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Service-level interventions

Collaborative care versus standard care

Quality assessment							Summary of findings					Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No. of patients		Effect		Quality	
							Collaborative care	Any standard care	Relative (95% CI)	Absolute		
Mortality												
9	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	117/1493 (7.8%)	121/1506 (8%)	RR 0.94 (0.74 to 1.19)	5 fewer per 1000 (from 21 fewer to 15 more)	⊕⊕○○ LOW	
Depression outcome. 1. Non-Response (<50% improvement) - sensitivity analysis - End of treatment												
11	randomised trials	serious ³	serious ⁴	no serious indirectness ⁵	no serious imprecision	none	1121/1797 (62.4%)	1390/1795 (77.4%)	RR 0.82 (0.76 to 0.89)	139 fewer per 1000 (from 85 fewer to 186 fewer)	⊕⊕○○ LOW	
Depression outcome. 1. Non-Response (<50% improvement) - sensitivity analysis - End of treatment - removing those with >50% drop out												
8	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	782/1322 (59.2%)	1016/1330 (76.4%)	RR 0.79 (0.73 to 0.85)	160 fewer per 1000 (from 115 fewer to 206 fewer)	⊕⊕⊕⊕ HIGH	
Depression outcome 2. Non-remission (scoring above cut-off e.g. >7 on HAM-D) - End of treatment												
6	randomised trials	serious ⁶	serious ⁴	no serious indirectness ⁵	no serious imprecision	none	611/1174 (52%)	763/1174 (65%)	RR 0.84 (0.73 to 0.96)	104 fewer per 1000 (from 26 fewer to 175 fewer)	⊕⊕○○ LOW	

Depression outcome 2. Non-remission (scoring above cut-off e.g. >7 on HAM-D) - End of treatment - papers with >50% drop out removed												
5	randomised trials	no serious limitations	serious ⁴	no serious indirectness	no serious imprecision	none	538/1096 (49.1%)	689/1095 (62.9%)	RR 0.81 (0.73 to 0.9)	120 fewer per 1000 (from 63 fewer to 170 fewer)	⊕⊕⊕O MODERATE	
Depression outcome 3. Diagnosis (at follow up) - End of treatment												
2	randomised trials	no serious limitations	serious ⁴	no serious indirectness	serious ^{2,7}	none	76/163 (46.6%)	97/158 (61.4%)	RR 0.77 (0.54 to 1.1)	141 fewer per 1000 (from 282 fewer to 61 more)	⊕⊕OO LOW	
Depression outcome 4. Continuous measures depression rating scale (Change score) - End of treatment (Better indicated by lower values)												
10	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1001	968	-	SMD 0.31 lower (0.4 to 0.22 lower)	⊕⊕⊕⊕ HIGH	
Physical health outcome: 2. Pain intensity (Brief Pain Inventory, author defined scale) - End of treatment (Better indicated by lower values)												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁷	none	725	693	-	SMD 0.15 lower (0.25 to 0.04 lower)	⊕⊕⊕O MODERATE	
Physical health outcome/ QoL: 1. General physical well-being/ functioning (SF-12 physical, etc) - End of treatment (Better indicated by lower values)												
5	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	941	915	-	SMD 0.26 lower (0.35 to 0.17 lower)	⊕⊕⊕O MODERATE	
Physical health outcome/ QoL: 2. General physical well-being/ functioning (Change scores) - End of treatment (Better indicated by lower values)												
6	randomised trials	serious ⁶	no serious inconsistency	no serious indirectness	no serious imprecision	none	566	584	-	SMD 0.12 lower (0.24 to 0.01 lower)	⊕⊕⊕O MODERATE	
Quality of Life 1. General QoL scales (Euroqol, 0-10 rating scale etc.) - End of treatment (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁷	none	484	480	-	SMD 0.14 lower (0.27 to 0.01 lower)	⊕⊕⊕O MODERATE	

Quality of Life 1. General QoL scales (Euroqol, 0-10 rating scale etc.) - Change score (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ^{2,7}	none	146	189	-	SMD 0.08 lower (0.29 lower to 0.14 higher)	⊕⊕⊕O	MODERATE
Service use/ Process of care: 1. Did not receive a consultation / specified number of mental health visits - End of treatment												
3	randomised trials	no serious limitations	serious ⁴	serious ⁵	no serious imprecision	none	239/428 (55.8%)	257/405 (63.5%)	RR 0.83 (0.67 to 1.02)	108 fewer per 1000 (from 209 fewer to 13 more)	⊕⊕OO	LOW
Service use / Process of care (64-66 combined) - End of treatment												
5	randomised trials	no serious limitations	serious ⁴	no serious indirectness ⁵	no serious imprecision	none	250/921 (27.1%)	485/886 (54.7%)	RR 0.5 (0.37 to 0.69)	274 fewer per 1000 (from 170 fewer to 345 fewer)	⊕⊕⊕O	MODERATE
Treatment acceptability - leaving the study early for any reason - End of treatment												
11	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	369/1875 (19.7%)	383/1867 (20.5%)	RR 0.96 (0.85 to 1.08)	8 fewer per 1000 (from 31 fewer to 16 more)	⊕⊕OO	LOW
Satisfaction with service - not satisfied with treatment/care - End of treatment												
3	randomised trials	no serious limitations	no serious inconsistency	serious ⁸	no serious imprecision	none	159/403 (39.5%)	223/442 (50.5%)	RR 0.78 (0.67 to 0.91)	111 fewer per 1000 (from 45 fewer to 166 fewer)	⊕⊕⊕O	MODERATE

Psychiatric liaison versus standard care

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychiatric consultation-liaison	standard care	Relative (95% CI)	Absolute		
Mortality												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	22/331 (6.6%)	19/338 (5.6%)	RR 1.18 (0.65 to 2.14)	10 more per 1000 (from 20 fewer to 64 more)	⊕⊕⊕O MODERATE	
Depression outcome 3. Diagnosis (at follow-up)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	245/331 (74%)	245/338 (72.5%)	RR 1.02 (0.93 to 1.12)	14 more per 1000 (from 51 fewer to 87 more)	⊕⊕⊕O MODERATE	
Physical health outcome/ QoL: 1. General physical well-being/ functioning (SF-12 physical etc) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	213	237	-	SMD 0.06 lower (0.25 lower to 0.12 higher)	⊕⊕⊕O MODERATE	
Treatment acceptability - leaving the study early for any reason												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	57/331 (17.2%)	40/338 (11.8%)	RR 1.46 (1 to 2.12)	54 more per 1000 (from 0 more to 133 more)	⊕⊕⊕O MODERATE	

¹ Sparse data

Multidisciplinary secondary mental healthcare teams versus standard care

Quality assessment							Summary of findings					Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No. of patients		Effect		Quality	
							Multidisciplinary secondary mental healthcare teams	Standard care	Relative (95% CI)	Absolute		
Mortality												
1	randomised trials	no serious limitations	no serious inconsistency	serious	serious ^{1,2}	none	4/33 (12.1%)	3/36 (8.3%)	RR 1.45 (0.35 to 6.02)	38 more per 1000 (from 54 fewer to 418 more)	⊕⊕○○ LOW	
Depression outcome 1. Diagnosis (at follow-up)												
1	randomised trials	no serious limitations	no serious inconsistency	serious ³	serious ¹	none	14/33 (42.4%)	25/36 (69.4%)	RR 0.61 (0.39 to 0.96)	271 fewer per 1000 (from 28 fewer to 424 fewer)	⊕⊕○○ LOW	
Depression outcome 2. Continuous measures depression rating scale (Change score) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious ³	serious ¹	none	33	36	-	SMD 1.03 lower (1.53 to 0.52 lower)	⊕⊕○○ LOW	
Treatment acceptability - leaving the study early for any reason												
1	randomised trials	no serious limitations	no serious inconsistency	serious ³	serious ^{1,2}	none	4/33 (12.1%)	4/36 (11.1%)	RR 1.09 (0.3 to 4.01)	10 more per 1000 (from 78 fewer to 334 more)	⊕⊕○○ LOW	

¹ Sparse data

² Compatible with benefit and no benefit

³ Participants not specifically recruited for a comorbid physical health problem

Psychological and psychosocial interventions

Physical activity versus standard care

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical activity	Standard care	Relative (95% CI)	Absolute		
Depression (end of treatment) (Better indicated by lower values)												
3	randomised trials	no serious limitations	serious ¹	serious ²	no serious imprecision	none	220	141	-	SMD 0.58 lower (1.2 lower to 0.05 higher)	⊕⊕OO LOW	
Depression (Change score) (Better indicated by lower values)												
3	randomised trials	no serious limitations	serious ¹	serious ²	no serious imprecision	none	83	81	-	SMD 0.29 lower (0.6 lower to 0.03 higher)	⊕⊕OO LOW	
Non remission (below cut-off)												
2	randomised trials	no serious limitations	serious ¹	serious ²	no serious imprecision	none	17/67 (25.4%)	29/72 (40.3%)	RR 0.64 (0.31 to 1.3)	145 fewer per 1000 (from 278 fewer to 121 more)	⊕⊕OO LOW	
Non remission (6-month follow-up)												
2	randomised trials	no serious limitations	no serious inconsistency	serious ²	no serious imprecision	none	11/63 (17.5%)	27/62 (43.5%)	RR 0.4 (0.23 to 0.69)	261 fewer per 1000 (from 135 fewer to 335 fewer)	⊕⊕⊕O MODERATE	
Quality of life (end of treatment) (Better indicated by lower values)												
3	randomised trials	no serious limitations	serious ¹	serious ²	no serious imprecision	none	220	141	-	SMD 0.62 lower (1.28 lower to 0.03 higher)	⊕⊕OO LOW	

Physical health outcomes (end of treatment) - Resting HR (beats/min) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	16	10	-	SMD 0.58 lower (1.39 lower to 0.23 higher)	⊕⊕⊕O	MODERATE

¹ I squared > 50%

² Population just below cut-off for depression (for some studies)

³ Sparse data

Peer support (self-help) programmes versus standard care

Quality assessment							Summary of findings				Importance	
							No. of patients		Effect			Quality
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Peer support (self-help)	Standard care	Relative (95% CI)	Absolute		
CES-D (end of treatment) (Better indicated by lower values)												
3	randomised trials	no serious limitations	serious ¹	no serious indirectness	no serious imprecision	none	89	102	-	SMD 0.32 lower (0.62 to 0.03 lower)	⊕⊕⊕O	MODERATE
CES-D (6 month follow-up) (Better indicated by lower values)												
3	randomised trials	no serious limitations	serious ¹	no serious indirectness	no serious imprecision	none	94	108	-	SMD 0.04 lower (0.32 lower to 0.24 higher)	⊕⊕⊕O	MODERATE
Physical Health Outcomes: HIV-1 RNA viral load - End of treatment (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	63	60	-	SMD 0.26 higher (0.09 lower to 0.62 higher)	⊕⊕⊕O	MODERATE
Physical Health Outcomes: HIV-1 RNA viral load - 3-month follow-up (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ^{2,3}	none	62	56	-	SMD 0.17 higher (0.2 lower to 0.53 higher)	⊕⊕⊕O	MODERATE

¹ I squared > 50%

² Sparse data

³ Compatible with benefit and no benefit

Peer support (self-help) programmes versus group-based cognitive and behavioural intervention

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Peer (self-help) support	Group-based cognitive and behavioural intervention	Relative (95% CI)	Absolute		
Depression (end of treatment) (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious ¹	no serious indirectness	no serious imprecision	none	35	54	-	SMD 0.23 lower (0.66 lower to 0.2 higher)	⊕⊕⊕O MODERATE	
Depression (6 month follow-up) (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ^{2,3}	none	38	54	-	SMD 0.34 lower (0.76 lower to 0.08 higher)	⊕⊕⊕O MODERATE	

¹ I squared > 50%

² Compatible with benefit and no benefit

³ Sparse data

Self-help intervention based on cognitive and behavioural principles versus standard care

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Self-help intervention based on CBT	Standard care	Relative (95% CI)	Absolute		Quality
Depression outcome (Better indicated by lower values)												
3	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	47	56	-	SMD 0.4 lower (0.79 lower to 0 higher)	⊕⊕⊕O MODERATE	
Physical health outcome - Visual Functioning Questionnaire (Better indicated by lower values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	12	20	-	MD 7.45 lower (18.58 lower to 3.68 higher)	⊕⊕OO LOW	

¹ Only looked at sub-group of depression (in one study) original sample not stratified for depression

² Sparse data

Group-based CBT versus standard care

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Group-based CBT	Standard care	Relative (95% CI)	Absolute		Quality
Depression (end of treatment) (Better indicated by lower values)												
8	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias ¹	296	265	-	SMD 0.30 lower (0.47 to 0.13 lower)	⊕⊕⊕O MODERATE	

Depression (follow-up - more than 6-months) (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	149	113	-	SMD 0.17 lower (0.42 lower to 0.07 higher)	⊕⊕⊕○	MODERATE
Non remission (below cut-off)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	8/25 (32%)	21/27 (77.8%)	RR 0.41 (0.22 to 0.75)	459 fewer per 1000 (from 194 fewer to 607 fewer)	⊕⊕⊕○	MODERATE
								77.8%		459 fewer per 1000 (from 195 fewer to 607 fewer)		
Non response (<50% reduction from baseline)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	9/25 (36%)	19/27 (70.4%)	RR 0.51 (0.29 to 0.91)	345 fewer per 1000 (from 63 fewer to 500 fewer)	⊕⊕⊕○	MODERATE
								70.4%		345 fewer per 1000 (from 63 fewer to 500 fewer)		
QoL - SF-30 (end of treatment) - Physical (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	20	28	-	SMD 0.28 lower (0.86 lower to 0.29 higher)	⊕⊕⊕○	MODERATE

¹ Possible publication bias

² Compatible with benefit and no benefit

³ Sparse data

Group-based CBT versus other psychosocial interventions

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Group-based CBT	Other psychosocial interventions	Relative (95% CI)	Absolute		
Depression (end of treatment) (Better indicated by lower values)												
5	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	257	209	-	SMD 0.09 higher (0.09 lower to 0.28 higher)	⊕⊕⊕O MODERATE	
Depression (follow-up - less than 6-months) (Better indicated by lower values)												
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	188	132	-	SMD 0.15 higher (0.08 lower to 0.37 higher)	⊕⊕⊕O MODERATE	

¹Compatible with benefit and no benefit

Individual-based cognitive and behavioural intervention versus standard care

Quality assessment							Summary of findings				Importance
							No. of patients		Effect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Individual-based cognitive and behavioural intervention	Standard care	Relative (95% CI)	Absolute	
Depression (end of treatment) (Better indicated by lower values)											
4	randomised	no serious	serious ¹	no serious	no serious	none	177	161	-	SMD 0.55 lower	⊕⊕⊕O

	trials	limitations		indirectness	imprecision					(0.97 to 0.13 lower)	MODERATE	
Non-remission (below cut-off)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	5/33 (15.2%)	8/33 (24.2%)	RR 0.63 (0.23 to 1.71)	90 fewer per 1000 (from 187 fewer to 172 more)	⊕⊕⊕O MODERATE	
							24.2%	90 fewer per 1000 (from 186 fewer to 172 more)				
Depression (16-month follow-up) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	122	111	-	SMD 0.07 lower (0.33 lower to 0.18 higher)	⊕⊕⊕O MODERATE	
QoL (end of treatment) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	21	16	-	SMD 0.00 higher (0.65 lower to 0.65 higher)	⊕⊕⊕O MODERATE	
Physical health outcome - CD4 cell count (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	21	16	-	SMD 0.09 lower (0.74 lower to 0.56 higher)	⊕⊕⊕O MODERATE	

¹ I squared = 56.4%

² Sparse data

Individual-based cognitive and behavioural intervention versus counselling

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Individual-based cognitive and behavioural intervention	Counselling	Relative (95% CI)	Absolute		
Depression (end of treatment) (Better indicated by lower values)												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	209	206	-	SMD 0.14 lower (0.46 lower to 0.18 higher)	⊕⊕⊕○ MODERATE	
Depression (end of treatment) - change score (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	20	20	-	SMD 0.30 higher (0.32 lower to 0.92 higher)	⊕⊕⊕○ MODERATE	
Physical health - CD4 Cell Count (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	13	13	-	SMD 0.34 lower (0.44 lower to 1.11 higher)	⊕⊕⊕○ MODERATE	

¹ Compatible with benefit and no benefit

² Sparse data

Group existential therapy versus standard care

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Group existential therapy	Standard care	Relative (95% CI)	Absolute		
Depression - BDI-21 (end of treatment) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious ¹	serious ^{2,3}	none	40	33	-	SMD 0.03 higher (0.43 lower to 0.49 higher)	⊕⊕⊕⊕ LOW	
Depression - HADS (change score - end of treatment) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ^{2,3}	none	15	15	-	SMD 0.42 lower (1.14 lower to 0.31 higher)	⊕⊕⊕⊕ MODERATE	
Non-remission (still meeting diagnosis of depression) - end of treatment												
1	randomised trials	serious ⁴	no serious inconsistency	no serious indirectness	serious ^{2,3}	none	13/34 (38.2%)	12/20 (60%)	RR 0.64 (0.37 to 1.11)	216 fewer per 1000 (from 378 fewer to 66 more)	⊕⊕⊕⊕ LOW	
								60%		216 fewer per 1000 (from 378 fewer to 66 more)		

¹ Subthreshold depression

² sparse data

³ Effect compatible with benefit and no benefit

⁴ Outcomes reported for a subgroup

Pharmacological interventions

SSRI versus placebo

Quality assessment							Summary of findings				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No. of patients		Effect		Quality
							SSRIs	Placebo	Relative (95% CI)	Absolute	
Leaving the study early: Any reason											
25	randomised trial	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	341/1608 (21.2%)	292/1529 (19.1%)	RR 1.1 (0.96 to 1.27)	19 more per 1000 (from 8 fewer to 50 more)	⊕⊕⊕O MODERATE
Leaving the study early: Lack of efficacy											
4	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	4/178 (2.2%)	11/180 (4.7%)	RR 0.43 (0.16 to 1.16)	25 fewer per 1,000	⊕⊕⊕O MODERATE
Leaving the study early: Due to adverse events											
11	randomised trial	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	55/841 (6.5%)	27/820 (3.3%)	RR 1.89 (1.23 to 2.89)	27 more per 1,000	⊕⊕⊕O MODERATE
Depression: 1. Not achieving success/remission (reaching a specified cut-off) - observer rated											
14	randomised trial	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	355/633 (56.1%)	394/564 (69.9%)	RR 0.81 (0.74 to 0.88)	140 fewer per 1,000	⊕⊕⊕O MODERATE

Depression: 2. Non-response (not achieving 50% reduction from baseline) - patient rated e.g. HADS, BDI											
3	randomised trial	no serious limitations	serious ³	no serious indirectness	serious ²	none	65/139 (46.8%)	85/140 (66.7%)	RR 0.73 (0.44 to 1.22)	180 fewer per 1,000	⊕⊕⊕ LOW
Depression: 2. Non-response (not achieving 50% reduction from baseline) - observer rated e.g. HAMD, MADRS											
17	randomised trial	serious ¹	serious ³	no serious indirectness	no serious imprecision	none	328/677 (48.4%)	402/656 (61.3%)	RR 0.83 (0.71 to 0.97)	109 fewer per 1,000	⊕⊕⊕ LOW
Depression: 3. Patient-rated continuous measures (Better indicated by less)											
13	randomised trial	serious	no serious inconsistency	no serious indirectness	no serious imprecision	none	468	455	-	SMD -0.17 (-0.3 to -0.04)	⊕⊕⊕ MODERATE
Depression: 4. Observer-rated continuous measures (Better indicated by less)											
25	randomised trial	serious	serious	no serious indirectness	no serious imprecision	none	1086	1030	-	SMD -0.33 (-0.47 to -0.19)	⊕⊕⊕ LOW
QoL: 1. continuous measures e.g. SQOL, FACT-G (Better indicated by less)											
7	randomised trial	serious	no serious inconsistency	no serious indirectness	no serious imprecision	none	263	261	-	SMD -0.27 (-0.44 to -0.1)	⊕⊕⊕ MODERATE
Physical outcome / QoL - General physical functioning/ well-being (SF-36 physical component) (Better indicated by less)											
5	randomised trial	serious	no serious inconsistency	no serious indirectness	no serious imprecision	none	168	170	-	SMD 0.02 (-0.19 to 0.23)	⊕⊕⊕ MODERATE

¹ Some studies did not clearly report whether double blinded

² CIs compatible with benefit and no benefit

³ I-squared >50%

TCAs versus placebo

Quality assessment							Summary of findings			
							No. of patients		Effect	
No. of	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other	TCAs	Placebo	Relative	Absolute

studies						considerations			(95% CI)		
Leaving the study early: Any reason											
6	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	40/150 (26.7%)	31/152 (20.4%)	RR 1.33 (0.88 to 2.01)	108 more per 1,000	⊕⊕⊕⊕ MODERATE
Leaving due to adverse events											
5	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	23/118 (19.5%)	12/121 (9.9%)	RR 2.00 (1.06 to 3.78)	111 more per 1,000	⊕⊕⊕⊕ HIGH
Depression: 1. Non-response (<50% improvement) - observer rated											
5	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/112 (38.9%)	84/112 (76.5%)	RR 0.53 (0.41 to 0.68)	374 fewer per 1,000	⊕⊕⊕⊕ HIGH
Depression: 2. Non-remission - patient rated											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	very serious ^{1,2}	none	11/35 (31.4%)	17/40 (47.5%)	RR 0.71 (0.4 to 1.29)	137 fewer per 1,000	⊕⊕⊕⊕ LOW
Depression: 3. Continuous measures (Change score) - patient rated											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	25	27	-	SMD -0.58 (-1.14 to -0.02)	⊕⊕⊕⊕ MODERATE
Depression: 3. Continuous measures (Change score) - observer rated											
8	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	151	173	-	SMD -0.69 (-0.92 to -0.47)	⊕⊕⊕⊕ HIGH

¹ CIs compatible with benefit and no benefit

² Two small studies

Mianserin versus placebo

Quality assessment	Summary of findings
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No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect		Quality
							Mianserin	Placebo	Relative (95% CI)	Absolute	
Leaving the study early: Any reason - At end of treatment - Cancer											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	13/64 (20.3%)	30/64 (48.1%)	RR 0.43 (0.25 to 0.75)	274 fewer per 1,000	⊕⊕⊕⊕ HIGH
Leaving the study early due to lack of efficacy - At end of treatment - Cancer											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/64 (3.1%)	13/64 (23.1%)	RR 0.18 (0.05 to 0.65)	189 fewer per 1,000	⊕⊕⊕⊕ HIGH
Leaving the study early: Due to adverse events - At end of treatment - Cancer											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	2/28 (7.1%)	4/27 (14.8%)	RR 0.48 (0.1 to 2.42)	76 fewer per 1,000	⊕⊕⊕○ MODERATE
Depression: 2. Non-response (not achieving 50% reduction from baseline) - observer rated e.g. HAMD, MADRS - At end of treatment - Cancer											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	17/64 (26.6%)	36/64 (57.2%)	RR 0.47 (0.3 to 0.74)	303 fewer per 1,000	⊕⊕⊕○ MODERATE
Depression: 3. Patient-rated continuous measures (Better indicated by less)											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	36	37	-	SMD -0.5 (-0.96 to -0.03)	⊕⊕⊕○ MODERATE
Depression: 4. Observer-rated continuous measures - Mean Change - Cancer (Better indicated by less)											
3	randomised trial	no serious limitations	serious ⁴	no serious indirectness	no serious imprecision	none	75	75	-	SMD -0.52 (-0.85 to -0.2)	⊕⊕⊕○ MODERATE

¹ Clear heterogeneity by visual inspection

² 2 small studies

³ 1 small study

⁴ No explanation was provided

SSRIs versus TCAs

Quality assessment							Summary of findings				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No. of patients		Effect		Quality
							Head-to-head SSRI	TCA	Relative (95% CI)	Absolute	
Leaving the study early - any reason											
10	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	68/355 (19.2%)	84/344 (24.4%)	RR 0.77 (0.58 to 1.01)	83 fewer per 1,000	⊕⊕⊕⊕ HIGH
Leaving study early due to adverse events											
8	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	30/228 (13.2%)	34/213 (16%)	RR 0.81 (0.52 to 1.27)	55 fewer per 1,000	⊕⊕⊕○ MODERATE
Leaving study early due to adverse cardiac events											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	1/41 (2.4%)	7/40 (17.5%)	RR 0.14 (0.02 to 1.08)	150 fewer per 1,000	⊕⊕⊕○ MODERATE
Leaving the study early: Due to lack of efficacy - At end of treatment											
1	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	2/13 (15.4%)	2/11 (18.2%)	RR 0.85 (0.14 to 5.06)	27 fewer per 1,000	⊕⊕⊕○ MODERATE
Depression: 1. Remission (below cut-off)											
5	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	43/87 (48.6%)	34/83 (46%)	RR 1.22 (0.88 to 1.67)	73 more per 1,000	⊕⊕⊕○ MODERATE
Depression: 2. Non-response (<50% reduction)											
8	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	150/311	155/314	RR 0.97	49 fewer per 1,000	⊕⊕⊕○

	trial	limitations	inconsistency	indirectness			(48.2%)	(49.4%)	(0.83 to 1.14)	1,000	MODERATE
Depression: 3. Continuous measures - observer-rated scales (Better indicated by less)											
9	randomised trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	241	230	-	SMD 0.04 (-0.14 to 0.22)	⊕⊕⊕○ MODERATE
Physical health outcome: 1. MMSE - PD - At end of treatment (Better indicated by less)											
2	randomised trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	26	24	-	MD -0.11 (-1.34 to 1.12)	⊕⊕⊕○ MODERATE

¹ CIs compatible with benefit and no benefit

² Just one study