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.

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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 asses	ssment				Su	mmary of	findings		
							No. of p	atients	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	it least 50% red	uction in depr	ession score	- SSRIs: dysthym	ia only					
5	randomised trials	no serious limitations		no serious indirectness	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	
							(10.170)	66.5%		19 fewer per 100 (from 12 fewer to 25 fewer)		
Number	of people no	ot achieving a	it least 50% red	uction in depr	ession score	- SSRIs: minor de	pression	only				
1	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)	MODERATE	
							,	52.3%	1.28)	1 fewer per 100 (from 12 fewer to 15 more)		

ımbe	r of people no	ot achieving a	at least 50% red	luction in dep	ression score	- TCAs: dysthym	ia only				
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	25/68 (36.8%)	54/76 (71.1%)	RR 0.52 (0.37 to	34 fewer per 100 (from 19 fewer to 45 fewer)	
							(30.870)	71.1%	0.73)	34 fewer per 100 (from 19 fewer to 45 fewer)	
ımbe	r of people no	ot achieving a	at least 50% red	luction in dep	ression score	- MAOIs: dysthy	mia only				
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	25/70 (35.7%)	54/76 (71.1%)	RR 0.5 (0.36 to	36 fewer per 100 (from 21 fewer to 45 fewer)	MODERATE
							(33.770)	71.1%	0.71)	36 fewer per 100 (from 21 fewer to 46 fewer)	WODENATE
umbe	r of people no	ot achieving r	emission - SSRI	s: dysthymia o	only						
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	167/317 (52.7%)	194/291 (66.7%)	RR 0.78 (0.68 to 0.89)	15 fewer per 100 (from 7 fewer to 21 fewer)	HIGH
								67.9%	3.33,	15 fewer per 100 (from 7 fewer to 22	

										fewer)		
Number	of people no	t achieving r	emission - SSRI	s: minor depre	ession only	1					Į Į	
		ŭ		·	,						_	
			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)	MODERATE	
							(00.07.5)	55.1%	1.34)	3 more per 100 (from 9 fewer to 19 more)		
Number	of people no	t achieving r	emission - TCAs	: dysthymia o	nly							
		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)	LOW	
Number	of people no	t achieving r	emission - MAC) Is: dysthymia	only							
					1 1						,	
	randomised trials		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)	29 fewer per 100 (from 14 fewer to 40 fewer)	MODERATE	
								77.6%		29 fewer per 100 (from 14		

										fewer to 40		
										fewer)		
ean	endpoint score	es (clinician r	ated) - SSRIs: dy	sthymia only	(Better indica	ted by lower val	lues)		•			
	randomised	no serious	no serious	no serious	no serious	none				SMD 0.56		
	trials	limitations	inconsistency	indirectness	imprecision		104	115	-	lower (0.83		
										to 0.29	HIGH	
										lower)		
ean	endpoint score	es (clinician r	ated) - SSRIs: m	inor depression	on only (Bette	r indicated by lo	wer value	s)				
	randomised	no serious	no serious	no serious	serious ³	none				SMD 0.19		
	trials	limitations	inconsistency	indirectness			155	167	_	lower (0.41		
										lower to	MODERATE	
										0.03 higher)		
ean	endpoint score	es (clinician r	। ated) - TCAs: dy	sthymia only	 (Better indica	ted by lower val	ues)					
ean	_	no serious	no serious		(Better indica	ted by lower val				SMD 0.62		
ean	_		1				ues) 107	105	-	lower (0.9 to	MODERATE	
ean	randomised	no serious	no serious	no serious				105	-		MODERATE	
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹		107		-	lower (0.9 to	MODERATE	
	randomised trials	no serious limitations es (clinician r	no serious inconsistency	no serious indirectness	serious ¹	none	107		-	lower (0.9 to	MODERATE	
	randomised trials endpoint score	no serious limitations es (clinician r	no serious inconsistency ated) - Antipsyc	no serious indirectness thotics: dysthy	serious ¹ ymia only (Bet	none ter indicated by	107	ues)	-	lower (0.9 to 0.35 lower) SMD 0.66 lower (0.94	MODERATE	
	randomised trials endpoint score	no serious limitations es (clinician r	no serious inconsistency ated) - Antipsyc	no serious indirectness chotics: dysthy	serious ¹ ymia only (Bet	none ter indicated by	107		-	SMD 0.66 lower (0.94 to 0.38	MODERATE MODERATE	
	randomised trials endpoint score	no serious limitations es (clinician r	no serious inconsistency ated) - Antipsyc	no serious indirectness chotics: dysthy	serious ¹ ymia only (Bet	none ter indicated by	107	ues)	-	lower (0.9 to 0.35 lower) SMD 0.66 lower (0.94	MODERATE	
ean	randomised trials endpoint score randomised trials	no serious limitations es (clinician r no serious limitations	no serious inconsistency ated) - Antipsyc	no serious indirectness chotics: dysthy no serious indirectness	serious ¹	none ter indicated by	107	ues)	-	SMD 0.66 lower (0.94 to 0.38	MODERATE	
ean	randomised trials endpoint score randomised trials	no serious limitations es (clinician r no serious limitations	no serious inconsistency ated) - Antipsyc no serious inconsistency	no serious indirectness chotics: dysthy no serious indirectness	serious ¹	none ter indicated by	107	ues)	-	SMD 0.66 lower (0.94 to 0.38	MODERATE	

	trials	limitations	inconsistency	indirectness						to 0.07 lower)	MODERATE	
lean	endpoint score	es (self rated) - SSRIs: minor	depression on	ly (Better ind	icated by lower	values)					
	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)	MODERATE	
lean	change (clinici	an rated) - SS	SRIs: dysthymia	only (Better i	ndicated by lo	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	
ean	change (clinici	an rated) - To	CAs: dysthymia	only (Better in	ndicated by lo	wer 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)	MODERATE	
lean	change (clinici	an rated) - A	Ps: dysthymia o	only (Better inc	dicated by low	ver values)					<u> </u>	
	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)	MODERATE	
						1						

Mean c	nange (clinici	an rated) - M	IAOIs: dysthymi	ia only (Better	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)	MODERATE	

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

			Quality asses	ssment				Su	mmary of	findings		
			Quality associ	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			No. of p	atients	E	ffect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Placebo	Relative (95% CI)	Absolute	Quality	
Leaving	the study ear	rly - SSRIs: dy	sthymia only	ı								
	randomised trials	no serious limitations	serious ¹	no serious indirectness	serious ²	none	101/535 (18.9%)	108/495 (21.8%) 21.5%	RR 0.84 (0.57 to 1.24)	3 fewer per 100 (from 9 fewer to 5 more) 3 fewer per 100 (from 9 fewer to 5 more)	LOW	

Single study

Significant heterogeneity - random effects model used

Non significant effect size

ving	the study ea	rly - SSRIs: m	inor depression	ı							
	randomised trials	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)	LOW
							(31.676)	26.4%	1.65)	5 more per 100 (from 3 fewer to 17 more)	2010
ving	the study ea	rly - TCAs: dy	sthymia only								
	randomised trials	no serious Iimitations	no serious inconsistency	no serious indirectness	serious ²	none	85/366 (23.2%)	78/368 (21.2%)	RR 1.1 (0.84 to	2 more per 100 (from 3 fewer to 9 more)	MODERATE
								22.3%	1.44)	2 more per 100 (from 4 fewer to 10 more)	
aving	the study ea	rly - MAOIs: (dysthymia only	'	'	'					
	randomised trials	no serious Iimitations	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)	LOW
							, ,	14.4%	1.67)	2 fewer per 100 (from 8 fewer to 10 more)	

										,
randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁴	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)	MODERATE
							20.4%	1.22)	7 fewer per 100 (from 13 fewer to 4 more)	
g the study ea	rly due to sid	e effects - SSRI	s: dysthymia o	nly						
randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁵	none	12/245 (4.9%)	7/252 (2.8%)	RR 1.77 (0.71 to	2 more per 100 (from 1 fewer to 9 more)	MODERATE
							2.7%	4.41)	2 more per 100 (from 1 fewer to 9 more)	
g the study ea	rly due to sid	e effects - SSRI	s: minor depre	ssion only		·				
randomised trials	no serious limitations	serious ¹	no serious indirectness	serious ²	none	17/187 (9.1%)	10/190 (5.3%)	RR 1.55 (0.51 to	3 more per 100 (from 3 fewer to 19 more)	LOW
							5.2%	4.68)	3 more per 100 (from 3 fewer to 19 more)	

randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/366	8/369 (2.2%)	RR 5.44 (2.66 to	10 more per 100 (from 4 more to 22 more)	
						(12.3%)	1.4%	11.11)	6 more per 100 (from 2 more to 14 more)	HIGH
the study ea	rly due to sid	le effects - MAC	Ols: dysthymia	only						
randomised trials	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)	5 more per 100 (from 1 fewer to 29 more) 5 more per 100 (from 1 fewer to 28 more)	MODERATE
the study ea	rly due to sid	le effects - APs:	dysthymia on	ly					,	
randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	3/104 (2.9%)	1/108 (0.9%)	RR 3.12 (0.33 to	2 more per 100 (from 1 fewer to 26 more)	MODERATE
							0.9%	29.47)	2 more per 100 (from 1 fewer to 26 more)	

tien	ts reporting si	de effects - S	SRIs: dysthymia	only							
	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 1.25)	4 more per 100 (from 2 fewer to 12 more) 4 more per 100 (from 2	HIGH
tien	ts reporting sid	de effects - S	SRIs: minor dep	ression only						fewer to 11 more)	
	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	7 fewer per 100 (from 16 fewer to 6 more)	MODERATE
								31.2%	1.18)	7 fewer per 100 (from 16 fewer to 6 more)	
ien			CAs: dysthymia	<u>, </u>		,					
	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)	MODERATE
							,	44.4%	1.81)	18 more per 100 (from 4 more to 36 more)	

randomised no serious no serious inconsistency indirectness inconsistency indirectness indirectn	Patients reporti	g side effects - A	intipsychotics: d	ysthymia only	1						
(54.8%) (0.94 to 1.62) MODERATE 1.62) 10 more per 100 (from 3 fewer to 28					serious ³	none	-	(44.4%)	RR 1.23 (0.94 to 1.62)	100 (from 3 fewer to 28 more) 10 more per 100 (from 3	

Significant heterogeneity - random effects model used

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

			Quality asses	ssment				S	ummary o	f findings		
							No. of p	atients	Е	ffect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Other drugs	Relative (95% CI)	Absolute	Quality	
Numbei	of people no	ot achieving a	t least 50% redu	uction in depre	ession score: S	SSRI - Dysthymia	=/> 50%	(fluvoxaı	mine vs ma	aprotiline)		
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)	LOW	

² Inconclusive effect size

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

⁶ Single study

Number	of people no	t achieving a	t least 50% redu	uction in depr	ession score: S	SSRI - Dysthymia	=/> 50%	75% (SSRI vs a	amisul prid	0 fewer per 100 (from 21 fewer to 29 more)		
2		no serious limitations		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 more)	HIGH	
1	randomised trials		no serious			none	30/126 (23.8%)	39/119 (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)	MODERATE	
2	randomised		no serious	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)	emide)	

umb	er of people no	ot achieving a	at least 50% red	uction in depr	ession score:	TCA - Dysthymia	a =/> 50%	(amitript	yline vs ar	100 (from 9 fewer to 21 more)	
	randomised trials	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)	LOW
Numb	er of neonle no	nt achieving r	emission: SSRI	. Dysthymia o	nly (sertraline	vs imipramine)		40.4%		100 (from 12 fewer to 13 more)	
1			no serious	no serious	serious ²	none		l		8 fewer per	T T
-	randomised trials	limitations	inconsistency	indirectness	scrious	none	71/134 (53%)	83/136 (61%)	RR 0.87 (0.7 to	100 (from 18 fewer to 4 more)	MODERATE
							(5073)	61%	1.07)	8 fewer per 100 (from 18 fewer to 4 more)	1
Numb	er of people no	ot achieving r	emission: SSRI	- Dysthymia =,	/> 50% (sertra	line vs amisulpr	ide)				
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	54/156 (34.6%)	42/157 (26.8%)	RR 1.29 (0.92 to 1.81)	8 more per 100 (from 2 fewer to 22 more)	MODERATE
								26.8%		8 more per 100 (from 2	

1 randomised no serious limitations Number of people not achieving 1 randomised no serious limitations Mean endpoint scores (clinician 1 randomised no serious limitations	ving remission: SSRI -	•		yndromal depres	ssive sym	ptomato	logy (49%	fewer to 22 more) vs 51%) (sertr	raline vs citalopram)
1 randomised no serious trials limitations Mean endpoint scores (clinician randomised no serious		no serious indirectness	serious ²	none	42/72 (58.3%)	31/66 (47%)	RR 1.24 (0.9 to 1.71)	11 more per 100 (from 5 fewer to 33 more)	MODERATE
trials limitations Mean endpoint scores (clinician randomised no serious	ving remission: TCA -	Dysthymia on	ly (imipramino	e vs moclobemid	e)	47%		100 (from 5 fewer to 33 more)	
randomised no serious		no serious indirectness	serious ²	none	37/68 (54.4%)	34/70 (48.6%)	RR 1.12 (0.81 to 1.55)	6 more per 100 (from 9 fewer to 27 more)	MODERATE
randomised no serious						48.6%		100 (from 9 fewer to 27 more)	
	cian rated): SSRI - Dys	thymia =/> 50	% (fluvoxamii	ne vs maprotiline	e) (Better	indicate	d by lower	values)	
		no serious indirectness	very serious ¹	none	21	21	-	SMD 0.01 lower (0.62 lower to 0.59 higher)	LOW

					1						_
	randomised		no serious	no serious	no serious	none				SMD 0.16	
	trials	limitations	inconsistency	indirectness	imprecision		279	295	-	higher (0 to HIGH	
										0.32 higher)	
an en	dpoint score	es (clinician r	ated): TCA - Dys	thymia only (i	mipramine vs	minaprine) (Bet	tter indica	ated by lo	wer value	es)	ļ
	randomised	no serious	no serious	no serious	very serious ¹	none				SMD 0.34	
ŀ	trials	limitations	inconsistency	indirectness			24	27		higher (0.1	
							24	27	_	lower to 0.77 LOW	
										higher)	
an an	dnoint score	 s (clinician r	 ated): TCA - Dys	thymia only (s	 mitrintyline v	s amicularida) (Retter inc	licated b	l v lower va	dues)	
call Cil	apoint score	es (chinician i	ateuj. TCA - Dys	cilyillia Olliy (a		s annisuipriue) (better int	ilcated D	y lower va	nues	
	randomised	no serious	no serious	no serious	serious ²	none				SMD 0.04	
	trials	limitations	inconsistency	indirectness			107	101	_	higher (0.23	
							107	101		lower to 0.31 MODERA	TE
										higher)	
								Į	l		,
ean en	dpoint score	। es (clinician r	i ated): TCA - Dys	thymia =/> 50	% (imipramin	e vs phenelzine)	(Better i	ndicated	by lower v	values)	
	•			1			(Better i	ndicated	by lower v		_
	randomised	no serious	no serious	no serious	% (imipramin serious ²	e vs phenelzine)) (Better ii	ndicated	by lower v	SMD 0.73	
	•			1			(Better in	ndicated 16	by lower v	SMD 0.73 higher (0.01	
	randomised	no serious	no serious	no serious					by lower v	SMD 0.73 higher (0.01 to 1.45 MODERA	TE
	randomised	no serious	no serious	no serious					by lower v	SMD 0.73 higher (0.01	TE
	randomised trials	no serious limitations	no serious	no serious indirectness	serious ²	none	16	16	-	SMD 0.73 higher (0.01 to 1.45 higher)	TE
ean en	randomised trials dpoint score	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	16 de) (Bette	16	-	SMD 0.73 higher (0.01 to 1.45 higher)	TE
ean en	randomised trials dpoint score	no serious limitations es (clinician r	no serious inconsistency ated): TCA - Dys	no serious indirectness thymia =/> 50	serious ² % (amitriptyli	none ne vs amisulprid	16	16	-	SMD 0.73 higher (0.01 to 1.45 higher) er values)	

ean	endpoint score	es (clinician r	ated): AP - Dyst	hymia only (flu	upenthixol vs I	ritanserin) (Betto	er indicat	ed by low	er values)	higher)	
	randomised trials	limitations	no serious inconsistency	no serious indirectness	very serious ¹		36	31		SMD 0.26 lower (0.74 ower to 0.22 higher)	LOW
1ean	change (clinici	an rated): SS	RI - Dysthymia o	only (sertraline	e vs imipramir	ne) (Better indica	ated by lo	wer value	s)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	134	136	-	SMD 0.05 higher (0.19 ower to 0.29 higher)	MODERATE
Mean	change (clinici	an rated): TO	A - Dysthymia c	only (imiprami	ne vs moclobe	emide) (Better in	dicated b	y lower va	alues)		
L	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	63	67		SMD 0.12 higher (0.23	
								67	-	ower to 0.46 higher)	MODERATE
Mean	change (clinici	an rated): TC	A - Dysthymia c	only (amitripty	line vs amisul	pride) (Better in					MODERATE

Inconclusive effect size; single study
Single study
Inconclusive effect size

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

			Quality asses	ssment			Su	ımmary of	findings			
			X • • • • • • • • • • • • • • • • • • •				No. of p	atients	E	ffect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Drugs	Others drugs	Relative (95% CI)	Absolute	Quality	
Leaving	the study ea	rly: SSRI - Dys	sthymia only (se	ertraline vs im	ipramine)				1		ı	
	randomised trials	no serious limitations		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)	MODERATE	
Leaving	the study ea	rlv: SSRI - Dvs	sthymia =/> 50%	6 (fluvoxamin	e vs maprotili	ne)		33.1%	0.75)	18 fewer per 100 (from 8 fewer to 23 fewer)		
		1		·	·	·				I	T	
	randomised trials	no serious limitations		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)	LOW	
								25%	2.07)	8 fewer per 100 (from 19 fewer to 27 more)		

	randomised trials	no serious Iimitations	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)	MODERATE
			or depression and subsyndromal depressive			17%	1.037	6 more per 100 (from 0 fewer to 15 more)			
avin	g the study ea	rly: SSRI - Mi	nor depression	and subsyndro	omal depressi	ve symptomato	logy (49%	vs 51%) (s	sertraline	vs citalopram)
	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
-	g the study ea	rly: TCA - Dys	thymia only (in	l nipramine vs n	l noclobemide)						
avin	randomised trials		no serious inconsistency	nipramine vs n	noclobemide) very serious ²		15/103 (14.6%)	13/108 (12%)	RR 1.21 (0.61 to	3 more per 100 (from 5 fewer to 17 more)	LOW
eavin	randomised	no serious	no serious	no serious	·		15/103 (14.6%)	· ·		100 (from 5 fewer to 17	LOW
	randomised trials	no serious limitations	no serious	no serious indirectness	very serious ²	none	-	(12%)	(0.61 to	100 (from 5 fewer to 17 more) 3 more per 100 (from 5 fewer to 17	LOW

l eaving	the study ea	rlv: TCA - Dvs	thymia =/> 50%	6 (iminramine	vs nhenelzine	.)		13.5%	2.51)	fewer to 20 more) 5 more per 100 (from 4 fewer to 20 more)	LOW	
1	randomised		_		very serious ²		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) 2 more per 100 (from 7 fewer to 35 more)	LOW	
1	randomised	no serious	no serious inconsistency		very serious ²		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) 3 more per 100 (from 8 fewer to 18 more)	LOW	
1	randomised		notics (flupenth no serious inconsistency		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 ear	rly due to sid	e effects: SSRI -	Dysthymia or	nly (sertraline	vs imipramine)					
	randomised trials		no serious inconsistency	no serious indirectness	serious ¹	none	8/134 (6%)	25/136 (18.4%)	RR 0.32 (0.15 to 0.69)		MODERATE
								18.4%	0.031	13 fewer per 100 (from 6 fewer to 16 fewer)	
Leaving	the study ear	rly due to sid	e effects: SSRI -	Dysthymia =/	> 50% (sertra	line/fluoxetine v	s amisulp	ride)			
	randomised trials		no serious inconsistency	no serious indirectness	very serious ²	none	22/295 (7.5%)	23/299 (7.7%)	RR 0.97 (0.55 to	0 fewer per 100 (from 3 fewer to 5 more)	LOW
								7.8%	1.7)	0 fewer per 100 (from 4 fewer to 5 more)	
Leaving	the study ear	rly due to sid	e effects: SSRI -	Minor depres	sion and subs	yndromal depres	ssive sym	ptomatol	ogy (49% v	vs 51%) (sertr	aline vs citalopram)
	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	

Leaving	the study ea	rly due to sid	e effects: TCA -	Dysthymia on	ly (imipramin	e vs minaprine/	mocloben	15.2%	1.75)	fewer to 11 more) 4 fewer per 100 (from 10 fewer to 11 more)	LOW	
2	randomised	•	no serious		very serious ⁴		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)	LOW	
1	randomised		no serious		very serious ²	ne vs amisulprio	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)	LOW	
1	randomised	_	no serious		> 50% (amitri)	none	11/87 (12.6%)	23/166 (13.9%)	RR 0.91 (0.47 to	1 fewer per 100 (from 7		

Lacrina	Abo abodo o		o official and in	nuckation Dur		fluo anthina luc		13.9%	1.78)	fewer to 11 more) 1 fewer per 100 (from 7 fewer to 11 more)	LOW	
1	randomised	_	no serious		very serious ²	none	2/36 (5.6%)	2/33 (6.1%) 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)	LOW	
2	randomised			no serious		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				ne vs minapr	none	20/34 (58.8%)	14/33 (42.4%)	RR 1.39 (0.85 to	17 more per 100 (from 6		

Patients	reporting sid	de effects: TC	A - Dysthymia c	only (amitripty	/line vs amisu	lpride)		42.4%	2.26)	fewer to 53 more) 17 more per 100 (from 6 fewer to 53 more)	MODERATE	
	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)	MODERATE	
1	randomised		A - Dysthymia = no serious inconsistency	no serious indirectness	serious ¹	nisulpride)	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)	MODERATE	
1	randomised		no serious		very serious ²		16/36 (44.4%)	15/33 (45.5%)	RR 0.98 (0.58 to	1 fewer per 100 (from 19		

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

Is relapse prevention effective in dysthymia?

			Quality assess	sment				Sumr	mary of fin	dings		
			X ,			No. of par	tients	E	Effect		Importance	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Relapse prevention	Control	Relative (95% CI)	Absolute	Quality	
Recurre	nce - TCAs										•	
	randomised trials				very serious ¹	none	0/14 (0%)	6/13 (46.2%)	RR 0.07 (0 to	43 fewer per 100 (from 46 fewer to 7 more)	LOW	
								46.2%	1.16)	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	ings		
							No. of pa	tients	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 - Numb	er not respo	onding	ı	'							
2	randomised trials		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) 8 fewer per 100 (from 18	MODERATE	
rff: oo ou	data Numb							30.570		fewer to 4 more)		
Епісасу	data - Numi		ving 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)	LOW	
								58.8%		8 fewer per 100 (from 18		

icac		-	ı	•		ated by lower va	lues)	ı			, , , , , , , , , , , , , , , , , , ,
	randomised trials			no serious indirectness	serious ¹	none	97	99	-	SMD 0.27 lower (0.55 lower to 0.01 higher)	MODERATE
cep	ability and to	lerability da	ta - Leaving tre	atment early	for any reas	on			•	•	· '
		no serious	no serious	no serious	corious ¹	none				2 fewer	T
	randomised trials			no serious indirectness	serious ¹	none	20/139 (14.4%)	23/138 (16.7%)	RR 0.86 (0.5 to	2 fewer per 100 (from 8 fewer to 8 more)	MODERATE

¹ Inconclusive effect

² Significant heterogeneity - random effects model used

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

			Quality asse	ssment				Summary	of finding	S		
								patients		fect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological therapies	Antidepressants	Relative (95% CI)	Absolute	Quality	
Efficac	y data - Num	ber not resp	oonding						•			
3	randomised trials		no serious inconsistency		no serious imprecision	none	92/162 (56.8%)	81/157 (51.6%)	(0.92 to	5 more per 100 (from 4 fewer to 15 more)	HIGH	
								51.9%		5 more per 100 (from 4 fewer to 15 more)		
Efficac	y data - Num	ber not rem	nitting									
2	randomised trials		no serious inconsistency		serious ¹	none	80/138 (58%)	70/135 (51.9%)	(0.92 to	former to	MODERATE	
								58.3%		8 more per 100		

										(from 5 fewer to 24 more)	
cac	cy data (conti	nuous) - Clii	nician-rated m	ean endpoin	t (Better indi	cated by lower	values)				
	randomised trials		no serious inconsistency		no serious imprecision	none	308	320	-	SMD 0.29 higher (0.13 to HIGH 0.45 higher)	1
cac	cy data (conti	nuous) - Cliı	nician-rated m	ean endpoint	t 6-month fo	llow-up (Better	indicated by lo	ower values)			
	randomised trials		no serious inconsistency		serious ²	none	167	186	-	SMD 0.19 higher (0.02 lower to 0.4 higher)	ATE
cac	y data (conti	nuous) - Clii	nician-rated m	ean endpoin	t 18-month f	ollow-up (Bette	r indicated by	lower values)		'	
	randomised trials		no serious inconsistency		serious ³	none	156	179	-	SMD 0.26 higher (0.05 to MODER 0.48 higher)	ATE
cac	cy data (conti	nuous) - Sel	f-rated mean o	endpoint (Bet	tter indicated	। d by lower value	es)				

2	randomicod	no corious	no corious	no corious	no corious	nono				CMD		
	randomised trials		no serious inconsistency		no serious imprecision	none	32	35	-	SMD 0.37 higher (0.11 lower to	HIGH	
										0.86 higher)		
Accept	ability and t	olerability d	ata - Leaving t	reatment ea	rly for any re	ason						
	randomised trials		no serious inconsistency		serious ¹	none	25/175 (14.3%)	39/175 (22.3%)	1111 0.07	7 fewer per 100 (from 13 fewer to 1 more)	MODERATE	
								23%	1.00)	8 fewer per 100 (from 13 fewer to 1 more)		
Accept	ability and t	olerability d	ata - Leaving t	reatment ea	rly due to sid	le effects						
	randomised trials		no serious inconsistency		very serious ⁴	none	0/13 (0%)	1/18 (5.6%)	RR 0.45 (0.02 to 10.3)	3 fewer per 100 (from 5 fewer to 52 more)		
								5.6%	-	3 fewer per 100 (from 5 fewer to		

						1
1					152 more)	
1					32 more,	

Inconclusive effect

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

			Quality asses	sment				Summary	of findings			
			. ,				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	
Efficacy	data - Numb	l er not respor	l nding	1								
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)	LOW	
								64.4%	1.79)	3 fewer per 100 (from 31 fewer to 51 more)		
Efficacy	data - Numb	er not remitt	ing									
1	randomised trials	no serious limitations	no serious inconsistency		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)	LOW	

² Single study

³ Significant heterogeneity - random effects model used

⁴ Single study; inconclusive effect size

								58.3%		10 fewer per 100 (from 31 fewer to 25 more)		
Efficacy	data (continu	ious) - Clinici	an-rated mean	endpoint (Bett	er indicated	by lower values)						
	randomised trials		no serious inconsistency	no serious indirectness	serious ²	none	233	220	-	SMD 0.09 higher (0.1 lower to 0.27 higher)	MODERATE	
Efficacy	data (continu	ious) - Clinici	an-rated mean	endpoint at 6-	month follow	w-up (Better indi	cated by lower valu	es)				
	randomised trials		no serious inconsistency	no serious indirectness	serious ⁴	none	196	186	-	SMD 0.01 higher (0.19 lower to 0.21 higher)	MODERATE	
Efficacy	data (continu	ıous) - Clinici	an-rated mean	endpoint at 18	-month follo	ow-up (Better inc	licated by lower val	ues)				
1	randomised trials		no serious inconsistency	no serious indirectness	serious ⁴	none	190	179	-	SMD 0.06 higher (0.14 lower to 0.27 higher)	MODERATE	
Accepta	bility and tole	erability data	- Leaving treat	ment early for	any reason							
	randomised trials		no serious inconsistency	no serious indirectness	serious ²	none	5/46 (10.9%)	5/46 (10.9%)	RR 1.09 (0.37 to	1 more per 100 (from 7 fewer to 24 more)	MODERATE	
								10.4%	3.25)	1 more per 100 (from 7 fewer to 23 more)		

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

			Quality asse	ssment				Summary o	of finding	s		
			~~~~				No. of pa	tients	Eff	ect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	theranies +	Psychological therapies	Relative (95% CI)	Absolute	Quality	
Efficacy	data - Num	ber not resp	onding									
	randomised trials		no serious inconsistency			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)	MODERATE	
								66.7%	0.91)	35 fewer per 100 (from 6 fewer to 50 fewer)		
										·		

¹ Significant heterogeneity - random effects model used

² Inconclusive effect

³ Single study; inconclusive effect

⁴ Single study

Efficacy	data (contir	nuous) - Clin	ician-rated me	ean endpoint	data (Bette	r indicated by lo	wer values)				
1	randomised trials		no serious inconsistency			none	212	178	-	SMD 0.17 lower (0.37 lower to 0.03 higher)	MODERATE
Efficacy	data (contir	nuous) - Clin	ician-rated me	ean endpoint	data 6-mon	th follow-up (Be	etter indicated by	lower values)		'
1	randomised trials		no serious inconsistency			none	196	167	-	SMD 0.18 lower (0.38 lower to 0.03 higher)	MODERATE
Efficacy	data (contir	nuous) - Clin	ician-rated me	ean endpoint	data 18-mo	nth follow-up (E	Better indicated I	y lower value	s)		
1	randomised trials		no serious inconsistency		serious ^{1,2}	none	190	156	-	SMD 0.2 lower (0.41 lower to 0.01 higher)	MODERATE
Accepta	ability and to	lerability da	ata - Leaving tr	eatment ear	ly for any re	ason	'				,
1	randomised	no serious	no serious	no serious	serious ^{1,2}	none	1/25 (4%)	0/24 (0%)	RR 2.88	0 more	

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	sment			S	ummary	of finding	gs		
			•				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	Importance
Efficacy	data - Self-ra	ited mean er	ndpoint (Better	indicated by	ower values	s)					ı	
1	randomised trials			no serious indirectness	very serious ¹	none	21	18	-	SMD 0.11 lower (0.74 lower to 0.52	LOW	

¹ Single study ² Inconclusive effect

									higher)	
cy data - Self-ra	ated mean e	ndpoint at 3-m	onth follow-u	o (Better ind	icated by lower	values)				
randomised trials		no serious inconsistency	no serious indirectness	,	none	21	18	-	SMD 0.26 lower (0.9 lower to 0.37 higher)	LOW
randomised trials			ous no serious	very serious ¹	none		3/21 (14.3%)	RR 0.32	10 fewer per 100 (from 14 fewer to 26	
						1/22 (4.5%)	14.3%	(0.04 to 2.82)	more) 10 fewer per 100 (from 14 fewer to 26	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 asses	sment								
			4 , 7				No. of pat	tients	E	ffect	Quality	Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Partial responders	Control	Relative (95% CI)	Absolute	Quality	
Number	of people no	i ot achieving a	t least 50% redu	ı ıction in depre	ssion score -	Psych/SSRI Com	i nbo 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	15 fewer per 100 (from 28 fewer to 23 more)	LOW	
								35%	1.65)	15 fewer per 100 (from 28 fewer to 23 more)		
Number	of people no	ot achieving a	t least 50% redu	iction in depre	ssion score:	12 week follow-	up - Psych/SS	RI Comb	o vs SSRI			
1	randomised trials			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)	LOW	
								70%	1.13)	25 fewer per 100 (from 44 fewer to 9 more)		

trials		no serious limitations	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)	
							50%	1.34)	20 fewer per 100 (from 37 fewer to 17 more)		
er c	of people no	t achieving r	emission: 12 we	ek follow-up -	Psych/SSRI	Combo vs SSRI					
	randomised rials	no serious limitations	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)	LOW
								70%	1.64)	10 more per 100 (from 14 fewer to 45 more)	
ing th	he study ear	ly - Psych/SS	RI Combo vs SSI	RI							
	randomised r trials l	no serious limitations		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)	LOW
								15%	3.57)	5 fewer per 100 (from 13 fewer to 39	7

¹ Single study; inconclusive effect