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 asse	ssment				Su	mmary of	findings		
			L ,				No. of p	patients	E	ffect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Placebo	Relative (95% CI)	Absolute	Quality	
Number	of people no	ot achieving a	at least 50% red	duction in dep	ression score	- SSRIs: dysthyr	nia only					
	randomised trials	no serious limitations	no serious inconsistency		no serious imprecision	none	176/382 (46.1%)	223/345 (64.6%)	RR 0.72 (0.63 to	18 fewer per 100 (from 12 fewer to 24 fewer)	⊕⊕⊕⊕ HIGH	
								66.5%		19 fewer per 100 (from 12 fewer to 25 fewer)	THE I	
Number	of people no	ot achieving a	at least 50% red	duction in dep	ression score	- SSRIs: minor d	lepressior	n only				
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	55/106 (51.9%)	57/109 (52.3%)	RR 0.99 (0.77 to	1 fewer per 100 (from 12 fewer to 15 more)	⊕⊕⊕O MODERATE	
							(0 2.0 / 0)	52.3%	1.28)	1 fewer per 100 (from 12 fewer to 15 more)		

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)	⊕⊕⊕O MODERATE
mber of people r	ot achieving	at least 50% re	duction in dep	ression score	- MAOIs: dysth	ymia only				
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)	⊕⊕⊕O MODERATE
umber of people r	ot achieving	remission - SSR	ls: dysthymia	only						
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	⊕⊕⊕⊕ HIGH

										fewer)		
Numbe	r of people no	t achieving	l remission - SSR	ls: minor den	 ression only	,				,		
	o people iii	, a a a a a a a a a a a a a a a a a a a										
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	62/106 (58.5%)	60/109 (55%)	RR 1.06 (0.84 to	3 more per 100 (from 9 fewer to 19 more)	⊕⊕⊕O MODERATE	
								55.1%	1.34)	3 more per 100 (from 9 fewer to 19 more)		
Numbe	r of people no	ot achieving	remission - TCA	s: dysthymia	only							
		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)	⊕⊕OO LOW	
Numbe	r of people no	ot achieving	remission - MA	Ols: dysthymi	ia only							
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	34/70 (48.6%)	59/76 (77.6%)	RR 0.63 (0.48 to 0.82)		⊕⊕⊕O MODERATE	
								77.6%		29 fewer per 100 (from 14		

										fewer to 40	
										fewer)	
ean	endpoint scor	es (clinician ı	rated) - SSRIs: d	ysthymia only	(Better indic	ated by lower	values)				
	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)	⊕⊕⊕⊕ HIGH
ean	endpoint scor	es (clinician ı	rated) - SSRIs: n	ninor depressi	on only (Bett	er indicated by	lower valu	es)			
	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)	⊕⊕⊕O MODERATE
				1							
ean	enapoint scor	es (clinician ı	rated) - TCAs: d	ysthymia only	(Better indic	ated by lower v	values)				
ean	randomised trials	,	no serious inconsistency	no serious indirectness	serious ¹	none	107	105	-	SMD 0.62 lower (0.9 to 0.35 lower)	⊕⊕⊕O MODERATE
	randomised trials	no serious limitations	no serious	no serious indirectness	serious ¹	none	107		-	lower (0.9 to	
	randomised trials	no serious limitations es (clinician I	no serious inconsistency	no serious indirectness	serious ¹	none	107		-	SMD 0.66 lower (0.94	
ean	randomised trials endpoint score randomised trials	no serious limitations es (clinician I no serious limitations	no serious inconsistency rated) - Antipsy no serious	no serious indirectness chotics: dysth no serious indirectness	serious ¹ ymia only (Be	none etter indicated	107	alues)	-	SMD 0.66 lower (0.94 to 0.38	MODERATE ⊕⊕⊕O

	trials	limitations	inconsistency	indirectness						to 0.07 lower)	MODERATE	
Mean e	ndpoint score	es (self rated) - SSRIs: minor	depression o	nly (Better in	dicated by lower	values)	1			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)	⊕⊕⊕O MODERATE	
Mean cl	nange (clinici	an rated) - S	SRIs: dysthymia	only (Better	indicated by I	ower values)						
	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)	⊕⊕⊕⊕ HIGH	
Mean cl	nange (clinici	an rated) - To	CAs: dysthymia	only (Better i	ndicated by l	ower values)		,				
	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)	⊕⊕⊕O MODERATE	
Mean cl	nange (clinici	an rated) - A	Ps: dysthymia (only (Better in	dicated by lo	wer values)						
	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)	⊕⊕⊕O MODERATE	

Mean	change (clinici	an rated) - M	1AOIs: dysthym	ia only (Bette	r indicated by	/ lower values)						
1	randomised trials			no serious indirectness	serious ¹	none	67	72	-	SMD 0.97 lower (1.32 to 0.62 lower)	⊕⊕⊕O MODERATE	

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

			Quality asse	ssment				Su	mmary of	findings		
			X ,				No. of	patients	E	ffect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Placebo	Relative (95% CI)	Absolute	Quality	
Leaving	the study ea	rly - SSRIs: d	ysthymia only									
	randomised trials	no serious limitations	serious ¹	no serious indirectness	serious ²	none	101/535 (18.9%)		RR 0.84 (0.57 to 1.24)	3 fewer per 100 (from 9 fewer to 5 more) 3 fewer per 100 (from 9	⊕⊕OO LOW	
								21.5%		fewer to 5 more)		

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

										_	
	andomised rials	no serious limitations	no serious inconsistency	no serious indirectness	very serious	none	59/187 (31.6%)	50/190 (26.3%)	RR 1.2 (0.87 to	5 more per 100 (from 3 fewer to 17 more)	⊕⊕OO LOW
								26.4%	1.65)	5 more per 100 (from 3 fewer to 17 more)	
aving th	he study ear	rly - TCAs: dy	sthymia only								
	andomised rials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	85/366 (23.2%)	78/368 (21.2%)	RR 1.1 (0.84 to 1.44)	2 more per 100 (from 3 fewer to 9 more)	⊕⊕⊕O MODERATE
								22.3%	1.44)	2 more per 100 (from 4 fewer to 10 more)	
eaving th	he study ear	rly - MAOIs:	dysthymia only	1							
	andomised rials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ³	none	13/108 (12%)	15/104 (14.4%)	RR 0.83 (0.42 to	2 fewer per 100 (from 8 fewer to 10 more)	⊕⊕OO LOW
								14.4%	1.67)	2 fewer per 100 (from 8 fewer to 10 more)	

	andomised rials	no serious limitations	no serious inconsistency	no serious indirectness	serious⁴	none	14/104 (13.5%)	22/108 (20.4%)	RR 0.66 (0.36 to	7 fewer per 100 (from 13 fewer to 4 more)	⊕⊕⊕O MODERATE
		rly due to side effects - SSRIs						20.4%	1.22)	7 fewer per 100 (from 13 fewer to 4 more)	
aving th	ne study ear	rly due to sid	le effects - SSR	s: dysthymia	only						
	andomised rials	no serious limitations	no serious inconsistency		serious ⁵	none	12/245 (4.9%)	7/252 (2.8%)	RR 1.77 (0.71 to - 4.41)	2 more per 100 (from 1 fewer to 9 more)	⊕⊕⊕O MODERATE
								2.7%		2 more per 100 (from 1 fewer to 9 more)	
eaving th	ne study ear	rly due to sic	le effects - SSR	s: minor depr	ession only						
	randomised no se				none	one 17/187 (9.1%)	37 (0	RR 1.55 (0.51 to 4.68)	3 more per 100 (from 3 fewer to 19 more)		
					(9.1%)	5.2%	4.08)	3 more per 100 (from 3 fewer to 19 more)			

	andomised rials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/366 (12.3%)	8/369 (2.2%)	RR 5.44 (2.66 to	10 more per 100 (from 4 more to 22 more)	⊕⊕⊕⊕ HIGH
		dy early due to side effects - MAOIs: dysthymia only			1.4%	11.11)	6 more per 100 (from 2 more to 14 more)				
aving th	he study ear	rly due to sid	le effects - MA	Ols: dysthymia	a only						
	andomised rials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁶	none	7/108 (6.5%)	2/104 (1.9%)	RR 3.37 (0.72 to 15.85)		⊕⊕⊕O MODERATE
								1.9%	,	5 more per 100 (from 1 fewer to 28 more)	
aving tr	ne study ear	rly due to sic	le effects - APs	: dysthymia oi							
					3/104 (2.9%)		RR 3.12 (0.33 to	2 more per 100 (from 1 fewer to 26 more)	⊕⊕⊕O MODERATE		
				0.9%		23.47)	2 more per 100 (from 1 fewer to 26 more)				

Patient	s reporting si	de effects - S	SRIs: dysthymi	a 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%)	RR 1.09 (0.95 to	4 more per 100 (from 2 fewer to 12 more)	⊕⊕⊕⊕ HIGH
								44.9%	1.25)	4 more per 100 (from 2 fewer to 11 more)	
Patient	s reporting sid	de effects - S	SRIs: minor de	pression only							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁴	none	25/106 (23.6%)	34/109 (31.2%)	RR 0.76 (0.49 to 1.18)	7 fewer per 100 (from 16 fewer to 6 more)	⊕⊕⊕O MODERATE
								31.2%	1.10)	7 fewer per 100 (from 16 fewer to 6 more)	
Patient	s reporting si	de effects - T	CAs: 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%)	RR 1.4 (1.08 to	18 more per 100 (from 4 more to 36 more)	⊕⊕⊕O MODERATE
								44.4%	1.81)	18 more per 100 (from 4 more to 36 more)	

Patient	reporting si	de effects - A	ntipsychotics:	dysthymia on	y							
1	randomised	no serious	no serious	no serious	serious ³	none				10 more per		
	trials	limitations	inconsistency	indirectness				48/108		100 (from 3		
							==/404	(44.4%)	RR 1.23	fewer to 28		
							57/104		(0.94 to	more)	⊕⊕⊕O	
							(54.8%)		1.62)		MODERATE	
										10 more per		
								44.4%		100 (from 3		
										fewer to 28 more)		

¹ Significant heterogeneity - random effects model used ² Inconclusive effect size

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

			Quality asses	ssment				S	ummary o	f findings		
						No. of p	atients	E	ffect		Importance	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Other drugs	Relative (95% CI)	Absolute	Quality	
Number	of people no	ot achieving a	it least 50% red	uction in depr	ession score:	SSRI - Dysthymi	a =/> 509	% (fluvox	amine vs r	naprotiline)		
1	randomised trials			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)	⊕⊕OO LOW	

Inconclusive effect size; single study
 Single study; non significant effect size
 Non significant effect size

⁶ Single study

Number	r of people no	ot achieving (at least 50% red	luction in dep	ression score:	SSRI - Dysthymi	a =/> 509	75% % (SSRI v	s amisulpr	0 fewer per 100 (from 21 fewer to 29 more) ide)		
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	89/295 (30.2%)	65/299 (21.7%)	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	⊕⊕⊕⊕ HIGH	
Number	r of people no	t achieving a	 at least 50% red	luction in dep	ression score:	SSRI - Minor de	pression	only (par	oxetine v	more) maprotiline)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	30/126 (23.8%)	39/119 (32.8%)	RR 0.73 (0.48 to	9 fewer per 100 (from 17 fewer to 3 more)	⊕⊕⊕O MODERATE	
								32.8%	1.09)	9 fewer per 100 (from 17 fewer to 3 more)		
Number	r of people no	ot achieving a	at least 50% red	luction in dep	ression score:	TCA - Dysthymi	a only (in	nipramin	e vs minar	orine or moclo	bemide)	
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ³	none	46/102 (45.1%)	43/103 (41.7%)	RR 1.07 (0.79 to 1.46)	3 more per 100 (from 9 fewer to 19 more)	⊕⊕OO LOW	

har of	naonio - a	at achievina	at least FO9/ year	luction in do-	roccion coord	TCA - Dysthymia	o = /> E00	/ lamituit	atulino va	100 (from 9 fewer to 21 more)	
inei oi t	people no	ot acmeving a	it least 50% rec	·			a -// 307	o (amuri)	Julille vs		
rand trial		no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	34/87 (39.1%)	67/166 (40.4%)	RR 0.97 (0.7 to 1.33)	1 fewer per 100 (from 12 fewer to 13 more)	⊕⊕OO LOW
								40.4%	1.33)	1 fewer per 100 (from 12 fewer to 13 more)	
mber of p	people no	ot achieving r	emission: SSRI	- Dysthymia o	nly (sertraline	vs imipramine)					
rand trial			no serious inconsistency	no serious indirectness	serious ²	none	71/134 (53%)	83/136 (61%)	RR 0.87 (0.7 to	8 fewer per 100 (from 18 fewer to 4 more)	⊕⊕⊕O MODERATE
					serious ²	none		_		100 (from 18 fewer to 4 more)	⊕⊕⊕O MODERATE
trial	als	limitations	inconsistency	indirectness		none aline vs amisulpr	(53%)	(61%)	(0.7 to	100 (from 18 fewer to 4 more) 8 fewer per 100 (from 18 fewer to 4	⊕⊕⊕O MODERATE
trial	people no	limitations ot achieving r	inconsistency	indirectness			(53%)	(61%)	(0.7 to	100 (from 18 fewer to 4 more) 8 fewer per 100 (from 18 fewer to 4 more) 8 more per 100 (from 2 fewer to 22	⊕⊕⊕O MODERATE

ımbe	randomised	no serious	no serious inconsistency	- Minor depre	ession and subserious ²	none	essive sy	31/66 (47%)		fewer to 22 more) % vs 51%) (se 11 more per 100 (from 5 fewer to 33		alopr
							42/72 (58.3%)		RR 1.24 (0.9 to 1.71)	more)	⊕⊕⊕O MODERATE	
umbe	er of people no	ot achieving I	remission: TCA	- Dysthymia o	nly (imiprami	ne vs moclobem	ide)	47%		fewer to 33 more)		
	randomised trials		no serious inconsistency	no serious indirectness	serious ²	none	37/68 (54.4%)	34/70 (48.6%)	RR 1.12 (0.81 to	6 more per 100 (from 9 fewer to 27 more)	⊕⊕⊕O MODERATE	
								48.6%	1.55)	6 more per 100 (from 9 fewer to 27 more)		
100n	endpoint score	es (clinician r	ated): SSRI - Dy	sthymia =/> 5	0% (fluvoxam	ine vs maprotili	ne) (Bett	er indica	ted by low	er values)		
vicali (no serious	no serious	very serious ¹	none				SMD 0.01		

	randomised	no serious	no serious	no serious	no serious	none				SMD 0.16	
	trials	limitations	inconsistency	indirectness	imprecision		279	295	-	higher (0 to	⊕⊕⊕⊕ HIGH
										0.32 higher)	nion
ean e	endpoint score	es (clinician r	ated): TCA - Dy	sthymia only (imipramine v	s minaprine) (Be	etter indi	cated by	lower val	ues)	
	randomised	no serious	no serious	no serious	very serious ¹	none				SMD 0.34	
	trials	limitations	inconsistency	indirectness			24	27		higher (0.1	⊕⊕OO
							24	27	-	lower to 0.77	LOW
										higher)	
lean e	endpoint score	es (clinician r	ated): TCA - Dy			vs amisulpride)	(Better i	ndicated	by lower		
	randomised		no serious		serious ²	none				SMD 0.04	
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	107	101	_	higher (0.23	⊕⊕⊕О
					serious	none	107	101	-	higher (0.23 lower to 0.31	
					serious	none	107	101	-	higher (0.23	
	trials	limitations	inconsistency	indirectness		none ne vs phenelzine			- d by lowe	higher (0.23 lower to 0.31 higher)	
1ean e	trials	limitations es (clinician r	inconsistency	indirectness					- d by lowe	higher (0.23 lower to 0.31 higher)	
Лean е	trials	limitations es (clinician r	inconsistency ated): TCA - Dy	indirectness sthymia =/> 50	0% (imipramii	ne vs phenelzine	e) (Better	indicated	- d by lowe	higher (0.23 lower to 0.31 higher)	
Лean е	trials andpoint score randomised	limitations es (clinician r	inconsistency ated): TCA - Dy	indirectness sthymia =/> 50	0% (imipramii	ne vs phenelzine			d by lowe	higher (0.23 lower to 0.31 higher) r values) SMD 0.73 higher (0.01	MODERATE
Лean є	trials andpoint score randomised	limitations es (clinician r	inconsistency ated): TCA - Dy	indirectness sthymia =/> 50	0% (imipramii	ne vs phenelzine	e) (Better	indicated	d by lowe	higher (0.23 lower to 0.31 higher) r values) SMD 0.73 higher (0.01	MODERATE
	endpoint score randomised trials	es (clinician r	ated): TCA - Dy no serious inconsistency	sthymia =/> 50 no serious indirectness	0% (imiprami serious ²	ne vs phenelzine	e) (Better	indicated	-	higher (0.23 lower to 0.31 higher) r values) SMD 0.73 higher (0.01 to 1.45 higher)	MODERATE
Лean є	endpoint score randomised trials	limitations es (clinician r no serious limitations es (clinician r	ated): TCA - Dy no serious inconsistency	sthymia =/> 50 no serious indirectness	0% (imiprami serious ²	ne vs phenelzine	16 (Better	indicated 16 er indica	-	higher (0.23 lower to 0.31 higher) r values) SMD 0.73 higher (0.01 to 1.45 higher)	⊕⊕⊕O MODERATE
1ean e	randomised trials	limitations es (clinician r no serious limitations es (clinician r	inconsistency ated): TCA - Dy no serious inconsistency ated): TCA - Dy	sthymia =/> 50 no serious indirectness sthymia =/> 50	o% (imipraminations) serious ² o% (amitripty	ne vs phenelzine none line vs amisulpri	e) (Better	indicated	-	higher (0.23 lower to 0.31 higher) r values) SMD 0.73 higher (0.01 to 1.45 higher) ver values) SMD 0.01	MODERATE

										higher)	
ean	endpoint score	es (clinician r	ated): AP - Dys	thymia only (f	upenthixol vs	ritanserin) (Bet	ter indica	ated by lo	ower valu	es)	
	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)	⊕⊕OO LOW
lean	change (clinici	an rated): SS	RI - Dysthymia	only (sertralin	e vs imiprami	ne) (Better indic	ated by I	ower val	ues)		
	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)	⊕⊕⊕O MODERATE
/lean	change (clinici	an rated): TC	A - Dysthymia	only (imipram	ine vs moclob	 emide) (Better i	ndicated	by lower	values)		
	randomised trials		no serious inconsistency		ine vs moclob	emide) (Better in	ndicated 63	by lower	values)	SMD 0.12 higher (0.23 lower to 0.46 higher)	⊕⊕⊕O MODERATE
L	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	T	63	67	-	higher (0.23 lower to 0.46	

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 asses	cement				Su	immary of	findings		
			Quality asses	ssinent			No. of p	oatients	E	ffect		Importanc
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Others drugs	Relative (95% CI)	Absolute	Quality	
Leaving	the study ea	rly: SSRI - Dy	sthymia only (s	sertraline vs in	nipramine)	l						
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	21/134 (15.7%)	45/136 (33.1%)	RR 0.47 (0.3 to	18 fewer per 100 (from 8 fewer to 23 fewer)	⊕⊕⊕O MODERATE	
								33.1%	0.75)	18 fewer per 100 (from 8 fewer to 23 fewer)		
Leaving	the study ea	rly: SSRI - Dy	sthymia =/> 50	% (fluvoxamir	ne vs maproti	line)						
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	4/24 (16.7%)	6/24 (25%)	RR 0.67 (0.22 to	8 fewer per 100 (from 19 fewer to 27 more)	⊕⊕OO LOW	
								25%	2.07)	8 fewer per 100 (from 19 fewer to 27 more)		

eaving	the study ea	rly: SSRI - Dy	sthymia =/> 50	% (sertraline	vs amisulpride	e)						
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	67/295 (22.7%)	50/299 (16.7%)	RR 1.36 (0.98 to 1.89)	6 more per 100 (from 0 fewer to 15 more) 6 more per 100 (from 0	⊕⊕⊕O MODERATE	
aving	the study ea	rly: SSRI - Mi	nor depression	and subsynd	romal depress	sive symptomat	ology (499	17% % vs 51%)	(sertralin	fewer to 15 more)	m)	
	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)	⊕⊕OO LOW	
aving	the study ea	rly: TCA - Dy	sthymia only (ii	mipramine vs	moclobemide	e)						
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	15/103 (14.6%)	13/108 (12%)	RR 1.21 (0.61 to	3 more per 100 (from 5 fewer to 17 more)	⊕⊕OO LOW	
								12%	2.42)	3 more per 100 (from 5 fewer to 17 more)		
aving	the study ea	rly: TCA - Dy	sthymia only (a	mitriptyline v	s amisulpride)						
	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	⊕⊕OO	

								13.5%	2.51)	fewer to 20 more) 5 more per 100 (from 4 fewer to 20 more)	LOW	
Leaving	the study ea	rly: TCA - Dy	sthymia =/> 50	% (imipramine	e vs phenelzin	e)	·		·			
	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)	⊕⊕OO LOW	
								11.1%	4.17)	2 more per 100 (from 7 fewer to 35 more)		
Leaving	the study ear	rly: TCA - Dys	sthymia =/> 509	% (amitriptylii	ne vs amisulp	ride)						
	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)	⊕⊕OO LOW	
								44%	1.42)	3 more per 100 (from 8 fewer to 18 more)		
Leaving	the study ea	rly: Antipsyc	hotics (flupentl	nixol vs ritans	erin)							
	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	⊕⊕ОО	

Leaving	the study ea	rly due to sid	le effects: SSRI	- Dysthymia o	only (sertraling	e vs imipramine)	6.5%	7.24)	fewer to 40 more) 2 more per 100 (from 5 fewer to 41 more)	LOW	
	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)	⊕⊕⊕O MODERATE	
Leaving	the study ea	rly due to sic	le effects: SSRI	- Dysthymia =	:/> 50% (sertr	aline/fluoxetine	vs amisu	18.4%		100 (from 6 fewer to 16 fewer)		
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	22/295 (7.5%)	23/299 (7.7%) 7.8%	RR 0.97 (0.55 to 1.7)	0 fewer per 100 (from 3 fewer to 5 more) 0 fewer per 100 (from 4 fewer to 5	⊕⊕OO LOW	
	the study ea	-	le effects: SSRI		very serious ²	psyndromal dep	ressive sy	mptomato			traline vs cit	:alopram)
		limitations		indirectness	3. 7 33.1003		(11.1%)	(15.2%)	RR 0.73 (0.31 to	4 fewer per 100 (from 10	⊕⊕ОО	

Leaving	the study ea	rly due to sic	le effects: TCA	- Dysthymia o	nly (imiprami	ne vs minaprine	/moclobe	15.2% emide)	1.75)	fewer to 11 more) 4 fewer per 100 (from 10 fewer to 11 more)	LOW	
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ⁴	none	15/137 (10.9%)	10/141 (7.1%) 7.8%	RR 1.54 (0.72 to 3.3)	4 more per 100 (from 2 fewer to 16 more) 4 more per 100 (from 2 fewer to 18 more)	⊕⊕OO LOW	
1	randomised		no serious		nly (amitripty very serious ²	line vs amisulpr	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) 3 more per 100 (from 2 fewer to 18 more)	⊕⊕OO LOW	
1	randomised	T	no serious		/> 50% (amitr very serious ²	iptyline vs amis none	11/87 (12.6%)	23/166 (13.9%)	RR 0.91 (0.47 to	1 fewer per 100 (from 7	⊕⊕⊙⊙	

Leaving	the study ea	rlv due to sid	le effects: Anti	osychotics - Dy	vsthvmia only	(flupenthixol v	s ritanseri	13.9%	1.78)	fewer to 11 more) 1 fewer per 100 (from 7 fewer to 11 more)	LOW	
1	randomised	no serious	no serious	no serious indirectness	very serious ²		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) 0 fewer per 100 (from 5 fewer to 31 more)	⊕⊕OO LOW	
2	randomised		no serious inconsistency	no serious	<u> </u>	none	130/293 (44.4%)	137/298 (46%) 46.1%	RR 0.96 (0.81 to 1.15)	2 fewer per 100 (from 9 fewer to 7 more) 2 fewer per 100 (from 9 fewer to 7 more)	⊕⊕⊕ HIGH	
1	randomised	no serious	no serious inconsistency		1	rine) none	20/34 (58.8%)	14/33 (42.4%)	RR 1.39 (0.85 to	17 more per 100 (from 6	⊕⊕⊕О	

Patients	reporting sid	de effects: T(CA - Dysthymia	only (amitript	cyline vs amis	ulpride)		42.4%	2.26)	fewer to 53 more) 17 more per 100 (from 6 fewer to 53 more)	MODERATE	
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)	⊕⊕⊕O MODERATE	
1	randomised					none	62/85 (72.9%)	106/165 (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)	⊕⊕⊕O MODERATE	
1	randomised	no serious		nly (flupenthino serious indirectness	very serious ²		16/36 (44.4%)	15/33 (45.5%)	RR 0.98 (0.58 to	1 fewer per 100 (from 19	⊕⊕00	

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

Is relapse prevention effective in dysthymia?

			Quality asses	sment				Sumi	mary of fir	ndings		
			X , ******				No. of pa	tients	ı	Effect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Relapse prevention	Control	Relative (95% CI)	Absolute	Quality	
Recurre	nce - TCAs				<u> </u>							
	randomised trials	no serious limitations			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)	⊕⊕OO LOW	
								46.2%	1.10)	43 fewer per 100 (from 46 fewer to 7 more)		

¹ Inconclusive effect size; single study

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

Are psychological therapies effective for subthreshold depressive symptoms?

			Quality asses	ssment				Summa	ary of find	lings		
							No. of pa	itients	Ef	fect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies	No treatment control	Relative (95% CI)	Absolute	Quality	
Efficacy	data - Numl	per not resp	onding									
2	randomised trials			no serious indirectness	serious ¹	none	72/139 (51.8%)	84/138 (60.9%)	RR 0.86 (0.7 to	9 fewer per 100 (from 18 fewer to 4 more)	⊕⊕⊕O MODERATE	
								58.9%	1.00)	8 fewer per 100 (from 18 fewer to 4 more)		
Efficacy	data - Numl	ta - Number not achieving remission	1									
1	randomised trials	no serious limitations			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)	⊕⊕OO LOW	
								58.8%		8 fewer per 100 (from 18		

cacy	data (contin	uous) - Clini	ician-rated and	noint scores	(Rotter indic	ated by lower v	ralues)			fewer to 5 more)	
	randomised	no serious	no serious			none	97	99	-	SMD 0.27 lower (0.55 lower to 0.01 higher)	⊕⊕⊕O MODERATE
	randomised	no serious			T 1	none	20/139 (14.4%)	23/138 (16.7%)	(0.5 to	2 fewer per 100 (from 8 fewer to 8 more)	⊕⊕⊕O MODERATE
								13.2%	1.47)	2 fewer per 100 (from 7 fewer to 6 more)	

¹ Inconclusive effect
² Significant heterogeneity - random effects model used

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

			Quality asse	essment				Summary	of finding	gs		
			~ ,					patients		fect		Importance
No. of studies	i Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies	Antidepressants	Relative (95% CI)	Ahsolute	Quality	
Efficac	y data - Nun	nber not res	ponding		<u> </u>							
	randomised trials		no serious inconsistency			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%	1.29)	5 more per 100 (from 4 fewer to 15 more)		
Efficac	y data - Nun	nber not rer	nitting									
	randomised trials		no serious inconsistency		serious ¹	none	80/138 (58%)	70/135 (51.9%)	(0.92 to	7 more per 100 (from 4 fewer to 21 more)	⊕⊕⊕O MODERATE	
								58.3%		8 more per 100		

										(from 5 fewer to 24 more)		
ffica	cy data (cont	inuous) - Cli	nician-rated m	nean endpoin	it (Better inc	dicated by lowe	r values)					
1	randomised trials		no serious inconsistency		no serious imprecision	none	308	320	-	SMD 0.29 higher (0.13 to 0.45 higher)	⊕⊕⊕ HIGH	
ffica	cy data (cont	inuous) - Cli	nician-rated m	nean endpoin	it 6-month f	ollow-up (Bette	er indicated by	lower values)				
L	randomised trials		no serious inconsistency		serious ²	none	167	186	-	SMD 0.19 higher (0.02 lower to 0.4 higher)	⊕⊕⊕O MODERATE	
Effica	cy data (cont	inuous) - Cli	nician-rated m	nean endpoin	it 18-month	follow-up (Bett	ter indicated b	y lower values)				
L	randomised trials		no serious inconsistency		serious ³	none	156	179		SMD 0.26 higher (0.05 to 0.48 higher)	⊕⊕⊕O MODERATE	
ffica	cy data (cont	inuous) - Se	lf-rated mean	endpoint (Be	etter indicate	ed by lower valu	ues)					

2 randomised no serious trials limitations inconsistency indirectness inprecision no n	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious trials limitations inconsistency indirectness indirectness 100 (from 13 fewer to 1 more) 100 (from 13 fewer to 1 mor	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious trials limitations inconsistency indirectness indirectness 100	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious trials limitations inconsistency indirectness indirectness 100	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious trials limitations inconsistency indirectness serious 1 none 1 39/175 (22.3%) RR 0.67 (0.42 to 1 more) 1	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious limitations inconsistency indirectness indirectness 10.86 higher	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious limitations inconsistency indirectness indirectness indirectness 100	
Acceptability and tolerability data - Leaving treatment early for any reason 4 randomised no serious limitations inconsistency indirectness indirectness 1 none 25/175 39/175 (22.3%) 1 none 39/175 (22.3%) 1 none 1 none 25/175 39/175 (22.3%) 1 none 1 none 25/175 39/175 (22.3%) 1 none 39/175 (22.3%) 1 none 39/175 (22.3%) 1 none 39/175 (22.3%)	
4 randomised no serious inconsistency indirectness serious none limitations inconsistency indirectness serious none 39/175 (22.3%) RR 0.67 (0.42 to 1 more)	
4 randomised no serious inconsistency indirectness serious none limitations inconsistency indirectness serious none 39/175 (22.3%) RR 0.67 (0.42 to 1 more)	
trials limitations inconsistency indirectness 39/175 (22.3%)	
trials limitations inconsistency indirectness 39/175 (22.3%) per 100 (from 13 RR 0.67 fewer to (0.42 to 1 more)	
39/175 (22.3%) (from 13 RR 0.67 fewer to 1 more) (0.42 to 1 more)	
25/175 RR 0.67 fewer to (0.42 to 1 more) $\oplus \oplus \oplus \ominus$	
(14.3%) MODERATE	
1.06) 1.06) 8 fewer	
per 100	
23% (from 13)	
fewer to	
1 more)	
Acceptability and tolerability data - Leaving treatment early due to side effects	
1 randomised no serious no serious very none 3 fewer	
trials limitations inconsistency indirectness serious ⁴ per 100	
1/18 (5.6%) (from 5	
RR 0.45 fewer to $\oplus \oplus OO$	
0/13 (0%) (0.02 to 52 more) LOW	
10.3) 10.3)	
3 fewer	
ner 100	
5.6%	

						,	
						152 morel	
						32 more)	

¹ Inconclusive effect

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

			Quality asses	sment				Summary o	of findings			
			4,				No. of pa	atients	E	ffect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies + antidepressants	Antidepressants	Relative (95% CI)	Absolute	Quality	portanec
Efficacy	data - Numb	er not respo	nding									
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	3 fewer per 100 (from 31 fewer to 52 more)	⊕⊕OO LOW	
							20/40 (00.9%)	64.4%	1.79)	3 fewer per 100 (from 31 fewer to 51 more)		
Efficacy	data - Numb	er not remit	ting									
1	randomised trials		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)	⊕⊕OO LOW	

² Single study

³ Significant heterogeneity - random effects model used

⁴ Single study; inconclusive effect size

fficacy	randomised		ian-rated mean no serious inconsistency		tter indicate	d by lower value	233	58.3%	-	10 fewer per 100 (from 31 fewer to 25 more) SMD 0.09 higher (0.1 lower to	⊕⊕⊕O MODERATE	
fficacy	data (continu	uous) - Clinic	ian-rated mean	endpoint at 6	-month follo	ow-up (Better in	dicated by lower va	lues)		0.27 higher)		
	randomised trials		no serious inconsistency	no serious indirectness	serious ⁴	none	196	186	-	SMD 0.01 higher (0.19 lower to 0.21 higher)	⊕⊕⊕O MODERATE	
icacy	data (continu	uous) - Clinic	ian-rated mean	endpoint at 1	.8-month fol	low-up (Better i	ndicated by lower v	alues)				
	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)	⊕⊕⊕O MODERATE	
cepta	bility and tol	erability data	a - Leaving trea	tment early fo	or any reasor							
	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)	⊕⊕⊕O MODERATE	
							, , , , , ,	10.4%	3.23)	1 more per 100 (from 7 fewer to 23 more)	er 7	

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

			Quality asse	ssment				Summary	of finding	gs		
			L ,				No. of pa	ntients	Ef	fect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	considerations	theranies +	Psychological therapies	Relative (95% CI)	Absolute	Quality	importance
Efficacy	data - Num	ber not res	oonding									
1	randomised trials		no serious inconsistency		serious ¹	none	8/25 (32%)	16/24 (66.7%)	RR 0.48 (0.25 to	35 fewer per 100 (from 6 fewer to 50 fewer)	⊕⊕⊕O MODERATE	
								66.7%	0.91)	35 fewer per 100 (from 6 fewer to 50 fewer)		
								00./%		fewer to		

¹ Significant heterogeneity - random effects model used

² Inconclusive effect

³ Single study; inconclusive effect

⁴ Single study

fficacy	data (conti	nuous) - Clii	nician-rated m	ean endpoin	t data (Bett	er indicated by	lower values)					
	randomised trials		no serious inconsistency		serious ^{1,2}	none	212	178	-	SMD 0.17 lower (0.37 lower to 0.03 higher)	⊕⊕⊕O MODERATE	
fficacy	data (conti	nuous) - Clii	nician-rated m	ean endpoin	t data 6-mo	nth follow-up (I	Better indicated	by lower value	es)		1	
	randomised trials		no serious inconsistency		serious ^{1,2}	none	196	167	-	SMD 0.18 lower (0.38 lower to 0.03 higher)	⊕⊕⊕O MODERATE	
fficacy	data (conti	nuous) - Clii	nician-rated m	ean endpoin	t data 18-m	onth follow-up	(Better indicated	l by lower val	ues)			
	randomised trials		no serious inconsistency		serious ^{1,2}	none	190	156	-	SMD 0.2 lower (0.41 lower to 0.01 higher)	⊕⊕⊕O MODERATE	
ccepta	ability and to	olerability d	ata - Leaving t	reatment ea	rly for any r	eason						
	randomised	no serious	no serious	no serious	serious ^{1,2}	none	1/25 (4%)	0/24 (0%)	RR 2.88	0 more	⊕⊕⊕О	

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

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

			Quality asses	ssment			\$	Summary	of finding	gs		
			4 ,				No. of patie	nts	Ef	fect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Short psychodynamic verbal vs short psychodynamic art	Control	Relative (95% CI)	Absolute	Quality	Importance
Efficacy	data - Self-ra	ated mean e	ndpoint (Bette	r indicated by	lower value	es)		•			•	
1	randomised trials		no serious inconsistency	no serious indirectness	very serious ¹	none	21	18	-	SMD 0.11 lower (0.74 lower to 0.52	⊕⊕OO LOW	

¹ Single study ² Inconclusive effect

										higher)		
fficacy	data - Self-ra	ated mean e	ndpoint at 3-m	onth follow-	up (Better in	dicated by lowe	r values)					
	randomised trials		no serious inconsistency	no serious indirectness	very serious ¹	none	21	18	-	SMD 0.26 lower (0.9 lower to 0.37 higher)	⊕⊕OO LOW	
ccepta	bility and to	lerability da	ta - Leaving tre	atment early	for any reas	on						
	randomised trials		no serious inconsistency	no serious indirectness	very serious ¹	none	1/22 (4.5%)	3/21 (14.3%)	(0.04 to	10 fewer per 100 (from 14 fewer to 26 more)	⊕⊕OO LOW	
								14.3%	2.82)	10 fewer per 100 (from 14 fewer to 26 more)		

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 asses	sment				Sum	mary of fir	ndings		
							No. of pa	tients	E	Effect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Partial responders	Control	Relative (95% CI)	Absolute	Quality	
Number	of people no	ot achieving a	t least 50% red	uction in depr	ession score	- Psych/SSRI Co	mbo vs SSRI				ļ.	
	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	15 fewer per 100 (from 28 fewer to 23 more)	⊕⊕OO LOW	
								35%	1.65)	15 fewer per 100 (from 28 fewer to 23 more)		
Number	of people no	ot achieving a	t least 50% red	uction in depr	ession score	: 12 week follow	-up - Psych/S	SSRI Com	ibo vs SSR	l		
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	25 fewer per 100 (from 44 fewer to 9 more)	⊕⊕OO LOW	
								70%	1.13)	25 fewer per 100 (from 44 fewer to 9 more)		

randor trials		no serious imitations	no serious inconsistency	no serious indirectness	very serious ¹	none	6/20 (30%)	10/20 (50%)	RR 0.6 (0.27 to	20 fewer per 100 (from 37 fewer to 17 more)	⊕⊕OO LOW
								50%	1.34)	20 fewer per 100 (from 37 fewer to 17 more)	
er of peo	ple not	achieving r	emission: 12 w	eek follow-up	- Psych/SSF	RI Combo vs SS	RI				
randor trials		no serious imitations	no serious inconsistency	no serious indirectness	very serious ¹	none	16/20 (80%)	14/20 (70%)	RR 1.14 (0.8 to	10 more per 100 (from 14 fewer to 45 more)	⊕⊕OO LOW
								70%	1.64)	10 more per 100 (from 14 fewer to 45 more)	
ing the stu	ıdy early	y - Psych/SS	SRI Combo vs SS	RI							
randor trials		no serious imitations	no serious inconsistency	no serious indirectness	very serious ¹	none	2/20 (10%)	3/20 (15%)	RR 0.67 (0.12 to	5 fewer per 100 (from 13 fewer to 39 more)	⊕⊕OO LOW
								15%	3.57)	5 fewer per 100 (from 13 fewer to 39 more)	

¹ Single study; inconclusive effect