National Institute for Health and Care Excellence

Consultation draft

Depression in adults: treatment and management

Appendix U2.6: Text from CG90 Appendix 16d that has been deleted

NICE Guideline

Appendices

May 2018

Disclaimer

Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Appendix 16d: Clinical evidence profiles for the management of subthreshold depressive symptoms

This appendix contains evidence profiles for reviews substantially updated or added to the guideline update (summary evidence profiles are included in the evidence chapters). The use of evidence profiles was introduced since the previous guideline was published.

Evidence profile tables summarise both the quality of the evidence and the results of the evidence synthesis. Each table includes details about the quality assessment of each outcome: quality of the included studies, number of studies and participants, limitations, information about the consistency of the evidence (based on heterogeneity – see Chapter 3), directness of the evidence (that is, how closely the outcome measures, interventions and participants match those of interest) and any other considerations (for example, effect sizes with wide confidence intervals [CIs] would be described as imprecise data). Each evidence profile also includes a summary of the findings: number of patients included in each group, an estimate of the magnitude of effect, quality of the evidence, and the importance of the evidence (where appropriate). The quality of the evidence was based on the quality assessment components (study design, limitations to study quality, consistency, directness and any other considerations) and graded using the following definitions:

High = further research is very unlikely to change our confidence in the estimate of the effects

Moderate = further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate

Low = further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate

Very low = any estimate of effect is very uncertain.

For further information about the process and the rationale of producing an evidence profile table see GRADE (2004) Grading quality of evidence and strength of recommendations. *British Medical Journal*, 328, 1490-1497.

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Are drugs effective for subthreshold depressive symptoms? (Efficacy data)

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Placebo	Relative (95% CI)	Absolute		
Number of people not achieving at least 50% reduction in depression score - SSRIs: dysthymia only												
5	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	176/382 (46.1%)	223/345 (64.6%) 66.5%	RR 0.72 (0.63 to 0.82)	18 fewer per 100 (from 12 fewer to 24 fewer) 19 fewer per 100 (from 12 fewer to 25 fewer)	[redacted] HIGH	
Number of people not achieving at least 50% reduction in depression score - SSRIs: minor depression only												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	55/106 (51.9%)	57/109 (52.3%) 52.3%	RR 0.99 (0.77 to 1.28)	1 fewer per 100 (from 12 fewer to 15 more) 1 fewer per 100 (from 12 fewer to 15 more)	[redacted] MODERATE	

Number of people not achieving at least 50% reduction in depression score - TCAs: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25/68 (36.8%)	54/76 (71.1%) 71.1%	RR 0.52 (0.37 to 0.73)	34 fewer per 100 (from 19 fewer to 45 fewer) 34 fewer per 100 (from 19 fewer to 45 fewer)	[redacted] MODERATE
Number of people not achieving at least 50% reduction in depression score - MAOIs: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25/70 (35.7%)	54/76 (71.1%) 71.1%	RR 0.5 (0.36 to 0.71)	36 fewer per 100 (from 21 fewer to 45 fewer) 36 fewer per 100 (from 21 fewer to 46 fewer)	[redacted] MODERATE
Number of people not achieving remission - SSRIs: dysthymia only											
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	167/317 (52.7%)	194/291 (66.7%) 67.9%	RR 0.78 (0.68 to 0.89)	15 fewer per 100 (from 7 fewer to 21 fewer) 15 fewer per 100 (from 7 fewer to 22	[redacted] HIGH

										fewer)		
Number of people not achieving remission - SSRIs: minor depression only												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	62/106 (58.5%)	60/109 (55%) 55.1%	RR 1.06 (0.84 to 1.34)	3 more per 100 (from 9 fewer to 19 more) 3 more per 100 (from 9 fewer to 19 more)	[redacted] MODERATE	
Number of people not achieving remission - TCAs: dysthymia only												
2	randomised trials	no serious limitations	serious[2]	no serious indirectness	serious[3]	none	120/204 (58.8%)	154/216 (71.3%) 72.7%	RR 0.81 (0.63 to 1.03)	14 fewer per 100 (from 26 fewer to 2 more) 14 fewer per 100 (from 27 fewer to 2 more)	[redacted] LOW	
Number of people not achieving remission - MAOIs: dysthymia only												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	34/70 (48.6%)	59/76 (77.6%) 77.6%	RR 0.63 (0.48 to 0.82)	29 fewer per 100 (from 14 fewer to 40 fewer) 29 fewer per 100 (from 14	[redacted] MODERATE	

										fewer to 40 fewer)		
Mean endpoint scores (clinician rated) - SSRIs: dysthymia only (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	104	115	-	SMD 0.56 lower (0.83 to 0.29 lower)	[redacted] HIGH	
Mean endpoint scores (clinician rated) - SSRIs: minor depression only (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	155	167	-	SMD 0.19 lower (0.41 lower to 0.03 higher)	[redacted] MODERATE	
Mean endpoint scores (clinician rated) - TCAs: dysthymia only (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	107	105	-	SMD 0.62 lower (0.9 to 0.35 lower)	[redacted] MODERATE	
Mean endpoint scores (clinician rated) - Antipsychotics: dysthymia only (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	101	105	-	SMD 0.66 lower (0.94 to 0.38 lower)	[redacted] MODERATE	
Mean endpoint scores (self rated) (Better indicated by lower values)												
1	randomised	no serious	no serious	no serious	serious[1]	none	73	74	-	SMD 0.4 lower (0.72	[redacted]	

	trials	limitations	inconsistency	indirectness						to 0.07 lower)	MODERATE	
Mean endpoint scores (self rated) - SSRIs: minor depression only (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	73	74	-	SMD 0.4 lower (0.72 to 0.07 lower)	[redacted] MODERATE	
Mean change (clinician rated) - SSRIs: dysthymia only (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	206	179	-	SMD 0.31 lower (0.51 to 0.11 lower)	[redacted] HIGH	
Mean change (clinician rated) - TCAs: dysthymia only (Better indicated by lower values)												
3	randomised trials	no serious limitations	serious[2]	no serious indirectness	no serious imprecision	none	306	317	-	SMD 0.61 lower (0.9 to 0.31 lower)	[redacted] MODERATE	
Mean change (clinician rated) - APs: dysthymia only (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	101	105	-	SMD 0.67 lower (0.95 to 0.39 lower)	[redacted] MODERATE	

Mean change (clinician rated) - MAOIs: dysthymia only (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	67	72	-	SMD 0.97 lower (1.32 to 0.62 lower)	[redacted] MODERATE	

[1] Single study
[2] Significant heterogeneity - random effects model used
[3] Non significant effect size

Are drugs effective for subthreshold depressive symptoms? (Acceptability/tolerability data)

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Placebo	Relative (95% CI)	Absolute		
Leaving the study early - SSRIs: dysthymia only												
6	randomised trials	no serious limitations	serious[1]	no serious indirectness	serious[2]	none	101/535 (18.9%)	108/495 (21.8%)	RR 0.84 (0.57 to 1.24)	3 fewer per 100 (from 9 fewer to 5 more)	[redacted] LOW	
								21.5%		3 fewer per 100 (from 9 fewer to 5 more)		

Leaving the study early - SSRIs: minor depression											
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious	none	59/187 (31.6%)	50/190 (26.3%) 26.4%	RR 1.2 (0.87 to 1.65)	5 more per 100 (from 3 fewer to 17 more) 5 more per 100 (from 3 fewer to 17 more)	[redacted] LOW
Leaving the study early - TCAs: dysthymia only											
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	85/366 (23.2%)	78/368 (21.2%) 22.3%	RR 1.1 (0.84 to 1.44)	2 more per 100 (from 3 fewer to 9 more) 2 more per 100 (from 4 fewer to 10 more)	[redacted] MODERATE
Leaving the study early - MAOIs: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[3]	none	13/108 (12%)	15/104 (14.4%) 14.4%	RR 0.83 (0.42 to 1.67)	2 fewer per 100 (from 8 fewer to 10 more) 2 fewer per 100 (from 8 fewer to 10 more)	[redacted] LOW

Leaving the study early - Antipsychotics: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	14/104 (13.5%)	22/108 (20.4%) 20.4%	RR 0.66 (0.36 to 1.22)	7 fewer per 100 (from 13 fewer to 4 more) 7 fewer per 100 (from 13 fewer to 4 more)	[redacted] MODERATE
Leaving the study early due to side effects - SSRIs: dysthymia only											
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[5]	none	12/245 (4.9%)	7/252 (2.8%) 2.7%	RR 1.77 (0.71 to 4.41)	2 more per 100 (from 1 fewer to 9 more) 2 more per 100 (from 1 fewer to 9 more)	[redacted] MODERATE
Leaving the study early due to side effects - SSRIs: minor depression only											
2	randomised trials	no serious limitations	serious[1]	no serious indirectness	serious[2]	none	17/187 (9.1%)	10/190 (5.3%) 5.2%	RR 1.55 (0.51 to 4.68)	3 more per 100 (from 3 fewer to 19 more) 3 more per 100 (from 3 fewer to 19 more)	[redacted] LOW

Leaving the study early due to side effects - TCAs: dysthymia only											
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/366 (12.3%)	8/369 (2.2%) 1.4%	RR 5.44 (2.66 to 11.11)	10 more per 100 (from 4 more to 22 more) 6 more per 100 (from 2 more to 14 more)	[redacted] HIGH
Leaving the study early due to side effects - MAOIs: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[6]	none	7/108 (6.5%)	2/104 (1.9%) 1.9%	RR 3.37 (0.72 to 15.85)	5 more per 100 (from 1 fewer to 29 more) 5 more per 100 (from 1 fewer to 28 more)	[redacted] MODERATE
Leaving the study early due to side effects - APs: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	3/104 (2.9%)	1/108 (0.9%) 0.9%	RR 3.12 (0.33 to 29.47)	2 more per 100 (from 1 fewer to 26 more) 2 more per 100 (from 1 fewer to 26 more)	[redacted] MODERATE

Patients reporting side effects - SSRIs: dysthymia only											
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	188/360 (52.2%)	153/313 (48.9%) 44.9%	RR 1.09 (0.95 to 1.25)	4 more per 100 (from 2 fewer to 12 more) 4 more per 100 (from 2 fewer to 11 more)	[redacted] HIGH
Patients reporting side effects - SSRIs: minor depression only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	25/106 (23.6%)	34/109 (31.2%) 31.2%	RR 0.76 (0.49 to 1.18)	7 fewer per 100 (from 16 fewer to 6 more) 7 fewer per 100 (from 16 fewer to 6 more)	[redacted] MODERATE
Patients reporting side effects - TCAs: dysthymia only											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[6]	none	69/111 (62.2%)	48/108 (44.4%) 44.4%	RR 1.4 (1.08 to 1.81)	18 more per 100 (from 4 more to 36 more) 18 more per 100 (from 4 more to 36 more)	[redacted] MODERATE

Patients reporting side effects - Antipsychotics: dysthymia only												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	57/104 (54.8%)	48/108 (44.4%) 44.4%	RR 1.23 (0.94 to 1.62)	10 more per 100 (from 3 fewer to 28 more) 10 more per 100 (from 3 fewer to 28 more)	MODERATE	

[1] Significant heterogeneity - random effects model used
[2] Inconclusive effect size
[3] Inconclusive effect size; single study
[4] Single study; non significant effect size
[5] Non significant effect size
[6] Single study

Which drugs are effective for subthreshold depressive symptoms? (Efficacy data)

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Other drugs	Relative (95% CI)	Absolute		
Number of people not achieving at least 50% reduction in depression score: SSRI - Dysthymia =/> 50% (fluvoxamine vs maprotiline)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	18/24 (75%)	18/24 (75%)	RR 1 (0.72 to 1.39)	0 fewer per 100 (from 21 fewer to 29 more)	LOW	

								75%		0 fewer per 100 (from 21 fewer to 29 more)		
Number of people not achieving at least 50% reduction in depression score: SSRI - Dysthymia =/> 50% (SSRI vs amisulpride)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	89/295 (30.2%)	65/299 (21.7%) 22%	RR 1.39 (1.06 to 1.83)	8 more per 100 (from 1 more to 18 more) 9 more per 100 (from 1 more to 18 more)	[redacted] HIGH	
Number of people not achieving at least 50% reduction in depression score: SSRI - Minor depression only (paroxetine vs maprotiline)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	30/126 (23.8%)	39/119 (32.8%) 32.8%	RR 0.73 (0.48 to 1.09)	9 fewer per 100 (from 17 fewer to 3 more) 9 fewer per 100 (from 17 fewer to 3 more)	[redacted] MODERATE	
Number of people not achieving at least 50% reduction in depression score: TCA - Dysthymia only (imipramine vs minaprine or moclobemide)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[3]	none	46/102 (45.1%)	43/103 (41.7%) 45.1%	RR 1.07 (0.79 to 1.46)	3 more per 100 (from 9 fewer to 19 more) 3 more per	[redacted] LOW	

										100 (from 9 fewer to 21 more)		
Number of people not achieving at least 50% reduction in depression score: TCA - Dysthymia =/> 50% (amitriptyline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	34/87 (39.1%)	67/166 (40.4%) 40.4%	RR 0.97 (0.7 to 1.33)	1 fewer per 100 (from 12 fewer to 13 more) 1 fewer per 100 (from 12 fewer to 13 more)	[redacted] LOW	
Number of people not achieving remission: SSRI - Dysthymia only (sertraline vs imipramine)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	71/134 (53%)	83/136 (61%) 61%	RR 0.87 (0.7 to 1.07)	8 fewer per 100 (from 18 fewer to 4 more) 8 fewer per 100 (from 18 fewer to 4 more)	[redacted] MODERATE	
Number of people not achieving remission: SSRI - Dysthymia =/> 50% (sertraline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	54/156 (34.6%)	42/157 (26.8%) 26.8%	RR 1.29 (0.92 to 1.81)	8 more per 100 (from 2 fewer to 22 more) 8 more per 100 (from 2	[redacted] MODERATE	

										fewer to 22 more)		
Number of people not achieving remission: SSRI - Minor depression and subsyndromal depressive symptomatology (49% vs 51%) (sertraline vs citalopram)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	42/72 (58.3%)	31/66 (47%) 47%	RR 1.24 (0.9 to 1.71)	11 more per 100 (from 5 fewer to 33 more) 11 more per 100 (from 5 fewer to 33 more)	[redacted] MODERATE	
Number of people not achieving remission: TCA - Dysthymia only (imipramine vs moclobemide)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	37/68 (54.4%)	34/70 (48.6%) 48.6%	RR 1.12 (0.81 to 1.55)	6 more per 100 (from 9 fewer to 27 more) 6 more per 100 (from 9 fewer to 27 more)	[redacted] MODERATE	
Mean endpoint scores (clinician rated): SSRI - Dysthymia =/> 50% (fluvoxamine vs maprotiline) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	21	21	-	SMD 0.01 lower (0.62 lower to 0.59 higher)	[redacted] LOW	

Mean endpoint scores (clinician rated): SSRI - Dysthymia =/> 50% (sertraline vs amisulpride) (Better indicated by lower values)											
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	279	295	-	SMD 0.16 higher (0 to 0.32 higher)	[redacted] HIGH
Mean endpoint scores (clinician rated): TCA - Dysthymia only (imipramine vs minaprine) (Better indicated by lower values)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	24	27	-	SMD 0.34 higher (0.1 lower to 0.77 higher)	[redacted] LOW
Mean endpoint scores (clinician rated): TCA - Dysthymia only (amitriptyline vs amisulpride) (Better indicated by lower values)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	107	101	-	SMD 0.04 higher (0.23 lower to 0.31 higher)	[redacted] MODERATE
Mean endpoint scores (clinician rated): TCA - Dysthymia =/> 50% (imipramine vs phenelzine) (Better indicated by lower values)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	16	16	-	SMD 0.73 higher (0.01 to 1.45 higher)	[redacted] MODERATE
Mean endpoint scores (clinician rated): TCA - Dysthymia =/> 50% (amitriptyline vs amisulpride) (Better indicated by lower values)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	85	165	-	SMD 0.01 lower (0.27 lower to 0.25	[redacted] MODERATE

										higher)		
Mean endpoint scores (clinician rated): AP - Dysthymia only (flupenthixol vs ritanserin) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	36	31	-	SMD 0.26 lower (0.74 lower to 0.22 higher)	LOW	
Mean change (clinician rated): SSRI - Dysthymia only (sertraline vs imipramine) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	134	136	-	SMD 0.05 higher (0.19 lower to 0.29 higher)	MODERATE	
Mean change (clinician rated): TCA - Dysthymia only (imipramine vs moclobemide) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	63	67	-	SMD 0.12 higher (0.23 lower to 0.46 higher)	MODERATE	
Mean change (clinician rated): TCA - Dysthymia only (amitriptyline vs amisulpride) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	107	101	-	SMD 0.06 higher (0.22 lower to 0.33 higher)	MODERATE	

[1] Inconclusive effect size; single study

[2] Single study

[3] Inconclusive effect size

Which drugs are effective for subthreshold depressive symptoms? (Acceptability/tolerability data)

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Others drugs	Relative (95% CI)	Absolute		
Leaving the study early: SSRI - Dysthymia only (sertraline vs imipramine)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	21/134 (15.7%)	45/136 (33.1%) 33.1%	RR 0.47 (0.3 to 0.75)	18 fewer per 100 (from 8 fewer to 23 fewer) 18 fewer per 100 (from 8 fewer to 23 fewer)	[redacted] MODERATE	
Leaving the study early: SSRI - Dysthymia =/> 50% (fluvoxamine vs maprotiline)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	4/24 (16.7%)	6/24 (25%) 25%	RR 0.67 (0.22 to 2.07)	8 fewer per 100 (from 19 fewer to 27 more) 8 fewer per 100 (from 19 fewer to 27 more)	[redacted] LOW	

Leaving the study early: SSRI - Dysthymia =/> 50% (sertraline vs amisulpride)											
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	67/295 (22.7%)	50/299 (16.7%) 17%	RR 1.36 (0.98 to 1.89)	6 more per 100 (from 0 fewer to 15 more) 6 more per 100 (from 0 fewer to 15 more)	MODERATE
Leaving the study early: SSRI - Minor depression and subsyndromal depressive symptomatology (49% vs 51%) (sertraline vs citalopram)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	20/72 (27.8%)	27.3%	RR 1.02 (0.59 to 1.75)	5 more per 1000 (from 112 fewer to 205 more)	LOW
Leaving the study early: TCA - Dysthymia only (imipramine vs moclobemide)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	15/103 (14.6%)	13/108 (12%) 12%	RR 1.21 (0.61 to 2.42)	3 more per 100 (from 5 fewer to 17 more) 3 more per 100 (from 5 fewer to 17 more)	LOW
Leaving the study early: TCA - Dysthymia only (amitriptyline vs amisulpride)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	20/111 (18%)	14/104 (13.5%)	RR 1.34 (0.71 to	5 more per 100 (from 4	

									2.51)	fewer to 20 more)	LOW	
								13.5%		5 more per 100 (from 4 fewer to 20 more)		
Leaving the study early: TCA - Dysthymia =/> 50% (imipramine vs phenelzine)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	5/37 (13.5%)	4/36 (11.1%)	RR 1.22 (0.35 to 4.17)	2 more per 100 (from 7 fewer to 35 more)	LOW	
								11.1%		2 more per 100 (from 7 fewer to 35 more)		
Leaving the study early: TCA - Dysthymia =/> 50% (amitriptyline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	41/87 (47.1%)	73/166 (44%)	RR 1.07 (0.81 to 1.42)	3 more per 100 (from 8 fewer to 18 more)	LOW	
								44%		3 more per 100 (from 8 fewer to 18 more)		
Leaving the study early: Antipsychotics (flupenthixol vs ritanserin)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	3/36 (8.3%)	2/31 (6.5%)	RR 1.29 (0.23 to	2 more per 100 (from 5		

									7.24)	fewer to 40 more)	LOW
								6.5%		2 more per 100 (from 5 fewer to 41 more)	
Leaving the study early due to side effects: SSRI - Dysthymia only (sertraline vs imipramine)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	8/134 (6%)	25/136 (18.4%)	RR 0.32 (0.15 to 0.69)	12 fewer per 100 (from 6 fewer to 16 fewer)	MODERATE
								18.4%		13 fewer per 100 (from 6 fewer to 16 fewer)	
Leaving the study early due to side effects: SSRI - Dysthymia =/> 50% (sertraline/fluoxetine vs amisulpride)											
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	22/295 (7.5%)	23/299 (7.7%)	RR 0.97 (0.55 to 1.7)	0 fewer per 100 (from 3 fewer to 5 more)	LOW
								7.8%		0 fewer per 100 (from 4 fewer to 5 more)	
Leaving the study early due to side effects: SSRI - Minor depression and subsyndromal depressive symptomatology (49% vs 51%) (sertraline vs citalopram)											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	8/72 (11.1%)	10/66 (15.2%)	RR 0.73 (0.31 to	4 fewer per 100 (from 10	

									1.75)	fewer to 11 more)	LOW	
								15.2%		4 fewer per 100 (from 10 fewer to 11 more)		
Leaving the study early due to side effects: TCA - Dysthymia only (imipramine vs minaprine/moclobemide)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[4]	none	15/137 (10.9%)	10/141 (7.1%)	RR 1.54 (0.72 to 3.3)	4 more per 100 (from 2 fewer to 16 more)	[redacted] LOW	
								7.8%		4 more per 100 (from 2 fewer to 18 more)		
Leaving the study early due to side effects: TCA - Dysthymia only (amitriptyline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	6/111 (5.4%)	3/104 (2.9%)	RR 1.87 (0.48 to 7.3)	3 more per 100 (from 1 fewer to 18 more)	[redacted] LOW	
								2.9%		3 more per 100 (from 2 fewer to 18 more)		
Leaving the study early due to side effects: TCA - Dysthymia =/> 50% (amitriptyline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	11/87 (12.6%)	23/166 (13.9%)	RR 0.91 (0.47 to	1 fewer per 100 (from 7	[redacted]	

									1.78)	fewer to 11 more)	LOW	
								13.9%		1 fewer per 100 (from 7 fewer to 11 more)		
Leaving the study early due to side effects: Antipsychotics - Dysthymia only (flupenthixol vs ritanserin)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	2/36 (5.6%)	2/33 (6.1%)	RR 0.92 (0.14 to 6.14)	0 fewer per 100 (from 5 fewer to 31 more)	LOW	
								6.1%		0 fewer per 100 (from 5 fewer to 31 more)		
Patients reporting side effects: SSRI - Dysthymia =/> 50% (sertraline vs amisulpride)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	130/293 (44.4%)	137/298 (46%)	RR 0.96 (0.81 to 1.15)	2 fewer per 100 (from 9 fewer to 7 more)	HIGH	
								46.1%		2 fewer per 100 (from 9 fewer to 7 more)		
Patients reporting side effects: TCA - Dysthymia only (imipramine vs minaprine)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	20/34 (58.8%)	14/33 (42.4%)	RR 1.39 (0.85 to	17 more per 100 (from 6		

								42.4%	2.26)	fewer to 53 more) 17 more per 100 (from 6 fewer to 53 more)	MODERATE	
Patients reporting side effects: TCA - Dysthymia only (amitriptyline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	69/111 (62.2%)	57/104 (54.8%) 54.8%	RR 1.13 (0.9 to 1.42)	7 more per 100 (from 5 fewer to 23 more) 7 more per 100 (from 5 fewer to 23 more)	[redacted] MODERATE	
Patients reporting side effects: TCA - Dysthymia =/> 50% (amitriptyline vs amisulpride)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	62/85 (72.9%)	106/165 (64.2%) 64.2%	RR 1.14 (0.96 to 1.35)	9 more per 100 (from 3 fewer to 22 more) 9 more per 100 (from 3 fewer to 22 more)	[redacted] MODERATE	
Patients reporting side effects: AP - Dysthymia only (flupenthixol vs ritanserin)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[2]	none	16/36 (44.4%)	15/33 (45.5%)	RR 0.98 (0.58 to	1 fewer per 100 (from 19	[redacted]	

									1.65)	fewer to 30 more)	LOW	
								45.5%		1 fewer per 100 (from 19 fewer to 30 more)		

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

Is relapse prevention effective in dysthymia?

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		
Recurrence - TCAs												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	0/14 (0%)	6/13 (46.2%)	RR 0.07 (0 to 1.16)	43 fewer per 100 (from 46 fewer to 7 more)	LOW	
								46.2%		43 fewer per 100 (from 46 fewer to 7 more)		

[1] Inconclusive effect size; single study

Are psychological therapies effective for subthreshold depressive symptoms?

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies	No treatment control	Relative (95% CI)	Absolute		
Efficacy data - Number not responding												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	72/139 (51.8%)	84/138 (60.9%)	RR 0.86 (0.7 to 1.06)	9 fewer per 100 (from 18 fewer to 4 more)	[redacted] MODERATE	
								58.9%		8 fewer per 100 (from 18 fewer to 4 more)		
Efficacy data - Number not achieving remission												
1	randomised trials	no serious limitations	serious[2]	no serious indirectness	serious[1]	none	62/115 (53.9%)	70/112 (62.5%)	RR 0.86 (0.69 to 1.08)	9 fewer per 100 (from 19 fewer to 5 more)	[redacted] LOW	
								58.8%		8 fewer per 100 (from 18		

										fewer to 5 more)		
Efficacy data (continuous) - Clinician-rated endpoint scores (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	97	99	-	SMD 0.27 lower (0.55 lower to 0.01 higher)	[redacted] MODERATE	
Acceptability and tolerability data - Leaving treatment early for any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	20/139 (14.4%)	23/138 (16.7%) 13.2%	RR 0.86 (0.5 to 1.47)	2 fewer per 100 (from 8 fewer to 8 more) 2 fewer per 100 (from 7 fewer to 6 more)	[redacted] MODERATE	

[1] Inconclusive effect

[2] Significant heterogeneity - random effects model used

Are psychological therapies more effective than antidepressants for subthreshold depressive symptoms?

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies	Antidepressants	Relative (95% CI)	Absolute		
Efficacy data - Number not responding												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	92/162 (56.8%)	81/157 (51.6%)	RR 1.09 (0.92 to 1.29)	5 more per 100 (from 4 fewer to 15 more)	HIGH	
								51.9%		5 more per 100 (from 4 fewer to 15 more)		
Efficacy data - Number not remitting												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	80/138 (58%)	70/135 (51.9%)	RR 1.14 (0.92 to 1.41)	7 more per 100 (from 4 fewer to 21 more)	MODERATE	
								58.3%		8 more per 100		

										(from 5 fewer to 24 more)		
Efficacy data (continuous) - Clinician-rated mean endpoint (Better indicated by lower values)												
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	308	320	-	SMD 0.29 higher (0.13 to 0.45 higher)	[redacted] HIGH	
Efficacy data (continuous) - Clinician-rated mean endpoint 6-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	167	186	-	SMD 0.19 higher (0.02 lower to 0.4 higher)	[redacted] MODERATE	
Efficacy data (continuous) - Clinician-rated mean endpoint 18-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	156	179	-	SMD 0.26 higher (0.05 to 0.48 higher)	[redacted] MODERATE	
Efficacy data (continuous) - Self-rated mean endpoint (Better indicated by lower values)												

2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	32	35	-	SMD 0.37 higher (0.11 lower to 0.86 higher)	[redacted] HIGH	
Acceptability and tolerability data - Leaving treatment early for any reason												
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25/175 (14.3%)	39/175 (22.3%) 23%	RR 0.67 (0.42 to 1.06)	7 fewer per 100 (from 13 fewer to 1 more) 8 fewer per 100 (from 13 fewer to 1 more)	[redacted] MODERATE	
Acceptability and tolerability data - Leaving treatment early due to side effects												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[4]	none	0/13 (0%)	1/18 (5.6%) 5.6%	RR 0.45 (0.02 to 10.3)	3 fewer per 100 (from 5 fewer to 52 more) 3 fewer per 100 (from 5 fewer to	[redacted] LOW	

										52 more)		

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

Are psychological therapies used in combination with antidepressants effective for subthreshold depressive symptoms?

Quality assessment							Summary of findings					
							No. of patients		Effect		Quality	Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies + antidepressants	Antidepressants	Relative (95% CI)	Absolute		
Efficacy data - Number not responding												
2	randomised trials	no serious limitations	serious[1]	no serious indirectness	serious[2]	none	28/46 (60.9%)	30/46 (65.2%)	RR 0.96 (0.52 to 1.79)	3 fewer per 100 (from 31 fewer to 52 more)	[redacted] LOW	
								64.4%		3 fewer per 100 (from 31 fewer to 51 more)		
Efficacy data - Number not remitting												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[3]	none	10/21 (47.6%)	14/24 (58.3%)	RR 0.82 (0.47 to 1.43)	10 fewer per 100 (from 31 fewer to 25 more)	[redacted] LOW	

								58.3%		10 fewer per 100 (from 31 fewer to 25 more)		
Efficacy data (continuous) - Clinician-rated mean endpoint (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	233	220	-	SMD 0.09 higher (0.1 lower to 0.27 higher)	[redacted] MODERATE	
Efficacy data (continuous) - Clinician-rated mean endpoint at 6-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	196	186	-	SMD 0.01 higher (0.19 lower to 0.21 higher)	[redacted] MODERATE	
Efficacy data (continuous) - Clinician-rated mean endpoint at 18-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	190	179	-	SMD 0.06 higher (0.14 lower to 0.27 higher)	[redacted] MODERATE	
Acceptability and tolerability data - Leaving treatment early for any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	5/46 (10.9%)	5/46 (10.9%)	RR 1.09 (0.37 to 3.25)	1 more per 100 (from 7 fewer to 24 more)	[redacted] MODERATE	
								10.4%		1 more per 100 (from 7 fewer to 23 more)		

[1] Significant heterogeneity - random effects model used
[2] Inconclusive effect
[3] Single study; inconclusive effect
[4] Single study

Are antidepressants used in combination with psychological therapies more effective for subthreshold depressive symptoms than psychological therapies alone?

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies + antidepressants	Psychological therapies	Relative (95% CI)	Absolute		
Efficacy data - Number not responding												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	8/25 (32%)	16/24 (66.7%)	RR 0.48 (0.25 to 0.91)	35 fewer per 100 (from 6 fewer to 50 fewer)	[redacted] MODERATE	
								66.7%		35 fewer per 100 (from 6 fewer to 50 fewer)		

Efficacy data (continuous) - Clinician-rated mean endpoint data (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none	212	178	-	SMD 0.17 lower (0.37 lower to 0.03 higher)	[redacted] MODERATE	
Efficacy data (continuous) - Clinician-rated mean endpoint data 6-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none	196	167	-	SMD 0.18 lower (0.38 lower to 0.03 higher)	[redacted] MODERATE	
Efficacy data (continuous) - Clinician-rated mean endpoint data 18-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none	190	156	-	SMD 0.2 lower (0.41 lower to 0.01 higher)	[redacted] MODERATE	
Acceptability and tolerability data - Leaving treatment early for any reason												
1	randomised	no serious	no serious	no serious	serious[1,2]	none	1/25 (4%)	0/24 (0%)	RR 2.88	0 more	[redacted]	

	trials	limitations	inconsistency	indirectness					(0.12 to 67.53)	per 100 (from 0 fewer to 0 more)	MODERATE	
								0%		0 more per 100 (from 0 fewer to 0 more)		

[1] Single study

[2] Inconclusive effect

Which type of short-term psychodynamic psychotherapy is more effective for subthreshold depressive symptoms – verbal or art?

Quality assessment							Summary of findings					Importance
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Short psychodynamic verbal vs short psychodynamic art	Control	Relative (95% CI)	Absolute	Quality	
Efficacy data - Self-rated mean endpoint (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	21	18	-	SMD 0.11 lower (0.74 lower to 0.52	LOW	

										higher)		
Efficacy data - Self-rated mean endpoint at 3-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	21	18	-	SMD 0.26 lower (0.9 lower to 0.37 higher)	LOW	
Acceptability and tolerability data - Leaving treatment early for any reason												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	1/22 (4.5%)	3/21 (14.3%) 14.3%	RR 0.32 (0.04 to 2.82)	10 fewer per 100 (from 14 fewer to 26 more) 10 fewer per 100 (from 14 fewer to 26 more)	LOW	

[1] Single study; inconclusive effect

Are psychological therapies used in combination with antidepressants effective for subthreshold depressive symptoms in people who have partially responded to initial treatment?

Quality assessment							Summary of findings					
							No. of patients		Effect		Quality	Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Partial responders	Control	Relative (95% CI)	Absolute		
Number of people not achieving at least 50% reduction in depression score - Psych/SSRI Combo vs SSRI												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	4/20 (20%)	7/20 (35%)	RR 0.57 (0.2 to 1.65)	15 fewer per 100 (from 28 fewer to 23 more)	LOW	
								35%		15 fewer per 100 (from 28 fewer to 23 more)		
Number of people not achieving at least 50% reduction in depression score: 12 week follow-up - Psych/SSRI Combo vs SSRI												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	9/20 (45%)	14/20 (70%)	RR 0.64 (0.37 to 1.13)	25 fewer per 100 (from 44 fewer to 9 more)	LOW	
								70%		25 fewer per 100 (from 44 fewer to 9 more)		

Number of people not achieving remission - Psych/SSRI Combo vs SSRI											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	6/20 (30%)	10/20 (50%) 50%	RR 0.6 (0.27 to 1.34)	20 fewer per 100 (from 37 fewer to 17 more) 20 fewer per 100 (from 37 fewer to 17 more)	[redacted] LOW
Number of people not achieving remission: 12 week follow-up - Psych/SSRI Combo vs SSRI											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	16/20 (80%)	14/20 (70%) 70%	RR 1.14 (0.8 to 1.64)	10 more per 100 (from 14 fewer to 45 more) 10 more per 100 (from 14 fewer to 45 more)	[redacted] LOW
Leaving the study early - Psych/SSRI Combo vs SSRI											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1]	none	2/20 (10%)	3/20 (15%) 15%	RR 0.67 (0.12 to 3.57)	5 fewer per 100 (from 13 fewer to 39 more) 5 fewer per 100 (from 13 fewer to 39 more)	[redacted] LOW

[1] Single study; inconclusive effect