching: single AD vs augmentation strategy (open-label data) be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Switching: single AD	augmentation strategy (open-label data)	Relative (95% CI)	Absolute	Quality	Importance
Number not achieving remission - Tranylcypromine vs venlafaxine ER + mirtazepine												
1	no methodology chosen					none	54/58 (93.1%)	44/51 (86.3%)	RR 1.08 (0.95 to 1.23)	69 more per 1,000		
Mean endpoint scores (self-rated) - Tranylcypromine vs venlafaxine ER + mirtazepine (range of scores: -; Better indicated by less)												
1	no methodology chosen					none	58	51	-	MD 1.1 (-1.06 to 3.26)		
Number leaving treatment early for any reason - Tranylcypromine vs venlafaxine + mirtazepine												
1	no methodology chosen					none	27/58 (46.6%)	11/51 (21.6%)	RR 2.16 (1.19 to 3.9)	250 more per 1,000		
Number leaving treatment early because of side effects - Tranylcypromine vs venlafaxine + mirtazepine												
1	no methodology chosen					none	24/58 (41.4%)	11/51 (21.6%)	RR 1.92 (1.05 to 3.52)	198 more per 1,000		

Author(s):
Date: 2009-01-15
Question: Switching: switching to single drug (open-label data) for
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Switching: switching to single drug (open-label data)	control	Relative (95% CI)	Absolute	Quality	Importance
Number not achieving remission - Venlafaxine versus sertraline or a range of antidepressants												
2	no methodology chosen					none	1051/2080 (50.5%)	1113/1910 (68.6%)	RR 0.87 (0.82 to 0.92)	89 fewer per 1,000		
Number not achieving remission - Mirtazepine vs nortripyline												
1	no methodology chosen					none	100/114 (87.7%)	97/121 (80.2%)	RR 1.09 (0.98 to 1.22)	72 more per 1,000		
Mean endpoint data - Venlafaxine versus sertraline or a range of antidepressants (range of scores: -; Better indicated by less)												
2	no methodology chosen					none	1882	1703	-	MD -0.78 (-1.21 to -0.35)		
Mean endpoint data - Venlafaxine versus buproprion (range of scores: -; Better indicated by less)												
1	no methodology chosen					none	250	239	-	MD -0.3 (-1.37 to 0.77)		
Mean endpoint data - Mirtazepine vs nortripyline (range of scores: -; Better indicated by less)												
1	no methodology chosen					none	114	121	-	MD 0.4 (-1.04 to 1.84)		
Leaving the study early for any reason - Venlafaxine versus sertraline or a range of antidepressants												

2	no methodology chosen	none	598/2080 (28.8%)	642/1910 (36.1%)	RR 0.86 (0.78 to 0.94)	50 fewer per 1,000
Leaving the study early for any reason - Mirtazepine vs nortripyline						
1	no methodology chosen	none	38/114 (33.3%)	37/121 (30.6%)	RR 1.09 (0.75 to 1.58)	27 more per 1,000
Leaving the study early due to side effects - Venlafaxine versus sertraline or a range of antidepressants						
2	no methodology chosen	none	273/2080 (13.1%)	172/1910 (14.2%)	RR 1.31 (0.81 to 2.13)	44 more per 1,000
Leaving the study early due to side effects - Mirtazepine vs nortripyline						
1	no methodology chosen	none	38/114 (33.3%)	42/121 (34.7%)	RR 0.96 (0.67 to 1.37)	13 fewer per 1,000
Number reporting side effects - Venlafaxine versus sertraline or a range of antidepressants						
2	no methodology chosen	none	481/2080 (23.1%)	459/1910 (48.5%)	RR 0.97 (0.89 to 1.07)	14 fewer per 1,000
Number reporting side effects - Mirtazepine vs nortripyline						
1	no methodology chosen	none	96/114 (84.2%)	104/121 (86%)	RR 0.98 (0.88 to 1.09)	17 fewer per 1,000

Author(s):
Date: 2009-01-15
Question: Should Augmentation: AD + AD vs AD + (placebo or nothing) be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Augmentation: AD + AD	AD + (placebo or nothing)	Relative (95% CI)	Absolute	Quality	Importance
Number not achieving response - SSRIs + Mianserin												
3	randomised trial	no serious limitations	serious[1]	no serious indirectness	serious[2]	none	49/141 (34.8%)	65/149 (43.6%) 63.2%	RR 0.71 (0.44 to 1.17)	13 fewer per 100 (from 24 fewer to 7 more) 18 fewer per 100	⊕⊕OOLOW	
Number not achieving response - Sertraline + mianserin v high dose sertraline + placebo												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	32/98 (32.7%)	45/98 (45.9%) 45.9%	RR 0.71 (0.5 to 1.02)	13 fewer per 100 (from 23 fewer to 1 more) 13 fewer per 100	⊕⊕⊕OMODERATE	
Number not achieving response - ADs + Mirtazapine												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	4/11 (36.4%)	12/15 (80%) 80%	RR 0.45 (0.2 to 1.03)	44 fewer per 100 (from 64 fewer to 2 more) 44 fewer per 100	⊕⊕⊕OMODERATE	
Number not achieving remission - SSRIs + Mianserin												
2	randomised trial	no serious limitations	serious[5]	no serious indirectness	serious[6]	none	73/130 (56.2%)	93/137 (67.9%)	RR 0.81 (0.62 to 1.04)	13 fewer per 100 (from 26 fewer to 3 more)	⊕⊕OOLOW	

								72.1%		13 fewer per 100	
Number not achieving remission - ADs + Mirtazapine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[7]	none	6/11 (54.5%)	13/15 (86.7%) 86.7%	RR 0.63 (0.35 to 1.12)	32 fewer per 100 (from 56 fewer to 10 more) 32 fewer per 100	⊕⊕⊕OMODERATE
Number not achieving remission - Sertraline + mianserin v high dose sertraline + placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[8]	none	55/98 (56.1%)	70/98 (71.4%) 71.4%	RR 0.79 (0.63 to 0.97)	15 fewer per 100 (from 2 fewer to -26 fewer) 14 fewer per 100	⊕⊕⊕OMODERATE
Number not achieving remission - Fluoxetine + desipramine v high dose fluoxetine											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[9]	none	33/46 (71.7%)	26/48 (54.2%) 52.1%	RR 1.32 (0.96 to 1.81)	17 more per 100 (from -2 fewer to 44 more) 16 more per 100	⊕⊕⊕OMODERATE
Mean endpoint or change scores - SSRIs + Mianserin (range of scores: -; Better indicated by less)											
3	randomised trial	no serious limitations	serious[10]	no serious indirectness	serious[11]	none	141	147	-	SMD -0.46 (-1.07 to 0.15)	⊕⊕OOLOW
Mean endpoint or change scores - Fluoxetine + desipramine v high dose fluoxetine (range of scores: -; Better indicated by less)											
2	randomised trial	no serious limitations	serious[12]	no serious indirectness	serious[13]	none	46	48	-	SMD 0.67 (0.05 to 1.28)	⊕⊕OOLOW
Mean endpoint or change scores - ADs + Mirtazapine (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[14]	none	11	15	-	SMD -0.83 (-1.64 to -0.01)	⊕⊕⊕OMODERATE
Mean endpoint or change scores - Amtriptyline + Moclobemide (range of scores: -; Better indicated by less)											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[15]	none	20	19	-	SMD -0.63 (-1.28 to 0.01)	⊕⊕⊕OMODERATE
Mean endpoint or change scores - AD + atomoxetine (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[16]	none	70	71	-	SMD -0.23 (-0.56 to 0.1)	⊕⊕⊕OMODERATE
Leaving the study early - SSRIs + Mianserin											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[17]	none	23/130 (17.7%)	17/137 (12.4%) 14.3%	RR 1.44 (0.81 to 2.58)	5 more per 100 (from -2 fewer to 20 more) 6 more per 100	⊕⊕OOLOW
Leaving the study early - Fluoxetine + desipramine v high dose fluoxetine											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[18]	none	8/46 (17.4%)	5/48 (10.4%) 11.2%	RR 1.71 (0.61 to 4.83)	7 more per 100 (from -4 fewer to 40 more) 7 more per 100	⊕⊕OOLOW
Leaving the study early - ADs + Mirtazapine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[19]	none	1/11 (9.1%)	2/15 (13.3%) 13.3%	RR 0.68 (0.07 to 6.61)	4 fewer per 100 (from 12 fewer to 75 more) 4 fewer per 100	⊕⊕OOLOW
Leaving the study early - AD + buspirone											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[20]	none	7/54 (13%)	9/54 (16.7%) 16.7%	RR 0.78 (0.31 to 1.94)	4 fewer per 100 (from 12 fewer to 16 more) 3 fewer per 100	⊕⊕OOLOW
Leaving the study early - Sertraline + mianserin v high dose sertraline + placebo											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[21]	none	17/98 (17.3%)	15/98 (15.3%) 15.3%	RR 1.13 (0.6 to 2.14)	2 more per 100 (from -6 fewer to 17 more) 1 more per 100	⊕⊕OOLOW
Leaving the study early - AD + atomoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[22]	none	13/72 (18.1%)	13/74 (17.6%) 17.6%	RR 1.03 (0.51 to 2.06)	1 more per 100 (from -9 fewer to 19 more) 0 more per 100	⊕⊕OOLOW
Leaving the study early due to side effects - SSRIs + Mianserin											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[23]	none	9/130 (6.9%)	6/137 (4.4%) 3%	RR 1.52 (0.58 to 3.96)	2 more per 100 (from -2 fewer to 13 more) 1 more per 100	⊕⊕OOLOW
Leaving the study early due to side effects - Fluoxetine + desipramine v high dose fluoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[24]	none	2/12 (16.7%)	0/15 (0%) 0%	RR 6.15 (0.32 to 117.21)	0 more per 100 (from 0 fewer to 0 more) 0 more per 100	⊕⊕OOLOW
Leaving the study early due to side effects - AD + atomoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[25]	none	7/72 (9.7%)	4/74 (5.4%) 5.4%	RR 1.8 (0.55 to 5.88)	4 more per 100 (from -2 fewer to 26 more) 4 more per 100	⊕⊕OOLOW
Patients reporting side effects - SSRIs + Mianserin											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[26]	none	75/98 (76.5%)	45/99 (45.5%)	RR 1.68 (1.32 to	31 more per 100 (from 15 more to 52 more)	⊕⊕⊕OMODERATE

								45.5%	2.14)	30 more per 100	
Patients reporting side effects - Sertraline + mianserin v high dose sertraline + placebo											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[27]	none	75/98 (76.5%)	54/98 (55.1%)	RR 1.39 (1.13 to 1.71)	21 more per 100 (from 7 more to 39 more)	⊕⊕⊕OMODERATE
								55.1%		21 more per 100	

[1] Significant heterogeneity - random effects model used[2] Inconclusive effect size[3] Single study[4] As 3[5] As 1[6] As 2[7] Single study; inconclusive effect size[8] As 3[9] As 2[10] As 1[11] As 2[12] As 2[13] As 2[14] As 3[15] As 3[16] As 3[17] As 2[18] As 2[19] As 7[20] As 7[21] As 7[22] As 7[23] As 2[24] As 7[25] As 7[26] As 3[27] No explanation was provided

Author(s):
Date: 2009-01-15
Question: Should Augmentation: AD + AP vs AD + (placebo or nothing) be used for depression which has not responded adequately to treatment?
Settings:
Bibliography:

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Augmentation: AD + AP	AD + (placebo or nothing)	Relative (95% CI)	Absolute	Quality	Importance
Number not achieving response (overall)												
9	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	557/866 (64.3%)	601/823 (73%) 72.4%	RR 0.88 (0.82 to 0.95)	9 fewer per 100 (from 4 fewer to -13 fewer) 8 fewer per 100	⊕⊕⊕⊕HIGH	
Number not achieving response - Aripiprazole												
2	randomised trial	no serious limitations	serious[1]	no serious indirectness	no serious imprecision	none	251/372 (67.5%)	259/362 (71.5%) 71.8%	RR 0.94 (0.81 to 1.1)	4 fewer per 100 (from 14 fewer to 7 more) 4 fewer per 100	⊕⊕⊕OMODERATE	
Number not achieving response - Olanzapine												
3	randomised trial	no serious limitations	serious[2]	no serious indirectness	serious[3]	none	124/210 (59%)	155/216 (71.8%) 71.2%	RR 0.81 (0.67 to 1)	14 fewer per 100 (from 24 fewer to 0 more) 13 fewer per 100	⊕⊕OOLOW	
Number not achieving response - Risperidone												
3	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	167/255 (65.5%)	166/216 (76.9%) 75.2%	RR 0.86 (0.77 to 0.97)	11 fewer per 100 (from 2 fewer to -18 fewer) 10 fewer per 100	⊕⊕⊕⊕HIGH	

Number not achieving response - Quetiapine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[4]	none	15/29 (51.7%)	21/29 (72.4%) 72.4%	RR 0.71 (0.47 to 1.08)	21 fewer per 100 (from 38 fewer to 6 more) 20 fewer per 100	⊕⊕OOLOW
Number not achieving remission (overall)											
8	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	640/857 (74.7%)	693/813 (85.2%) 84.2%	RR 0.88 (0.84 to 0.92)	10 fewer per 100 (from 7 fewer to -14 fewer) 10 fewer per 100	⊕⊕⊕⊕HIGH
Number not achieving remission - Aripiprazole											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	278/372 (74.7%)	307/362 (84.8%) 84.8%	RR 0.88 (0.82 to 0.95)	10 fewer per 100 (from 4 fewer to -15 fewer) 10 fewer per 100	⊕⊕⊕⊕HIGH
Number not achieving remission - Olanzapine											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	146/200 (73%)	172/206 (83.5%) 83.5%	RR 0.87 (0.79 to 0.97)	11 fewer per 100 (from 3 fewer to -18 fewer) 10 fewer per 100	⊕⊕⊕⊕HIGH
Number not achieving remission - Risperidone											
3	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	196/256 (76.6%)	190/216 (88%) 84%	RR 0.88 (0.81 to 0.96)	11 fewer per 100 (from 4 fewer to -17 fewer) 10 fewer per 100	⊕⊕⊕⊕HIGH
Number not achieving remission - Quetiapine											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[5]	none	20/29 (69%)	24/29 (82.8%) 82.8%	RR 0.83 (0.62 to 1.12)	14 fewer per 100 (from 31 fewer to 10 more) 14 fewer per 100	⊕⊕⊕OMODERATE
Mean endpoint (overall) (range of scores: -; Better indicated by less)											
6	randomised trial	no serious limitations	serious[6]	no serious indirectness	no serious imprecision	none	568	578	-	SMD -0.45 (-0.62 to -0.28)	⊕⊕⊕OMODERATE
Mean endpoint - Aripiprazole (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[7]	none	185	184	-	SMD -0.32 (-0.53 to -0.12)	⊕⊕⊕OMODERATE
Mean endpoint - Olanzapine (range of scores: -; Better indicated by less)											
2	randomised trial	no serious limitations	serious[8]	no serious indirectness	serious[9]	none	198	203	-	SMD -0.35 (-0.77 to 0.07)	⊕⊕OOLOW
Mean endpoint - Risperidone (range of scores: -; Better indicated by less)											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	156	162	-	SMD -0.56 (-0.78 to -0.33)	⊕⊕⊕⊕HIGH
Mean endpoint - Quetiapine (range of scores: -; Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[10]	none	29	29	-	SMD -0.77 (-1.3 to -0.23)	⊕⊕⊕OMODERATE
Number leaving treatment early for any reason											
7	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[11]	none	121/626 (19.3%)	95/583 (16.3%) 18.6%	RR 1.19 (0.93 to 1.51)	3 more per 100 (from -1 fewer to 8 more) 3 more per 100	⊕⊕⊕OMODERATE
Number leaving treatment early for any reason - Aripiprazole											

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[12]	none	22/182 (12.1%)	16/172 (9.3%) 9.3%	RR 1.3 (0.71 to 2.39)	3 more per 100 (from -3 fewer to 13 more) 2 more per 100	⊕⊕OOLOW
Number leaving treatment early for any reason - Olanzapine											
3	randomised trial	no serious limitations	no serious inconsistency[13]	no serious indirectness	serious[14]	none	53/210 (25.2%)	43/216 (19.9%) 20.2%	RR 1.29 (0.9 to 1.84)	6 more per 100 (from -2 fewer to 17 more) 5 more per 100	⊕⊕⊕OMODERATE
Number leaving treatment early for any reason - Risperidone											
2	randomised trial	no serious limitations	serious[15]	no serious indirectness	very serious[16]	none	35/205 (17.1%)	22/166 (13.3%) 15.1%	RR 1.21 (0.64 to 2.29)	3 more per 100 (from -5 fewer to 17 more) 3 more per 100	⊕OOOVERY LOW
Number leaving treatment early for any reason - Quetiapine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[17]	none	11/29 (37.9%)	14/29 (48.3%) 48.3%	RR 0.79 (0.43 to 1.43)	10 fewer per 100 (from 28 fewer to 21 more) 10 fewer per 100	⊕⊕OOLOW
Number leaving treatment early due to side effects (overall)											
7	randomised trial	no serious limitations	serious[18]	no serious indirectness	no serious imprecision	none	64/807 (7.9%)	23/763 (3%) 2.3%	RR 2.43 (1.18 to 5.03)	4 more per 100 (from 1 more to 12 more) 3 more per 100	⊕⊕⊕OMODERATE
Number leaving treatment early due to side effects - Aripiprazole											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[19]	none	13/373 (3.5%)	6/362 (1.7%)	RR 2.01 (0.76 to	2 more per 100 (from 0 fewer to 7 more)	⊕⊕⊕OMODERATE

								1.7%	5.33)	1 more per 100	
Number leaving treatment early due to side effects - Olanzapine											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	27/200 (13.5%)	5/206 (2.4%) 2.4%	RR 5.53 (2.17 to 14.08)	11 more per 100 (from 3 more to 31 more) 10 more per 100	⊕⊕⊕⊕HIGH
Number leaving treatment early due to side effects - Risperidone											
2	randomised trial	no serious limitations	serious[20]	no serious indirectness	serious[21]	none	16/205 (7.8%)	10/166 (6%) 11.7%	RR 1.13 (0.27 to 4.74)	1 more per 100 (from -4 fewer to 22 more) 1 more per 100	⊕⊕OOLOW
Number leaving treatment early due to side effects - Quetiapine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[22]	none	8/29 (27.6%)	2/29 (6.9%) 6.9%	RR 4 (0.93 to 17.25)	21 more per 100 (from 0 fewer to 100 more) 20 more per 100	⊕⊕OOLOW
Number reporting side effects - (overall)											
3	randomised trial	no serious limitations	serious[23]	no serious indirectness	serious[24]	none	113/229 (49.3%)	104/191 (54.5%) 56.7%	RR 1.06 (0.82 to 1.38)	3 more per 100 (from -10 fewer to 21 more) 3 more per 100	⊕⊕OOLOW
Number reporting side effects - Aripiprazole											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[25]	none	19/30 (63.3%)	17/30 (56.7%) 56.7%	RR 1.12 (0.74 to 1.69)	7 more per 100 (from -15 fewer to 39 more) 6 more per 100	⊕⊕OOLOW

Number reporting side effects - Risperidone											
2	randomised trial	no serious limitations	serious[26]	no serious indirectness	serious[27]	none	129/199 (64.8%)	87/161 (54%) 67.9%	RR 1.11 (0.94 to 1.31)	6 more per 100 (from -3 fewer to 17 more) 7 more per 100	⊕⊕OOLOW

[1] Significant heterogeneity - random effects model used[2] As 1[3] Inconclusive effect size[4] Single study; inconclusive effect size[5] As 4[6] As 1[7] Single study[8] As 1[9] As 3[10] As 7[11] As 3[12] As 4[13] [footnote inserted in error][14] As 3[15] As 1[16] As 1[17] As 4[18] As 1[19] As 3[20] As 1[21] As 3[22] As 4[23] As 1[24] As 3[25] As 4[26] As 1[27] As 3

Author(s): , Rachel Burbeck
Date: 2009-01-27
Question: Augmentation: AD + other psychotropic drug vs AD + (placebo or nothing) for
Settings:
Bibliography: , Burbeck R. Depression update: pharmacology - next-step treatments. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Augmentation: AD + other psychotropic drug	AD + (placebo or nothing)	Relative (95% CI)	Absolute	Quality	
Number not achieving response - ADs + lithium												
6	randomised trial	no serious limitations	serious[1]	no serious indirectness	no serious imprecision[2]	none	56/87 (64.4%)	68/86 (79.1%) 81.8%	RR 0.83 (0.66 to 1.03)	13 fewer per 100 (from 27 fewer to 2 more) 13 fewer per 100	⊕⊕⊕OMODERATE	
Number not achieving remission - AD + lithium												
3	randomised trial	no serious limitations	serious[3]	no serious indirectness	serious[4]	none	57/107 (53.3%)	53/109 (48.6%) 53.3%	RR 1.26 (0.72 to 2.17)	13 more per 100 (from 14 fewer to 57 more) 13 more per 100	⊕⊕OOLOW	
Number not achieving remission - AD + atomoxetine												
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[5]	none	43/72 (59.7%)	36/74 (48.6%) 48.7%	RR 1.23 (0.91 to 1.66)	11 more per 100 (from -4 fewer to 32 more) 11 more per 100	⊕⊕OOLOW	
Mean endpoint or change scores - AD + lithium (range of scores: -; Better indicated by less)												
7	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	135	138	-	SMD -0.32 (-0.56 to -0.08)	⊕⊕⊕⊕HIGH	
Mean endpoint or change scores - AD + atomoxetine (range of scores: -; Better indicated by less)												

1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[6]	none	70	71	-	SMD -0.23 (-0.56 to 0.1)	⊕⊕OOLOW
Leaving the study early - AD + lithium											
8	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	55/178 (30.9%)	31/178 (17.4%) 9.8%	RR 1.79 (1.23 to 2.6)	14 more per 100 (from 4 more to 28 more) 7 more per 100	⊕⊕⊕⊕HIGH
Leaving the study early - AD + atomoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[7]	none	13/72 (18.1%)	13/74 (17.6%) 17.6%	RR 1.03 (0.51 to 2.06)	1 more per 100 (from -9 fewer to 19 more) 0 more per 100	⊕⊕OOLOW
Leaving the study early due to side effects - AD + atomoxetine											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious[8]	none	7/72 (9.7%)	4/74 (5.4%) 5.4%	RR 1.8 (0.55 to 5.88)	4 more per 100 (from -2 fewer to 26 more) 4 more per 100	⊕⊕OOLOW

[1] Significant heterogeneity - random effects model used[2] Not needed[3] As 2[4] Inconclusive effect size[5] Single study; inconclusive effect size[6] As 5[7] As 5[8] As 5

Author(s):
Date: 2009-01-26
Question: Should Comparisons involving ECT be used for severe depression?
Settings:
Bibliography:

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Comparisons involving ECT	control	Relative (95% CI)	Absolute	Quality	
Low-dose bilateral ECT vs low-dose unilateral ECT - non-responders												
4	randomised trial	no serious limitations	serious[1]	no serious indirectness	very serious[2]	none	51/98 (52%)	83/119 (69.7%) 67.9%	RR 0.65 (0.35 to 1.21)	24 fewer per 100 (from 45 fewer to 15 more) 23 fewer per 100	⊕OOOVERY LOW	
Low-dose bilateral ECT vs low-dose unilateral ECT - non-remission												
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	43/67 (64.2%)	46/67 (68.7%) 57.8%	RR 0.93 (0.77 to 1.14)	5 fewer per 100 (from 16 fewer to 10 more) 4 fewer per 100	⊕⊕⊕⊕HIGH	
Low-dose bilateral vs low-dose unilateral - mean endpoint depression scores (range of scores: -; Better indicated by less)												
2	randomised trial	no serious limitations	serious[3]	no serious indirectness	very serious[4]	none	49	42	-	SMD -0.46 (-1.69 to 0.76)	⊕OOOVERY LOW	
Low-dose bilateral ECT vs high-dose unilateral ECT - non-responders												
7	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	63/179 (35.2%)	66/183 (36.1%) 38.5%	RR 0.98 (0.74 to 1.29)	1 fewer per 100 (from 9 fewer to 10 more) 0 fewer per 100	⊕⊕⊕⊕HIGH	
Low-dose bilateral ECT vs high-dose unilateral ECT - non-remission												

5	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[5]	none	62/118 (52.5%)	51/119 (42.9%) 31.8%	RR 1.24 (0.97 to 1.6)	10 more per 100 (from -1 fewer to 26 more) 7 more per 100	⊕⊕⊕OMODERATE
Bilateral ECT (low dose) vs high-dose unilateral ECT - mean endpoint scores (range of scores: -; Better indicated by less)											
4	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious[6]	none	107	97	-	SMD 0.01 (-0.27 to 0.29)	⊕⊕⊕OMODERATE

[1] Significant heterogeneity - random effects model used[2] Inconclusive effect size[3] As 1[4] As 2[5] As 2[6] As 2