# Depression in adults: treatment and management

**Appendix L: GRADE profiles** 

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# Organisation and service delivery (chapter 5)

- 4 Service delivery
- Collaborative care versus control

			Quality as:	sessment			No of patien	ıts		Effect		
											Quality	Importar
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	COLLABORATIVE CARE	CONTROL	Relative (95% CI)	Absolute		
epressi	on symptoms	s- 6 month	s (follow-up mear	6; Better indica	ted by lower va	alues)						
7		very serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	0	-	-	SMD 0.31 lower (0.39 to 0.23 lower)	⊕OOO VERY LOW	CRITIC
	on symptoms	s- Simple o		(follow-up mean	n 6 months; Bet	ter indicated by lo	ower values)					
6		very serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	0	-	-	SMD 0.32 lower (0.41 to 0.22 lower)	⊕000 VERY LOW	CRITIC
epressi	on symptoms	s- Complex	collaborative ca	re (follow-up me	an 6 months; B	Setter indicated by	lower values)					
1		very serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	0	-	-	SMD 0.28 lower (0.43 to 0.13 lower)	⊕OOO VERY LOW	CRITIC
epression	on symptoms	at follow-	up (follow-up me	an 12 months; E	etter indicated	by lower values)						

	randomised	very	no serious	no serious	no serious	none	1264	1304	-	SMD 0.21 lower (0.3	⊕⊕00	CRITICA
	trials	serious <sup>1</sup>	inconsistency	indirectness	imprecision					to 0.12 lower)	LOW	
			,							,		
pression	on symptoms	at follow	-up - Complex co	ollaborative care	(follow-up me	an 12 months; B	etter indicated by low	ver values)				
	randomised	very	very serious <sup>3</sup>	no serious	serious4	none	995	976	-	SMD 0.27 lower (0.72	⊕000	CRITIC
	trials	serious <sup>1</sup>		indirectness						lower to 0.17 higher)	VERY	
											LOW	
on-resp	onse at follo	w-up (follo	w-up mean 12 m	nonths)								
)	randomised	very	serious <sup>2</sup>	no serious	no serious	none	872/1732	1156/1546	RR 0.72	209 fewer per 1000	⊕000	CRITIC
	trials	serious <sup>1</sup>	33.1343	indirectness	imprecision		(50.3%)	(74.8%)	(0.63 to	(from 142 fewer to	VERY	0
							(0010,0)	(* 115,5)	0.81)	277 fewer)	LOW	
										191 fewer per 1000		
								68.1%		(from 129 fewer to		
										252 fewer)		
on-resp	onse at follo	w-up- Sim	ple collaborative	care (follow-up	mean 12 mont	hs)						
	randomised	very	serious <sup>2</sup>	no serious	serious <sup>4</sup>	none	181/482	247/413	RR 0.66	203 fewer per 1000	⊕000	CRITIC
	trials	serious <sup>1</sup>		indirectness			(37.6%)	(59.8%)	(0.47 to	(from 48 fewer to 317	VERY	
									0.92)	fewer)	LOW	
										134 fewer per 1000		
								39.4%		(from 32 fewer to 209		
				1		1				fewer)		
on-resp	onse at follo	w-up - Cor	nplex collaborat	ive care (follow-	up mean 12 mc	onths)						
	randomised	very	no serious	no serious	no serious	none	691/1250	909/1133	RR 0.75	201 fewer per 1000	⊕⊕00	CRITIC
	trials	serious <sup>1</sup>	inconsistency	indirectness	imprecision		(55.3%)	(80.2%)	(0.66 to	(from 120 fewer to	LOW	
									0.85)	273 fewer)		
										188 fewer per 1000		
								75%		(from 112 fewer to		
										255 fewer)		
ntidepre	essant use- 6	months (1	follow-up mean 6	6 months)								
	randomised	very	serious <sup>2</sup>	no serious	no serious	none	-	-	RR 1.39	-	⊕000	CRITIC
	trials	serious <sup>1</sup>		indirectness	imprecision				(1.26 to		VERY	
								0%	1.52)	-	LOW	
	1	I			1	1					1	1
tidone	occept	months	Simple collabora	ativo core								

22			serious <sup>2</sup>						RR 1.45		0000	CRITICAL
<u> </u>	randomised trials	very serious <sup>1</sup>	serious	no serious indirectness	no serious	none	-	-	_	-	⊕000	CRITICAL
	แเลเร	serious		maneciness	imprecision				(1.26 to		VERY	
								0%	1.66)	-	LOW	
				4								
Antidep	ressant use- 6	months -	Complex collabo	rative care								
0	randomised	very	no serious	no serious	serious <sup>4</sup>	none	-	-	RR 1.29 (1.2	-	⊕000	CRITICAL
	trials	serious <sup>1</sup>	inconsistency	indirectness					to 1.38)		VERY	
								0%		_	LOW	
								0 70				
Antidep	ressant use at	follow-up	(follow-up mean	12 months)								
0	randomised	verv	serious <sup>2</sup>	no serious	serious <sup>4</sup>	none	1156/1799	972/1819	RR 1.18	96 more per 1000	⊕000	CRITICAL
	trials	serious <sup>1</sup>		indirectness			(64.3%)	(53.4%)	(1.03 to	(from 16 more to 187		
							(5 115 / 5 /	(001170)	1.35)	more)	LOW	
									,	/		
										99 more per 1000		
								55%		(from 16 more to 193		
										more)		
Antidep	ressant use a	follow-up	- Simple collabo	rative care (foll	ow-up mean 12	months)						
2	randomised	very	serious <sup>2</sup>	no serious	serious <sup>4</sup>	none	358/686	338/697	RR 1.14 (0.9	68 more per 1000	0000	CRITICAL
)	trials	serious <sup>1</sup>	serious-	indirectness	serious	none	(52.2%)	(48.5%)	to 1.46)	(from 48 fewer to 223	⊕000 VERY	CRITICA
	liiais	Scrious		indirectriess			(32.270)	(40.576)	10 1.40)	more)	LOW	
										more)	LOW	
										53 more per 1000		
								38%		(from 38 fewer to 175		
										(IIOIII OO ICWCI tO 170		
										more)	۱ ۱	
ntidep	ressant use a	follow-up	- Complex collab	porative care (fo	ollow-up mean	12 months)				more)		
Antidep			- Complex collab							,		
Antidep	randomised	very	no serious	no serious	ollow-up mean of serious <sup>4</sup>	12 months)	798/1113	634/1122	RR 1.26	147 more per 1000	⊕000	CRITICAL
Antidep							798/1113 (71.7%)	634/1122 (56.5%)	(1.17 to	147 more per 1000 (from 96 more to 198	⊕000 VERY	CRITICAL
Antidep	randomised	very	no serious	no serious						147 more per 1000	⊕000	CRITICAL
Antidep	randomised	very	no serious	no serious					(1.17 to	147 more per 1000 (from 96 more to 198 more)	⊕000 VERY	CRITICAL
Antidep	randomised	very	no serious	no serious				(56.5%)	(1.17 to	147 more per 1000 (from 96 more to 198 more)	⊕000 VERY	CRITICAL
Antidep	randomised	very	no serious	no serious					(1.17 to	147 more per 1000 (from 96 more to 198 more) 161 more per 1000 (from 105 more to	⊕000 VERY	CRITICAL
	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness				(56.5%)	(1.17 to	147 more per 1000 (from 96 more to 198 more)	⊕000 VERY	CRITICAL
	randomised trials	very serious <sup>1</sup>	no serious	no serious indirectness				(56.5%)	(1.17 to	147 more per 1000 (from 96 more to 198 more) 161 more per 1000 (from 105 more to	⊕000 VERY	CRITICAL
	randomised trials	very serious <sup>1</sup>	no serious inconsistency ole collaborative	no serious indirectness care)	serious <sup>4</sup>	none	(71.7%)	(56.5%) 61.9%	(1.17 to 1.35)	147 more per 1000 (from 96 more to 198 more) 161 more per 1000 (from 105 more to 217 more)	⊕OOO VERY LOW	
	randomised trials  nission at 6 me	very serious <sup>1</sup> onths (sing	no serious inconsistency  ole collaborative no serious	no serious indirectness  care)			64/115	(56.5%) 61.9%	(1.17 to 1.35)	147 more per 1000 (from 96 more to 198 more)  161 more per 1000 (from 105 more to 217 more)	⊕OOO VERY LOW	
	randomised trials	very serious <sup>1</sup>	no serious inconsistency ole collaborative	no serious indirectness care)	serious <sup>4</sup>	none	(71.7%)	(56.5%) 61.9%	(1.17 to 1.35)	147 more per 1000 (from 96 more to 198 more) 161 more per 1000 (from 105 more to 217 more)	⊕OOO VERY LOW	CRITICAL

#### Non-remission at follow-up (follow-up mean 12 months) randomised serious<sup>6</sup> very serious<sup>3</sup> serious4 88/197 156/198 RR 0.58 331 fewer per 1000 ⊕000 **CRITICAL** no serious none trials indirectness (44.7%) (78.8%)(0.38 to (from 87 fewer to 488 **VERY** 0.89) fewer) LOW Non-remission at follow-up - simple collaborative care (follow-up mean 12 months) RR 0.47 CRITICAL randomised serious<sup>6</sup> serious<sup>7</sup> 47/110 95/104 484 fewer per 1000 no serious no serious none $\oplus \oplus OO$ indirectness (42.7%) (91.3%)(0.37 to (from 375 fewer to trials inconsistency LOW 0.59) 575 fewer) Non-remission at follow-up - complex collaborative care (follow-up mean 12 months) randomised serious<sup>6</sup> no serious no serious serious4 none 41/87 61/954 RR 0.73 17 fewer per 1000 $\oplus \oplus OO$ **CRITICAL** indirectness (47.1%) (0.56 to (from 3 fewer to 28 trials inconsistency (6.4%)LOW 0.95) fewer)

#### Collaborative care versus active intervention

			Quality ass	sessment			No of patients Effect				Quality	Importance
No of studies	Design   Inconsistancy   Indirectness		Indirectness	Imprecision	Other considerations	COLLABORATIVE CARE	OTHER COMPARISON	Relative (95% CI)	Absolute			
Simple c	ollaborative	care: Stai	ndards CC vs pa	tient centred Co	C- remission a	t follow-up (follow	v-up mean 12 month	s)				
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	27/65 (41.5%)	22/67 (32.8%)	RR 1.27 (0.81 to 1.98)	89 more per 1000 (from 62 fewer to 322 more)		CRITICAL

ROB high or unclear across multiple domains in most studies

<sup>&</sup>lt;sup>2</sup> 12 >50%

<sup>3</sup> I2 >80%

<sup>&</sup>lt;sup>4</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>5</sup> ROB high or unclear across multiple domains

<sup>&</sup>lt;sup>6</sup> ROB high or unclear across a two to three domains

<sup>&</sup>lt;sup>7</sup> OIS not met (<300 events)

randomised serious

randomised serious1

ROB high or unclear across two to three domains

<sup>2</sup> 95% CI crosses one clinical decision threshold

trials

trials

Telebased CC vs Practice based CC- response- 6 months (follow-up mean 6 months)

Telebased CC vs practice based CC- response at follow-up (follow-up mean 12 months)

no serious

no serious

indirectness

indirectness

no serious

imprecision

serious<sup>2</sup>

none

no serious

no serious

inconsistency

inconsistency

	care versus											
			Quality asse	essment			No of pa	atients		Effect		
											Quality	Importance
No of	Design   Inconsiste					Other	STEPPED COUTROL		Relative			
studies	Design	bias	Inconsistency	Indirectness	Imprecision	considerations	CARE	CONTROL	(95% CI)	Absolute		
Remission	n at endpoint											
1	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	40/74	29/74	RR 1.38 (0.97	149 more per 1000 (from	⊕⊕00	CRITICAL
	trials		inconsistency	indirectness			(54.1%)	(39.2%)	to 1.96)	12 fewer to 376 more)	LOW	
								39.2%		149 more per 1000 (from		
								39.2 /0		12 fewer to 376 more)		
Depression	n symptoms	at endpoin	t (measured with:	PHQ-9; Better in	dicated by lo	wer values)	•	•	•			•

CRITICAL

CRITICAL

 $\oplus \oplus \oplus O$ 

MODERATE

 $\oplus \oplus OO$ 

LOW

89 more per 1000 (from 62 fewer to

321 more)

306 more per

1000 (from 155

more to 532 more)

307 more per

1000 (from 155 more to 534 more)

320 more per

1000 (from 164

more to 543 more)

320 more per

1000 (from 164 more to 543 more

32.8%

25/165

(15.2%)

15.2%

31/149

(20.8%)

20.8%

RR 3.02

(2.02 to

4.51)

RR 2.54

(1.79 to

3.61)

70/153

(45.8%)

73/138

(52.9%)

7		
_		
С		

### Medication management versus control

randomised

trials

trials

serious1

serious<sup>3</sup>

Antidepressant use (follow-up mean 6 months)

randomised very

1 ROB high or unclear in two to three domains

<sup>2</sup> 95% CI crosses one clinical decision threshold <sup>3</sup> High or unclear ROB in most domains 4 95% CI crosses two clinical decision thresholds

no serious

no serious

inconsistency

inconsistency

no serious

no serious

indirectness

indirectness

serious<sup>2</sup>

very

serious4

none

none

	3												
			Quality as	sessment			No of patier	nts		Effect			
											Quality	Importance	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MEDICATION MANAGEMENT	CONTROL	Relative (95% CI)	Absolute			
									,				
Mean cl	Mean change in depression scores (Better indicated by lower values)												
	Total olithings in depression socies (Botton indicated by total values)												
9	randomised	very	serious <sup>2</sup>	no serious	no serious	none	0	-	-	SMD 0.13 lower	⊕000	CRITICAL	
	trials	serious <sup>1</sup>		indirectness	imprecision					(0.33 lower to 0.06	VERY		
										higher)	LOW		
Mean ch	ange in depre	ssion sco	res at follow-up (fo	ollow-up mean 1	2 months; Bette	r indicated by low	er values)						
1	randomised	serious <sup>3</sup>	no serious	no serious	very serious <sup>4,5</sup>	none	113	106	-	MD 2 lower (4.86	$\oplus$ OOO	CRITICAL	
	trials		inconsistency	indirectness						lower to 0.86 higher)	VERY		
											LOW		
Antidep	essant use at	endpoint											
4	randomised	serious <sup>3</sup>	serious <sup>2</sup>	no serious	serious <sup>6</sup>	none	-	-	Not	-	$\oplus$ OOO	CRITICAL	
	trials			indirectness					estimable		VERY		
											LOW		

137

28/86

(32.6%)

64

23/84

(27.4%)

CRITICAL

CRITICAL

 $\oplus \oplus OO$ 

LOW

⊕000

**VERY** LOW

MD 1.4 lower (2.87 lower

to 0.07 higher)

68 fewer to 244 more)

RR 1.19 (0.75 52 more per 1000 (from

to 1.89)

3 4 5 6	<sup>1</sup> ROB high or unclear across multiple domains <sup>2</sup> I2 > 50% <sup>3</sup> ROB high or unclear across two to three domains <sup>4</sup> OIS not met (<400 participants) <sup>5</sup> 95% CI crosses two clinical decision thresholds <sup>6</sup> 95% CI crosses one clinical decision threshold												
8	Care co-	ordination (	versus cor	ntrol									
				Quality as:	sessment			No of pati	ents		Effect		
												Quality	Importance
	No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CARE CO- ORDINATION	CONTROL	Relative (95% CI)	Absolute		
	Mean cha	nge in depre	ssion score	es at endpoint (Be	tter indicated by	lower values)							
		randomised trials	very serious <sup>1,2</sup>	no serious inconsistency		no serious imprecision	none	0	-	-	SMD 0.05 lower (0.35 lower to 0.25 higher)	⊕⊕OO LOW	CRITICAL
	Antidepre	essant adhere	ence at follo	ow-up (follow-up r	nean 12 months								
			serious <sup>1</sup>	serious <sup>3</sup>	no serious	very serious <sup>4</sup>	none	-	-	RR 1.79	-	⊕000	CRITICAL
		trials			indirectness				0%	(0.68 to 4.72)	-	VERY LOW	
9 10 11 12	<ul><li>ROB high</li><li>12 &gt; 50%</li></ul>	n or unclear in n or unclear ac crosses two cli	cross multipl	e domains									

13

#### Integrated care versus control 14

Quality assessment	No of patients	Effect	Quality	Importance

1
2
_
3
4
5
6

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	INTEGRATED CARE	CONTROL	Relative (95% CI)	Absolute		
Mean cha	inge in depres	sion scor	es at endpoint (Be	tter indicated by	lower values)							
3	randomised	very	serious <sup>2</sup>		no serious	none	0	-	-	SMD 0.05 lower (0.26	⊕000	CRITICAL
	trials	serious <sup>1</sup>		indirectness	imprecision					lower to 0.16 higher)	VERY LOW	
											2011	
lean cha	inge in depres	ssion scor	es at endpoint - In		·	ndicated by lower	values)					
2	randomised	very	serious <sup>2</sup>		serious <sup>3,4</sup>	none	0	-	-	SMD 0.19 lower (0.55	$\oplus$ OOO	CRITICA
	trials	serious <sup>1</sup>		indirectness						lower to 0.17 higher)	VERY LOW	
		L.										
lean cha	inge in depres	ssion scor	es at endpoint - In	tegrated care vs	speciality referr	al system (Better i	ndicated by high	er values)				
1	randomised	very	no serious		no serious	none	0	-	-	SMD 0.08 higher (0.03	$\oplus \oplus OO$	CRITICAL
	trials	serious <sup>1</sup>	inconsistency	indirectness	imprecision					lower to 0.19 higher)	LOW	
lean cha	inge in depres	sion scor	es at follow-up (fo	llow-up mean 12	months; Better	indicated by highe	r values)	L				
1	randomised	serious <sup>5</sup>	no serious	no serious	serious <sup>6</sup>	none	189	186	-	MD 0.01 higher (0.11	⊕⊕ОО	CRITICAL
	trials		inconsistency	indirectness						lower to 0.13 higher)	LOW	
Antidepre	essant adhere	nce										
2	randomised	verv	serious <sup>2</sup>	no serious	very serious <sup>3</sup>	none	-	_	Not	-	⊕000	CRITICAL
	trials	serious <sup>1</sup>		indirectness					estimable		VERY	
											LOW	
ROB hig	h or unclear in	multiple do	mains		<u>l</u>							

<sup>&</sup>lt;sup>2</sup> I2 > 50%

## Service delivery models for relapse prevention

Quality assessment	No of patients	Effect	Quality	Importance

<sup>&</sup>lt;sup>3</sup> 95% CI crosses two clinical decision thresholds

<sup>4 95%</sup> CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>5</sup> ROB high or unclear in two to three domains <sup>6</sup> OIS not met (<400 participants)

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RELAPSE PREVENTION	Control	Relative (95% CI)	Absolute		
Collabora	tive care (sim	ple)- depr	ession symptoms	at endpoint (Bett	er indicated	by lower values)						
1	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	174	153	-	MD 0.09 lower (0.2 lower to 0.02 higher)	⊕OOO VERY LOW	CRITICAL
Collabora	tive care (sim	ple)- relap	se at follow-up (fo	llow-up mean 12	months)							
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	67/192 (34.9%)	67/194 (34.5%)	RR 1.01 (0.77 to 1.33)	3 more per 1000 (from 79 fewer to 114 more)	⊕⊕OO LOW	CRITICAL
								34.5%		3 more per 1000 (from 79 fewer to 114 more)		
Stepped o	care at follow-	up (follow	-up mean 12 mont	hs)								
	randomised trials	very serious <sup>1</sup>	no serious inconsistency		very serious <sup>4</sup>	none	24/74 (32.4%)	16/62 (25.8%)		67 more per 1000 (from 67 fewer to 297 more)	⊕000 VERY LOW	CRITICAL
	or unclear in							25.8%		67 more per 1000 (from 67 fewer to 297 more)		

<sup>&</sup>lt;sup>1</sup> ROB high or unclear in multiple domains <sup>2</sup> OIS not met (<400 participants)

# Settings for care

Crisis resolution team care versus standard care

			Quality asses	sment			No of patie	ents		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Crisis resolution team care	Standard care	Relative (95% CI)	Absolute		
Lost to foll	low-up (follov	v-up mean	12 months; asses	ssed with: Nu	mber of part	icipants lost to fo	llow-up by the end	of the stud	ly)			

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>4</sup> 95% CI crosses two clinical decision thresholds

	randomised	very	no serious	serious <sup>2</sup>	very	none	17/135	17/125	RR 0.93 (0.49		⊕OOO
	trials	serious <sup>1</sup>	inconsistency		serious <sup>3</sup>		(12.6%)	(13.6%)	to 1.73)	69 fewer to 99 more)	VERY
											LOW
								13.6%		10 fewer per 1000 (from	
										69 fewer to 99 more)	
ton	n severity (BP	RS) (follow	w-up mean 8 weel	ks; measure	d with: Brief I	Psychiatric Rating	Scale (BPRS) 8 we	eeks after cr	isis; Better ind	icated by lower values)	
	randomised	von	no serious	serious <sup>2</sup>	serious <sup>4</sup>	none	107	104		SMD 0.29 lower (0.56 to	0000
	trials	very serious <sup>1</sup>	inconsistency	Serious	Serious	none	107	104	-	0.02 lower)	⊕OOO VERY
	lilais	Sellous	inconsistency							0.02 lower)	LOW
											LOVV
issi	on as inpatien	t (follow-u	p mean 6 months	: assessed v	vith: Number	of participants th	at had been admitt	ed to a psvc	hiatric ward wi	thin 6 months after crisis	)
				,							,
	randomised	very	no serious	serious <sup>2</sup>	serious <sup>5</sup>	none	39/134	84/124	RR 0.43 (0.32	386 fewer per 1000 (from	⊕ООО
	trials	serious1	inconsistency				(29.1%)	(67.7%)	to 0.57)	291 fewer to 461 fewer)	VERY
											LOW
								67.7%		386 fewer per 1000 (from	
										291 fewer to 460 fewer)	
days	s in hospital (f	ollow-up r	mean 6 months; n	neasured wit	h: Number o	f bed days in hosp	oital for those admi	tted within 6	months after	crisis; Better indicated by	lower value
	1		1	1	1	1	1		1		
		1001	no serious	serious <sup>2</sup>	serious4	none	134	123	_	MD 18.9 lower (29.38 to	⊕OOO
	randomised	very		SCHOUS	oonoao	110110	104			•	
	randomised trials	serious <sup>1</sup>	inconsistency	3011003	Conodo		104			8.42 lower)	VERY
				SCHOUS	Conodo		104	1.20		•	
-ft	trials	serious <sup>1</sup>	inconsistency						for origin Date	8.42 lower)	VERY LOW
sfact	trials	serious <sup>1</sup>	inconsistency						fter crisis; Bett	•	VERY LOW
isfact	trials ion (follow-up	serious <sup>1</sup> mean 8 w	inconsistency reeks; measured	with: Client S	Satisfaction C	Questionnaire - 8 if	tem version (CSQ-	B) 8 weeks at	fter crisis; Bett	8.42 lower) er indicated by lower valu	VERY LOW
sfact	trials  ion (follow-up  randomised	serious <sup>1</sup> mean 8 w	reeks; measured v						fter crisis; Bett	8.42 lower) er indicated by lower valu SMD 0.23 higher (0.03	VERY LOW
sfact	trials ion (follow-up	serious <sup>1</sup> mean 8 w	inconsistency reeks; measured	with: Client S	Satisfaction C	Questionnaire - 8 if	tem version (CSQ-	B) 8 weeks at	fter crisis; Bett	8.42 lower) er indicated by lower valu	VERY LOW  Jes)  +000 VERY
sfact	trials  ion (follow-up  randomised	serious <sup>1</sup> mean 8 w	reeks; measured v	with: Client S	Satisfaction C	Questionnaire - 8 if	tem version (CSQ-	B) 8 weeks at	fter crisis; Bett	8.42 lower) er indicated by lower valu SMD 0.23 higher (0.03	VERY LOW
	ion (follow-up randomised trials	mean 8 wery serious <sup>1</sup>	reeks; measured voncessions inconsistency	with: Client \$	Satisfaction C	Questionnaire - 8 it	tem version (CSQ-t	3) 8 weeks at	-	8.42 lower) er indicated by lower valu SMD 0.23 higher (0.03	VERY LOW Jes) ⊕OOO VERY LOW
	trials  ion (follow-up  randomised trials  f life (follow-u	very serious <sup>1</sup>	no serious inconsistency weeks; measured weeks; measured	serious <sup>2</sup>	serious <sup>4</sup>	none assessment of qua	tem version (CSQ-4	108 108 8 weeks at	-	8.42 lower)  er indicated by lower values  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower values	VERY LOW  Jes)  #000 VERY LOW  Jes)
	trials  ion (follow-up  randomised trials  f life (follow-u	mean 8 w very serious¹  p mean 8 very	no serious inconsistency weeks; measured weeks; we well we weeks; measured weeks; measured weeks; we well we well we well we well we well we w	with: Client \$	Satisfaction C	Questionnaire - 8 it	tem version (CSQ-t	3) 8 weeks at	-	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37	VERY LOW  Des)  Description  De
	trials  ion (follow-up  randomised trials  f life (follow-u	very serious <sup>1</sup>	no serious inconsistency weeks; measured weeks; measured	serious <sup>2</sup>	serious <sup>4</sup>	none assessment of qua	tem version (CSQ-4	108 108 8 weeks at	-	8.42 lower)  er indicated by lower values  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower values	VERY LOW  Des)  Description  De
	trials  ion (follow-up  randomised trials  f life (follow-u	mean 8 w very serious¹  p mean 8 very	no serious inconsistency weeks; measured weeks; we well we weeks; measured weeks; measured weeks; we well we well we well we well we well we w	serious <sup>2</sup>	serious <sup>4</sup>	none assessment of qua	tem version (CSQ-4	108 108 8 weeks at	-	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37	VERY LOW  Des)  Description  De
ality o	ion (follow-up randomised trials  f life (follow-u randomised trials	mean 8 w very serious¹  p mean 8 very serious¹	no serious inconsistency  weeks; measured weeks; measured no serious inconsistency	serious <sup>2</sup> I with: Mancl	serious <sup>4</sup> hester short a	none assessment of quantum	118 ality of life (MANSA	108 108 108 103	ter crisis; Bett	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37 lower to 0.16 higher)	VERY LOW  Des)  Description  De
ality o	ion (follow-up randomised trials  f life (follow-u randomised trials	mean 8 w very serious¹  p mean 8 very serious¹	no serious inconsistency  weeks; measured weeks; measured no serious inconsistency	serious <sup>2</sup> I with: Mancl	serious <sup>4</sup> hester short a	none assessment of quantum	tem version (CSQ-4	108 108 108 103	ter crisis; Bett	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37 lower to 0.16 higher)	VERY LOW  Des)  Description  De
ality o	ion (follow-up randomised trials  f life (follow-u randomised trials	mean 8 w very serious¹  p mean 8 very serious¹	no serious inconsistency  weeks; measured weeks; measured no serious inconsistency	serious <sup>2</sup> I with: Mancl	serious <sup>4</sup> hester short a	none assessment of quantum	118 ality of life (MANSA	108 108 108 103	ter crisis; Bett	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37 lower to 0.16 higher)	VERY LOW  Des)  Description  De
ality o	trials  ion (follow-up  randomised trials  f life (follow-u  randomised trials  nctioning (8 w	mean 8 w very serious¹  p mean 8  very serious¹  very serious¹	no serious inconsistency  weeks; measured weeks; measured weeks; measured no serious inconsistency  r crisis) (follow-up	serious <sup>2</sup> I with: Mancle serious <sup>2</sup> o mean 8 week	serious <sup>4</sup> hester short a serious <sup>4</sup> serious <sup>4</sup>	none none none none none	ality of life (MANSA	108 108 108 108 103 er indicated	ter crisis; Bett	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37 lower to 0.16 higher)	VERY LOW  Des)  Des)  Description of the control of
lity o	trials  ion (follow-up  randomised trials  f life (follow-up  randomised trials  nctioning (8 was  randomised	mean 8 w very serious¹  p mean 8 very serious¹  very serious¹  very serious¹	no serious inconsistency  weeks; measured weeks; measured weeks; measured no serious inconsistency  r crisis) (follow-up no serious	serious <sup>2</sup> I with: Mancle serious <sup>2</sup> o mean 8 week	serious <sup>4</sup> hester short a serious <sup>4</sup> serious <sup>4</sup>	none none none none none	ality of life (MANSA	108 108 108 108 103 er indicated	ter crisis; Bett	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37 lower to 0.16 higher)  s)  SMD 0.2 higher (0.05	VERY LOW  Des)  Door VERY LOW  Des)  Door VERY LOW  Design
lity o	trials  ion (follow-up  randomised trials  f life (follow-up  randomised trials  nctioning (8 was  randomised	mean 8 w very serious¹  p mean 8 very serious¹  very serious¹  very serious¹	no serious inconsistency  weeks; measured weeks; measured weeks; measured no serious inconsistency  r crisis) (follow-up no serious	serious <sup>2</sup> I with: Mancle serious <sup>2</sup> o mean 8 week	serious <sup>4</sup> hester short a serious <sup>4</sup> serious <sup>4</sup>	none none none none none	ality of life (MANSA	108 108 108 108 103 er indicated	ter crisis; Bett	8.42 lower)  er indicated by lower value  SMD 0.23 higher (0.03 lower to 0.49 higher)  er indicated by lower value  SMD 0.11 lower (0.37 lower to 0.16 higher)  s)  SMD 0.2 higher (0.05	VERY LOW  Des)  Des)  Description  Descripti

•	1	randomised	very	no serious	serious <sup>2</sup>	serious4	none	133	122	-	SMD 0.06 higher (0.18	⊕000	
		trials	serious <sup>1</sup>	inconsistency							lower to 0.31 higher)	VERY	1
												LOW	
													1

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups and baseline and non-blind participants, intervention administrator(s) and outcome assessor(s)

Acute day hospital care versus inpatient care

	/ 1		3 Inputient cure				1		i		1	I
			Quality ass	sessment			No of pa	tients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acute day hospital care	Inpatient care	Relative (95% CI)	Absolute		
Lost to fo	llow-up (follow	v-up 3-14 r	months; assessed	with: Number of	participants los	st to follow-up by t	he end of the s	study)				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	310/907 (34.2%)	270/856 (31.5%)	RR 1.25 (0.96 to 1.63)	79 more per 1000 (from 13 fewer to 199 more)	⊕000 VERY LOW	
								17.8%		44 more per 1000 (from 7 fewer to 112 more)		
Death (sui	icide) (follow-	up mean 1	4 months; assess	ed with: Number	of participants	that committed su	icide during th	e study pei	riod)			
	randomised trials	very serious <sup>4</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	0/596 (0%)	3/521 (0.6%)	RR 0.12 (0.01 to 2.41)	5 fewer per 1000 (from 6 fewer to 8 more)	⊕000 VERY LOW	
								0.6%		5 fewer per 1000 (from 6 fewer to 8 more)		
Remission	n of psychiatr	ic symptor	ns (follow-up 3-13	months; assess	ed with: Presen	t State Examinatio	n: Index of Def	finition≤4/<	7 on Hamiltor	Rating Scale for Dep	ression (	HAM-D))
	randomised trials	- ,	no serious inconsistency	serious <sup>2</sup>	very serious <sup>7</sup>	reporting bias <sup>8</sup>	33/80 (41.3%)	33/71 (46.5%)	RR 0.91 (0.65 to 1.26)	42 fewer per 1000 (from 163 fewer to 121 more)		

<sup>&</sup>lt;sup>2</sup> Not depression-specific population <sup>3</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>4</sup> N<400

<sup>&</sup>lt;sup>5</sup> Events<300

								20.00/		33 fewer per 1000	⊕000 VERY
								36.9%		(from 129 fewer to 96 more)	LOW
on	se (follow-up n	nean 3 mor	ths; assessed wi	th: Number of p	eople showing ≥	47% improvement of	on Hamilton R	lating Scale	for Depression	on (HAM-D))	
	randomised	very	no serious	no serious	very serious <sup>7</sup>	reporting bias <sup>10</sup>	6/24	8/20	RR 0.62	152 fewer per 1000	⊕000
	trials	serious <sup>9</sup>	inconsistency	indirectness	very serious	reporting bias	(25%)	(40%)		(from 296 fewer to 200	VERY
	tilais	3011003	inconsistency	indirectiness			(2370)	(4070)	(0.20 to 1.5)	more)	LOW
											2011
										152 fewer per 1000	
								40%		(from 296 fewer to 200	
										more) PRS; change score)/Br	
.9 .	randomised trials	very serious <sup>11</sup>	serious <sup>12</sup>	serious <sup>2</sup>	no serious imprecision	none	682	599	-	SMD 0.05 higher (0.22 lower to 0.33 higher)	⊕OOO VERY
											LOW
	Scale (BPRS; c	hange sco	re); Better indicate	ed by lower valu	ies)					le (CPRS; change scor	
						red with: Compreh	ensive Psycho	ppathologic 586	al Rating Sca	SMD 0.19 lower (0.81 lower to 0.42 higher)	e)/Brief Psyc
ing S	randomised trials	very serious <sup>11</sup>	very serious <sup>13</sup>	serious <sup>2</sup>	serious <sup>14</sup>		663	586	-	SMD 0.19 lower (0.81 lower to 0.42 higher)	⊕000 VERY
ing S	randomised trials	very serious <sup>11</sup>	very serious <sup>13</sup>	serious <sup>2</sup>	serious <sup>14</sup>	none	663	586	-	SMD 0.19 lower (0.81 lower to 0.42 higher)	⊕000 VERY
ng S	randomised trials  n of index adm	very serious <sup>11</sup>	very serious <sup>13</sup> ow-up 12-14 month	serious <sup>2</sup> ths; measured w	serious <sup>14</sup>	none lays/months in hos	663 pital; Better ir	586	-	SMD 0.19 lower (0.81 lower to 0.42 higher)	⊕OOO VERY LOW
ng S	randomised trials  n of index adm	very serious <sup>11</sup> ission (foll	very serious <sup>13</sup> ow-up 12-14 month no serious	serious <sup>2</sup> ths; measured w	serious <sup>14</sup> vith: Number of o	none lays/months in hos	663 pital; Better ir	586	-	SMD 0.19 lower (0.81 lower to 0.42 higher) SMD 0.55 higher (0.44	⊕000 VERY LOW
ing s	randomised trials  n of index adm  randomised trials	very serious <sup>11</sup> ission (foll very serious <sup>11</sup>	very serious <sup>13</sup> ow-up 12-14 montons inconsistency	serious <sup>2</sup> ths; measured w	serious <sup>14</sup> vith: Number of o	none lays/months in hos	663 pital; Better ir	586	-	SMD 0.19 lower (0.81 lower to 0.42 higher) SMD 0.55 higher (0.44	⊕OOO VERY LOW ⊕OOO VERY
ation	randomised trials  n of index adm  randomised trials  randomised trials	very serious <sup>11</sup> ission (foll very serious <sup>11</sup> p mean 12	very serious <sup>13</sup> ow-up 12-14 monton on serious inconsistency  months; assesse	serious <sup>2</sup> ths; measured w serious <sup>2</sup> d with: Number	serious <sup>14</sup> vith: Number of o	none lays/months in hos none mitted to hospital)	663  pital; Better ir	586  Indicated by	lower values)	SMD 0.19 lower (0.81 lower to 0.42 higher)  SMD 0.55 higher (0.44 to 0.65 higher)	⊕OOO VERY LOW ⊕OOO VERY
ation	randomised trials  n of index adm  randomised trials  randomised trials  ssion (follow-upper randomised)	very serious <sup>11</sup> ission (foll very serious <sup>11</sup>	very serious <sup>13</sup> ow-up 12-14 montons inconsistency	serious <sup>2</sup> ths; measured w	serious <sup>14</sup> vith: Number of o	none lays/months in hos	663  pital; Better ir  800	735	lower values)	SMD 0.19 lower (0.81 lower to 0.42 higher)  SMD 0.55 higher (0.44 to 0.65 higher)	#000 VERY LOW #000 VERY LOW #000
ration	randomised trials  n of index adm  randomised trials  randomised trials	very serious <sup>11</sup> ission (foll very serious <sup>11</sup> p mean 12	very serious <sup>13</sup> ow-up 12-14 monton on serious inconsistency  months; assesse	serious <sup>2</sup> ths; measured w serious <sup>2</sup> d with: Number	serious <sup>14</sup> vith: Number of o	none lays/months in hos none mitted to hospital)	663  pital; Better ir	586  Indicated by	lower values)	SMD 0.19 lower (0.81 lower to 0.42 higher)  SMD 0.55 higher (0.44 to 0.65 higher)	⊕000 VERY LOW ⊕000 VERY LOW
ation	randomised trials  n of index adm  randomised trials  randomised trials  ssion (follow-upper randomised)	very serious <sup>11</sup> ission (foll very serious <sup>11</sup> p mean 12	very serious <sup>13</sup> ow-up 12-14 monton on serious inconsistency  months; assesse	serious <sup>2</sup> ths; measured w serious <sup>2</sup> d with: Number	serious <sup>14</sup> vith: Number of o	none lays/months in hos none mitted to hospital)	663  pital; Better ir  800	735	lower values)	SMD 0.19 lower (0.81 lower to 0.42 higher)  SMD 0.55 higher (0.44 to 0.65 higher)  52 fewer per 1000 (from 147 fewer to 129	#000 VERY LOW #000 VERY LOW #000 VERY LOW

	andomised	serious <sup>15</sup>	no serious	serious <sup>2</sup>	serious <sup>16</sup>	reporting bias8	17/41	33/48	RR 0.6 (0.4	275 fewer per 1000	⊕OOO
t	rials		inconsistency				(41.5%)	(68.8%)	to 0.91)	(from 62 fewer to 412	VERY
										fewer)	LOW
										275 fewer per 1000	
								68.8%		(from 62 fewer to 413	
								00.070		fewer)	
e uti	lisation: Em	ergency co	ontacts (follow-up	mean 4 mont	hs; assessed with	: Number of partici	pants making o	emergency	contacts with	in 4 months post-adm	ission)
r	andomised	serious <sup>17</sup>	no serious	serious <sup>2</sup>	serious <sup>3</sup>	reporting bias8	12/38	6/45	RR 2.37	183 more per 1000	⊕OOO
t	rials		inconsistency				(31.6%)	(13.3%)	(0.98 to 5.71)	(from 3 fewer to 628	VERY
			·				, ,		,	more)	LOW
										182 more per 1000	
								13.3%		(from 3 fewer to 626	
								10.070		more)	
e uti	lisation: Out	patient co	ntact (follow-up r	nean 4 months	s; assessed with: I	Number of participa	ints making ou	tpatient co	ntacts within	1 months post-admiss	ion)
r	andomised	serious <sup>17</sup>	no serious	serious <sup>2</sup>	very serious <sup>5</sup>	reporting bias8	14/38	12/45	RR 1.38	101 more per 1000	⊕000
t	rials		inconsistency		·	. 0	(36.8%)	(26.7%)	(0.73 to 2.62)	(from 72 fewer to 432	VERY
			,				,	,	,	more)	LOW
										101 more per 1000	
								26.7%		(from 72 fewer to 433	
								20.1 70		more)	
actio	n (follow-up	mean 4 m	onths; assessed	with: Number	of participants sat	tisfied or very satisf	ied with their t	treatment)			
r	andomised	very	no serious	serious <sup>2</sup>	serious <sup>16</sup>	reporting bias8	31/38	19/45	RR 1.93	393 more per 1000	⊕OOO
t	rials	serious <sup>17</sup>	inconsistency			, 0	(81.6%)	(42.2%)		(from 139 more to 764	VERY
			, , , , , , , , , , , , , , , , , , , ,				(2 2 2 2 )	( 11)	,	more)	LOW
										392 more per 1000	
								42.2%		(from 139 more to 764	
								72.270		more)	
factio	n (follow-up	mean 2 m	onths; measured	with: Cliet As:	sessment of Treat	ment (CAT); Better	indicated by lo	wer values		,	
lr	andomised	verv	no serious	serious <sup>2</sup>	no serious	none	596	521		SMD 0.03 higher (0.09	⊕000
	rials	serious <sup>11</sup>	inconsistency	0011000	imprecision	110110	000	021		lower to 0.15 higher)	VERY
ľ	TIGIO .	CONTOUC	in consistency		impredicion					ionor to o. ro migner)	LOW
			1				1	1			

	randomised	very	no serious	serious <sup>2</sup>	no serious	none	596	521	-	SMD 0.01 higher (0.11	⊕000	
	trials	serious <sup>11</sup>	inconsistency		imprecision					lower to 0.13 higher)	VERY	
										-	LOW	
ty of	f life (14-mon	ths post-ad	lmission) (follow-	up mean 14 mor	iths; measured v	vith: Manchester sl	nort assessme	ent of quality	y of life (MAN	SA); Better indicated b	y lower v	alues
	randomised	very	no serious	serious <sup>2</sup>	no serious	none	596	521	-	SMD 0.01 higher (0.11	⊕000	
	trials	serious <sup>11</sup>	inconsistency		imprecision					lower to 0.13 higher)	VERY	
											LOW	
						lities or less on Gro mance and behavio				SDS)/Number of partic	cipants liv	ing i
	randomicad	von	no corious	serious <sup>2</sup>	serious <sup>19</sup>	reporting bias8	41/91	30/90	RR 1.36	120 more per 1000	0000	
	randomised trials	very serious <sup>18</sup>	no serious inconsistency	Sellous-	Sellous	reporting bias	(45.1%)	(33.3%)		(from 20 fewer to 320	⊕000 VERY	
	liidis	Serious	inconsistency				(45.1%)	(33.3%)	(0.94 to 1.90)	more)	LOW	
										123 more per 1000		
								34.2%		(from 21 fewer to 328		
								0.11270		more)	1	
	randomised trials	very serious <sup>11</sup>	no serious inconsistency	serious <sup>2</sup>	no serious imprecision	none	596	521	-	SMD 0.3 lower (0.42 to 0.19 lower)	⊕000 VERY	
	liidis	Serious	inconsistency		Imprecision					(0 0.19 lower)	LOW	
											1	
	nctioning imp by lower valu		I-months post-ad	mission) (follow	-up mean 14 mo	nths; measured wit	th: Groningen	Social Disa	bilities Sched	ule, Second revision (	GSDS-II);	Bette
	by lower valu	ues)	·	, ,					bilities Sched			Bette
	randomised	very	no serious	mission) (follow serious <sup>2</sup>	no serious	nths; measured wit	th: Groningen	Social Disa	bilities Sched	SMD 0.15 lower (0.27	⊕000	Bette
	by lower valu	ues)	·	, ,					bilities Sched			Bette
cated	randomised trials	very serious <sup>11</sup>	no serious inconsistency	serious <sup>2</sup>	no serious imprecision	none	596	521	-	SMD 0.15 lower (0.27	⊕000 VERY LOW	
cated	randomised trials	very serious <sup>11</sup>	no serious inconsistency	serious <sup>2</sup>	no serious imprecision	none	596	521	-	SMD 0.15 lower (0.27 to 0.04 lower)	⊕000 VERY LOW	
cated	randomised trials tress (3-mont	very serious <sup>11</sup>	no serious inconsistency mission) (follow-u	serious <sup>2</sup> up mean 3 montl	no serious imprecision hs; measured wi	none th: General Health	596  Questionnaire	521 (GHQ; cha	nge score); Bo	SMD 0.15 lower (0.27 to 0.04 lower)	⊕OOO VERY LOW	
cated	randomised trials tress (3-mont	very serious <sup>11</sup> hs post-ad	no serious inconsistency mission) (follow-uno serious	serious <sup>2</sup> up mean 3 montl	no serious imprecision hs; measured wi	none th: General Health	596  Questionnaire	521 (GHQ; cha	nge score); Bo	SMD 0.15 lower (0.27 to 0.04 lower)  etter indicated by lower  MD 1.1 lower (3.15	⊕000 VERY LOW er values)	

	- 3	no serious	serious <sup>2</sup>	serious <sup>14</sup>	none	24	31	-	MD 0.4 lower (2.98	⊕000	·
trials	serious <sup>15</sup>	inconsistency							lower to 2.18 higher)	VERY	ı
										LOW	l
											ı

- <sup>1</sup> Randomisation method was unclear (or high risk associated with it due to significant baseline differences). Non-blind participants, intervention administrator(s) and unclear blinding of, or non-blind, outcome assessor(s)
  - <sup>2</sup> Non depression-specific population
  - <sup>3</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)
  - <sup>4</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline. Non-blind participants, intervention administrator(s) and outcome assessor(s).
  - Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)
  - <sup>5</sup> 95% CI crosses line of no effect and both threshold for clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

    <sup>6</sup> Unclear randomisation method and method of allocation concealment. Non-blind participants and intervention administrator(s) and unclear blinding of outcome assessment
  - onclear randomisation method or anocation concealment. Non-olino participants and intervention administrator(s) and unclear billioning or outcome assessment
  - <sup>7</sup> 95% CI crosses line of no effect and threshold for clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)
- 10 <sup>8</sup> Data cannot be extracted for all outcomes (measure of variance not reported)
  - <sup>9</sup> Unclear blinding of allocation concealment. Non-blind participants and intervention administrator(s) and unclear blinding of outcome assessment. Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)
  - <sup>10</sup> A non-standard definition of response selected (e.g. 47% rather than 50%)
- 14 High risk of bias associated with randomisation method due to significant difference between groups at baseline. Non-blind participants, intervention administrator(s) and outcome assessment.

  15 Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)
- 16 <sup>12</sup> I-squared>50%
- 17 <sup>13</sup> I-squared>80%

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- 18 14 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD -0.5)
  - <sup>15</sup> Non-blind participants, intervention administrator(s) and outcome assessment
- 20 <sup>16</sup> Events<300
  - <sup>17</sup> Unclear randomisation method and allocation concealment, and non-blind participants, intervention administrator(s) and outcome assessment
  - <sup>18</sup> Non-blind participants and intervention administrator(s) and non-blind, or unclear blinding of, outcome assessment. Unclear risk of attrition bias (drop-out>20% but difference between groups<20%)
  - <sup>19</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

#### Non-acute day hospital care versus outpatient care

			Quality asses	sment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Non-acute day hospital care versus outpatient care		Relative (95% CI)	Absolute		
Lost to f	ollow-up (follo	w-up 6-24	months; assesse	d with: Numb	er of particip	ants lost to follow	-up by the end of the stu	dy)				
3		serious <sup>1</sup>	serious <sup>2</sup>	serious <sup>3</sup>	very serious <sup>4</sup>	reporting bias <sup>5</sup>	24/136	30/145		39 fewer per 1000		
	trials						(17.6%)	(20.7%)	(0.24 to 2.7)	(from 157 fewer to 352 more)		

		1					1	_	1			
										39 fewer per 1000	⊕000	
								20.7%		(from 157 fewer to 352	VERY	
										more)	LOW	
41- /-1	/6 - 11		04		N				4			
eath (ai	i causes) (foii	ow-up me	an 24 months; ass	sessea witn:	Number of pa	rticipants who die	ed due to any causes dur	ing the s	tuay perioa)			
	randomised	serious <sup>6</sup>	no serious	serious <sup>3</sup>	very serious <sup>4</sup>	none	2/48	1/58	RR 2.42	24 more per 1000	⊕000	
	trials		inconsistency				(4.2%)	(1.7%)	(0.23 to	(from 13 fewer to 428	VERY	
									25.85)	more)	LOW	
										24 more per 1000		
								1.7%		(from 13 fewer to 422		
								1.7 /0		more)		
mnton	severity (4-6	months n	ost-admission) (fo	ollow-up 4-6	months: meas	sured with: Psychi	iatric Evaluation Form (c	hange so	ore)/Present	,	nge score):	Bette
	by lower value		oot uumiooion) (ii	onow up + o	months, mout	dica with i Syon	iddio Evaluation i oim (o	nunge se	010,71 1000110	otato Examination (one	inge score,	Dotte
		,										
	randomised	serious <sup>7</sup>	very serious <sup>8</sup>	serious <sup>3</sup>	very serious9	none	75	69	-	SMD 0.08 higher (0.72	⊕OOO	
	trials									lower to 0.88 higher)	VERY	
											LOW	
etter ind	dicated by lov	ver values		ionow up o	12 monuis, me	asureu witii. Fsyt	chiatric Evaluation Form	(cnange	score)/Prese	nt State Examination (C	nange score	=),
etter in	,		)						score//Prese			<b>5</b> ),
etter inc	randomised	serious <sup>7</sup>	no serious	serious <sup>3</sup>		reporting bias <sup>11</sup>	73	66	-	SMD 0.15 lower (0.49	⊕000	<del>5</del> ),
etter in	,		)						-		⊕OOO VERY	=), 
etter in	randomised		no serious						-	SMD 0.15 lower (0.49	⊕000	<i>=)</i> ,
	randomised trials	serious <sup>7</sup>	no serious inconsistency	serious <sup>3</sup>	serious <sup>10</sup>	reporting bias <sup>11</sup>		66	-	SMD 0.15 lower (0.49	⊕OOO VERY	<i>=</i> ),
	randomised trials on as inpatien	serious <sup>7</sup>	no serious inconsistency p 6-12 months; as	serious <sup>3</sup>	serious <sup>10</sup> 1: Number of pa	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)	⊕OOO VERY LOW	<i>5</i> ),
	randomised trials	serious <sup>7</sup>	no serious inconsistency p 6-12 months; as	serious <sup>3</sup>	serious <sup>10</sup>	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66 ring the s	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000	⊕000 VERY LOW	<i>5</i> ),
	randomised trials on as inpatien	serious <sup>7</sup>	no serious inconsistency p 6-12 months; as	serious <sup>3</sup>	serious <sup>10</sup> 1: Number of pa	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66 ring the s	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170	⊕000 VERY LOW	<i>=</i> 1,
	randomised trials	serious <sup>7</sup>	no serious inconsistency p 6-12 months; as	serious <sup>3</sup>	serious <sup>10</sup> 1: Number of pa	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66 ring the s	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000	⊕000 VERY LOW	<i>=</i> ),
	randomised trials	serious <sup>7</sup>	no serious inconsistency p 6-12 months; as	serious <sup>3</sup>	serious <sup>10</sup> 1: Number of pa	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66 ring the s	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170	⊕000 VERY LOW	<i>=</i> ),
	randomised trials	serious <sup>7</sup>	no serious inconsistency p 6-12 months; as	serious <sup>3</sup>	serious <sup>10</sup> 1: Number of pa	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66 ring the s	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)	⊕000 VERY LOW	<b>3</b> ),
dmissio	randomised trials on as inpatien randomised trials	serious <sup>7</sup> t (follow-u	no serious inconsistency  p 6-12 months; as no serious inconsistency	serious <sup>3</sup> sessed with	serious <sup>10</sup> 1: Number of particular very serious <sup>4</sup>	reporting bias <sup>11</sup> articipants admitte	ed into inpatient care du	66  12/145 (8.3%)	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)  21 more per 1000	⊕000 VERY LOW	<b>3</b> ),
dmissio	randomised trials on as inpatien randomised trials	serious <sup>7</sup> t (follow-u	no serious inconsistency  p 6-12 months; as no serious inconsistency	serious <sup>3</sup> sessed with	serious <sup>10</sup> 1: Number of particular very serious <sup>4</sup>	reporting bias <sup>11</sup> articipants admitte	73 ed into inpatient care du	66  12/145 (8.3%)	- study period)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)  21 more per 1000 (from 38 fewer to 165	⊕000 VERY LOW	, , , , , , , , , , , , , , , , , , ,
dmissio	randomised trials on as inpatien randomised trials trials	serious <sup>7</sup> t (follow-u serious <sup>12</sup>	no serious inconsistency  p 6-12 months; as no serious inconsistency	serious <sup>3</sup> sessed with serious <sup>3</sup>	serious <sup>10</sup> 1: Number of participants serious <sup>4</sup>	reporting bias <sup>11</sup> articipants admittent one	73  ed into inpatient care du  16/136 (11.8%)	66 12/145 (8.3%) 8%	- RR 1.26 (0.52 to 3.06)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)  21 more per 1000 (from 38 fewer to 165 more)	⊕OOO VERY LOW ⊕OOO VERY LOW	9),
dmissio	randomised trials on as inpatien randomised trials ion (follow-up	serious <sup>7</sup> t (follow-u	no serious inconsistency  p 6-12 months; as no serious inconsistency	serious <sup>3</sup> sessed with	serious <sup>10</sup> 1: Number of participants serious <sup>4</sup> very serious <sup>4</sup>	reporting bias <sup>11</sup> articipants admitte	73  ed into inpatient care du  16/136 (11.8%)  tisfied with their treatme	66  12/145 (8.3%)  8%  ent)	- RR 1.26 (0.52 to 3.06)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)  21 more per 1000 (from 38 fewer to 165 more)  0 fewer per 1000 (from	⊕OOO VERY LOW  ⊕OOO VERY LOW	9),
dmissio	randomised trials on as inpatien randomised trials trials	serious <sup>7</sup> t (follow-u serious <sup>12</sup>	no serious inconsistency  p 6-12 months; as no serious inconsistency	serious <sup>3</sup> sessed with serious <sup>3</sup>	serious <sup>10</sup> 1: Number of participants serious <sup>4</sup>	reporting bias <sup>11</sup> articipants admittent one	73  ed into inpatient care du  16/136 (11.8%)	66 12/145 (8.3%) 8%	- RR 1.26 (0.52 to 3.06)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)  21 more per 1000 (from 38 fewer to 165 more)	⊕OOO VERY LOW  ⊕OOO VERY LOW  ⊕OOO VERY LOW	9),
dmissio	randomised trials on as inpatien randomised trials ion (follow-up	serious <sup>7</sup> t (follow-u serious <sup>12</sup>	no serious inconsistency  p 6-12 months; as no serious inconsistency	serious <sup>3</sup> sessed with serious <sup>3</sup>	serious <sup>10</sup> 1: Number of participants serious <sup>4</sup> very serious <sup>4</sup>	reporting bias <sup>11</sup> articipants admittent one	73  ed into inpatient care du  16/136 (11.8%)  tisfied with their treatme	66  12/145 (8.3%)  8%  ent)	- RR 1.26 (0.52 to 3.06)	SMD 0.15 lower (0.49 lower to 0.19 higher)  22 more per 1000 (from 40 fewer to 170 more)  21 more per 1000 (from 38 fewer to 165 more)  0 fewer per 1000 (from	⊕OOO VERY LOW  ⊕OOO VERY LOW	9),

r	randomised	very	no serious	serious <sup>3</sup>	very serious <sup>9</sup>	none	34	18	-	SMD 0.04 higher (0.53	⊕OOO
t	trials	serious <sup>14</sup>	inconsistency							lower to 0.61 higher)	VERY
											LOW
oal fun	ctioning (12	-months p	ost-admission) (fo	ollow-up mea	an 12 months;	measured with: G	Blobal Assessment Sca	le (GAS; c	hange score)	Better indicated by lov	wer values
r	randomised	very	no serious	serious <sup>3</sup>	serious15	none	33	18	-	SMD 0.12 lower (0.7	⊕000
	t! - 1 -	serious14	inconsistency							lower to 0.45 higher)	VERY
t	trials	0011040									
ial fund	ctioning (4-6	months p	ost-admission) (fo	ollow-up 4-6	months; mea	sured with: Social	Adjustment Scale-Self	Report (S	AS-SR; chanç	ge score)/Social Function	LOW oning Scale
ial fund	ctioning (4-6 ore); Better	months p	by lower values)						AS-SR; chang	, , , , , , , , , , , , , , , , , , ,	oning Scale
ial fund nge sc	ctioning (4-6 ore); Better	months p	no serious	ollow-up 4-6		sured with: Social	Adjustment Scale-Self	F Report (Sa	1	SMD 0.2 lower (0.54	oning Scale
rial fundinge sc	ctioning (4-6 core); Better	months p	by lower values)						1	, , , , , , , , , , , , , , , , , , ,	oning Scale
cial fundange score	ctioning (4-6 core); Better randomised trials ctioning (8-1	s months pindicated serious <sup>7</sup>	no serious inconsistency	serious <sup>3</sup>	serious <sup>15</sup>	reporting bias <sup>11</sup>	74	67	-	SMD 0.2 lower (0.54	⊕OOO VERY LOW
r t tial func- tial func- nge sco	ctioning (4-6 core); Better randomised trials ctioning (8-1	s months pindicated serious <sup>7</sup>	no serious inconsistency post-admission) (	serious <sup>3</sup>	serious <sup>15</sup>	reporting bias <sup>11</sup>	74	67	-	SMD 0.2 lower (0.54 lower to 0.14 higher)	⊕OOO VERY LOW

<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and non-blind participants and intervention administrator(s)

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<sup>&</sup>lt;sup>2</sup> I-squared>50%

<sup>&</sup>lt;sup>3</sup> Non-depression specific population

<sup>&</sup>lt;sup>4</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>5</sup> Data cannot be extracted or is not reported for all outcomes

<sup>&</sup>lt;sup>6</sup> Unclear randomisation method and non-blind participants and intervention administrator(s). Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>&</sup>lt;sup>7</sup> Unclear randomisation method and non-blind participants and intervention administrator(s). Risk of attrition bias is unclear or high (drop-out>20% and ITT analysis not used)

<sup>8</sup> I-squared>80%

<sup>&</sup>lt;sup>9</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (SMD -0.5) and clinically important harm (SMD 0.5)

<sup>10 &</sup>lt;sup>10</sup> N<400

<sup>&</sup>lt;sup>11</sup> Data is not reported for longest follow-up

<sup>12</sup> Unclear randomisation method and method of allocation concealment. Non-blind participants and intervention administrator(s) and unclear blinding of outcome assessment. Unclear risk of attrition bias (drop-out>20%)

<sup>&</sup>lt;sup>13</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>14</sup> Unclear randomisation method and method of allocation concealment. Non-blind participants and intervention administrator(s) and unclear blinding of outcome assessment. High risk of attrition bias as drop-out>20%, difference between groups>20% and completer analysis used

<sup>&</sup>lt;sup>15</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD-0.5)

			Quality ass	essment			No of	oatients		Effect		
											Quality	Importar
No of tudies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Specialist depression service	Usual specialist mental health care	Relative (95% CI)	Absolute		
st to fo	ollow-up (folio	ow-up me	an 18 months; as	sessed with: Nu	mber of part	icipants lost to fo	llow-up by the en	d of the study)				
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	31/93	46/94	RR 0.68	157 fewer per 1000	⊕⊕00	
	trials		inconsistency	indirectness			(33.3%)	(48.9%)	(0.48 to	(from 15 fewer to 254	LOW	
			,				,	,	0.97)	fewer)		
										156 fewer per 1000		
								48.9%		(from 15 fewer to 254		
								101070		fewer)		
	randomised		no serious	serious	very	none	1/93	2/94	RR 0.51	10 fewer per 1000	⊕000	
	trials		inconsistency		serious <sup>4</sup>		(1.1%)	(2.1%)	(0.05 to 5.48)	(from 20 fewer to 95 more)	VERY LOW	
										10 fewer per 1000		
								2.1%		(from 20 fewer to 94 more)		
spons	e (follow-up r	nean 18 n	nonths; assessed	with: Hamilton	Rating Scale	for Depression (	HAM-D) - definitio	n for response no	t reported)			
	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	none	37/93	23/94	RR 1.63	154 more per 1000	⊕⊕00	
	trials		inconsistency	indirectness			(39.8%)	(24.5%)	(1.05 to	(from 12 more to 369	LOW	
									2.51)	more)		
	I									154 more per 1000		
								24.5%		(from 12 more to 370		

	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	none	24/93	12/94	RR 2.02	130 more per 1000	⊕⊕00	
	trials		inconsistency	indirectness			(25.8%)	(12.8%)	(1.08 to 3.8)	(from 10 more to 357	LOW	
										more)		
										·		
										131 more per 1000		
								12.8%		(from 10 more to 358		
										more)		
pression	on symptoma	tology (fo	ollow-up mean 18	months; measi	ured with: Ha	milton Rating Sca	le for Depression	(HAM-D; change	score); Bette	er indicated by lower	values)	
	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>5</sup>	none	93	94	-	SMD 0.62 lower	⊕⊕ОО	
	trials		inconsistency	indirectness						(0.92 to 0.33 lower)	LOW	
		1										
obal fur	nctioning (fo	llow-up m	l lean 18 months; r	neasured with:	 Global Asses	ssment of Functio	ning (GAF; chang	e score); Better in	dicated by lo	ower values)		
obal fui	nctioning (fo	llow-up m	lean 18 months; r	neasured with:	Global Asses	ssment of Functio	ning (GAF; chang	e score); Better in	dicated by lo	ower values)		
	,		nean 18 months; r	neasured with:		none	ning (GAF; chang	e score); Better in	dicated by Id	ower values)  SMD 0.49 higher	⊕⊕00	
	,	serious <sup>3</sup>						"	dicated by Id	,		
	randomised	serious <sup>3</sup>	no serious	no serious				"	dicated by lo	SMD 0.49 higher		
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	93	"	-	SMD 0.49 higher (0.19 to 0.78 higher)		
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	93	94	-	SMD 0.49 higher (0.19 to 0.78 higher)		
ocial fur	randomised trials nctioning (fol	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	93	94	-	SMD 0.49 higher (0.19 to 0.78 higher)	LOW	
ocial fur	randomised trials nctioning (fol	serious <sup>3</sup> low-up m	no serious inconsistency ean 18 months; n	no serious indirectness neasured with: \$	serious <sup>5</sup> Social Adjust	none ment Scale-modif	93	94 ge score); Better i	-	SMD 0.49 higher (0.19 to 0.78 higher)	LOW ⊕⊕OO	

<sup>&</sup>lt;sup>1</sup> Non-blind participants and intervention administrator(s)

## Community mental health teams (CMHTs) versus standard care

			0				No of west out			F# 4		
			Quality asses	sment			No of patients			Effect		
											Quality	Importance
No of		Rick of				Other	Community mental health		Relative			
studies							teams (CMHTs) versus	Control	(95% CI)	Absolute		
Studies		Dias				Considerations	standard care		(30 /8 01)			
Lost to fo	llow-up (follo	w-up mea	an 3 months; asse	essed with: N	umber of pa	rticipants lost to f	follow-up by the end of the st	udy)				
1	randomised	serious1	no serious	serious <sup>2</sup>	very	reporting bias⁴	8/48	7/52	RR 1.24	32 more per 1000		
	trials inconsistency serious s						(16.7%)	(13.5%)	(0.49 to	(from 69 fewer to 291		
									3.16)	more)		

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Non-blind participants and intervention administrator(s). Risk of attrition bias is unclear (drop-out>20% but difference between groups<20% and ITT analysis used) <sup>4</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>5</sup> N<400

	1											
										32 more per 1000	⊕000	
								13.5%		(from 69 fewer to 292	VERY	
								707070		more)	LOW	
										,		
ath (a	II causes) (fol	low-up m	ean 3 months; as	ssessed with	: Number of	participants who di	ed due to any causes dur	ring the stud	y period)			
	randomised	serious <sup>1</sup>	no serious	serious <sup>2</sup>	very	reporting bias4	1/48	2/52	RR 0.54	18 fewer per 1000	⊕000	
	trials		inconsistency		serious <sup>3</sup>		(2.1%)	(3.8%)	(0.05 to	(from 37 fewer to 184	VERY	
									5.78)	more)	LOW	
										18 fewer per 1000		
								3.9%		(from 37 fewer to 186		
										more)		
mptor	n severity (fol	llow-up m	ean 3 months; m	neasured wit	h: Comprehe	nsive Psychopatho	logical Rating Scale (CPF	RS) at endpo	int; Better in	dicated by lower value	es)	
	randomised	serious <sup>1</sup>	no serious	serious <sup>2</sup>	serious <sup>5</sup>	reporting bias⁴	48	52	-	SMD 0.06 lower (0.45	⊕OOO	
	trials		inconsistency							lower to 0.33 higher)	VERY	
											LOW	
missi	on as innatier	nt (follow-	un mean 3 mont	he, accesse	d with: Numb	er of narticinants a	dmitted into innatient car	e during the	study period	4)		
missi			-				dmitted into inpatient care				0000	
dmissi	randomised	serious <sup>1</sup>	no serious	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias4	7/48	16/52	RR 0.47	163 fewer per 1000	⊕000 VEDY	
lmissi			-						RR 0.47 (0.21 to	163 fewer per 1000 (from 243 fewer to 15	VERY	
lmissi	randomised		no serious				7/48	16/52	RR 0.47	163 fewer per 1000		
dmissi	randomised		no serious				7/48	16/52	RR 0.47 (0.21 to	163 fewer per 1000 (from 243 fewer to 15 more) 163 fewer per 1000	VERY	
lmissi	randomised		no serious				7/48	16/52	RR 0.47 (0.21 to	163 fewer per 1000 (from 243 fewer to 15 more)	VERY	
missi	randomised		no serious				7/48	16/52 (30.8%)	RR 0.47 (0.21 to	163 fewer per 1000 (from 243 fewer to 15 more) 163 fewer per 1000	VERY	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48	16/52 (30.8%) 30.8%	RR 0.47 (0.21 to 1.05)	163 fewer per 1000 (from 243 fewer to 15 more) 163 fewer per 1000 (from 243 fewer to 15 more)	VERY LOW	od)
	randomised trials on as inpatier	serious¹	no serious inconsistency	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48 (14.6%)	16/52 (30.8%) 30.8%	RR 0.47 (0.21 to 1.05)	163 fewer per 1000 (from 243 fewer to 15 more) 163 fewer per 1000 (from 243 fewer to 15 more) an 10 days during the	VERY LOW	od)
	randomised trials on as inpatier	serious¹	no serious inconsistency days (follow-up)	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48 (14.6%) rticipants admitted into in	16/52 (30.8%) 30.8%	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more) 163 fewer per 1000 (from 243 fewer to 15 more) an 10 days during the	VERY LOW	od)
	randomised trials  on as inpatier	serious¹	no serious inconsistency days (follow-up inconsistency)	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48 (14.6%) rticipants admitted into in	16/52 (30.8%) 30.8% npatient care	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the	VERY LOW study peri	od)
	randomised trials  on as inpatier	serious¹	no serious inconsistency days (follow-up inconsistency)	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48 (14.6%) rticipants admitted into in	16/52 (30.8%) 30.8% npatient care	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201	VERY LOW study peri	od)
	randomised trials  on as inpatier	serious¹	no serious inconsistency days (follow-up inconsistency)	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48 (14.6%) rticipants admitted into in	16/52 (30.8%) 30.8% npatient care	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201	VERY LOW study peri	od)
	randomised trials  on as inpatier	serious¹	no serious inconsistency days (follow-up inconsistency)	serious <sup>2</sup>	serious <sup>6</sup>	reporting bias <sup>4</sup>	7/48 (14.6%) rticipants admitted into in	16/52 (30.8%) 30.8% npatient care	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201 fewer)	VERY LOW study peri	od)
lmissi	randomised trials  on as inpatier  randomised trials	serious¹  nt for >10  serious¹	no serious inconsistency  days (follow-up inconsistency	serious <sup>2</sup> mean 3 mon  serious <sup>2</sup>	serious <sup>6</sup> ths; assessed serious <sup>7</sup>	reporting bias <sup>4</sup> d with: umber of pa  reporting bias <sup>4</sup>	7/48 (14.6%)  rticipants admitted into in  2/48 (4.2%)	16/52 (30.8%) 30.8% npatient care 11/52 (21.2%)	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201 fewer)  170 fewer per 1000	VERY LOW study peri	od)
lmissi	randomised trials  on as inpatier  randomised trials	serious¹  nt for >10  serious¹	no serious inconsistency  days (follow-up inconsistency	serious <sup>2</sup> mean 3 mon  serious <sup>2</sup>	serious <sup>6</sup> ths; assessed serious <sup>7</sup>	reporting bias <sup>4</sup>	7/48 (14.6%)  rticipants admitted into in  2/48 (4.2%)	16/52 (30.8%) 30.8% npatient care 11/52 (21.2%)	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201 fewer)  170 fewer per 1000 (from 34 fewer to 201 fewer to 201 fewer to 201 fewer)	VERY LOW study peri	od)
dmissi	randomised trials  on as inpatier  randomised trials	serious¹  nt for >10  serious¹	no serious inconsistency  days (follow-up inconsistency	serious <sup>2</sup> mean 3 mon  serious <sup>2</sup>	serious <sup>6</sup> ths; assessed serious <sup>7</sup>	reporting bias <sup>4</sup> d with: umber of pa  reporting bias <sup>4</sup>	7/48 (14.6%)  rticipants admitted into in  2/48 (4.2%)	16/52 (30.8%) 30.8% npatient care 11/52 (21.2%)	RR 0.47 (0.21 to 1.05) for more that	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201 fewer)  170 fewer per 1000 (from 34 fewer to 201 fewer to 201 fewer to 201 fewer)	VERY LOW study peri	od)
dmissi	randomised trials  on as inpatier  randomised trials  tion (follow-up	serious¹  nt for >10  serious¹	no serious inconsistency  days (follow-up inconsistency  no serious inconsistency	serious <sup>2</sup> mean 3 mon  serious <sup>2</sup>	serious <sup>6</sup> ths; assessed serious <sup>7</sup>	reporting bias <sup>4</sup> d with: umber of pa reporting bias <sup>4</sup>	7/48 (14.6%)  rticipants admitted into in  2/48 (4.2%)  n their treatment)	16/52 (30.8%) 30.8% npatient care 11/52 (21.2%) 21.2%	RR 0.47 (0.21 to 1.05) for more that RR 0.2 (0.05 to 0.84)	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201 fewer)  170 fewer per 1000 (from 34 fewer to 201 fewer)	VERY LOW study peri	od)
dmissi	randomised trials  on as inpatier  randomised trials  tion (follow-up	serious¹  nt for >10  serious¹	no serious inconsistency  days (follow-up inconsistency in	serious <sup>2</sup> mean 3 mon  serious <sup>2</sup>	serious <sup>6</sup> ths; assessed serious <sup>7</sup>	reporting bias <sup>4</sup> d with: umber of pa reporting bias <sup>4</sup>	7/48 (14.6%)  rticipants admitted into in  2/48 (4.2%)	16/52 (30.8%) 30.8% npatient care 11/52 (21.2%) 21.2%	RR 0.47 (0.21 to 1.05) for more that RR 0.2 (0.05 to 0.84)	163 fewer per 1000 (from 243 fewer to 15 more)  163 fewer per 1000 (from 243 fewer to 15 more)  an 10 days during the  169 fewer per 1000 (from 34 fewer to 201 fewer)  170 fewer per 1000 (from 34 fewer to 201 fewer)	VERY LOW study peri	od)

								54.4%		288 more per 1000 (from 71 more to 577 more)	⊕000 VERY LOW	
Satisfacti	on (follow-up	mean 3 r	months; measure	d with: Service	e Satisfaction	on Score; Better in	dicated by lower values)					
1	randomised trials		no serious inconsistency	serious <sup>2</sup>	serious <sup>5</sup>	reporting bias <sup>4</sup>	41	46	-	SMD 0.85 higher (0.41 to 1.29 higher)	⊕OOO VERY	
											LOW	

<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and non-blind participants and intervention administrator(s)

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# First-line treatment (chapter 7)

- 10 NMA sub-analysis
- Nortriptyline for depression in older adults
- 12 Nortriptyline versus placebo

		sment		No of patien	nts		Effect					
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nortriptyline versus placebo	Control	Relative (95% CI)	Absolute		
Depression	on symptoma	tology at en	dpoint (measured	with: HAMD; Be	etter indicate	d by lower values	)					
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	53	56	-	MD 6.24 lower (9.17 to 3.3 lower)	⊕⊕OO LOW	CRITICAL
Depression	on symptoma	tology at en	dpoint - milder de	pression (measi	red with: HA	AMD; Better indica	ated by lower value	es)				•

<sup>&</sup>lt;sup>2</sup> Non-depression specific population

<sup>&</sup>lt;sup>3</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>4</sup> Data cannot be extracted for all outcomes (no measure of variance reported)

<sup>5</sup> N<400

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)

<sup>&</sup>lt;sup>7</sup> Events<300

LOW  O to	CRITICAL  CRITICAL  CRITICAL
0 to	CRITICAL
LOW  00	CRITICAL
00	
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Treatment discontinuations due to side effects - more severe depression

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### Pairwise comparisons: Acupuncture

#### Acupuncture versus sham acupuncture

	Quality assessment						No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acupuncture versus sham acupuncture	Control	Relative (95% CI)	Absolute		
Discontin	uation due to	side effe	cts - Mild/modera	te symptom seve	erity (follow-	up 8-12 weeks)						
2	randomised trials			no serious indirectness	very serious²	none	1/53 (1.9%)	0/54 (0%)	RR 3.1 (0.13 to 73.12)	-	⊕000 VERY LOW	
Discontin	uation for an	y reason -	Mild/moderate sy	mptom severity	(follow-up 8	I-12 weeks)					L	L

<sup>&</sup>lt;sup>2</sup> OIS not met (<400 participants)

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

<sup>4</sup> I2 >50% but <80%

<sup>&</sup>lt;sup>5</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>6</sup> OIS not met (<300 events)

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Acupuncture versus fluoxetine

<sup>&</sup>lt;sup>3</sup> Allocation sequence not concealed

<sup>&</sup>lt;sup>4</sup> Events<300

<sup>&</sup>lt;sup>5</sup> I-squared is over 80%

<sup>&</sup>lt;sup>6</sup> 95% CI crosses line of no effect and two clinical decision thresholds (SMD -0.5 and 0.5)

		Quality asse	essment			No of patient	ts		Quality	Importance			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acupuncture versus fluoxetine	Control	Relative (95% CI)	Absolute			
Discontinuation due to side effects - Mild/moderate symptom severity (follow-up mean 6 weeks)													
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/50 (0%)	0/25 (0%)	not pooled	not pooled	⊕⊕OO LOW		
								0%		not pooled			
Discontin	uation for an	y reason -	Mild/moderate sy	mptom severity	(follow-up m	ean 6 weeks)							
1	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	14/50 (28%)	0/25 (0%)	See comment	-	⊕OOO VERY LOW		
								0%		-	LOW		
Response	e - Mild/mode	rate symp	tom severity (follo	w-up mean 6 we	eks; assesse	ed with: HAMD red	uction of at least 50	% from t	he baseline so	ore)			
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	27/36 (75%)	15/25 (60%)	RR 1.25 (0.86 to 1.81)	150 more per 1000 (from 84 fewer to 486 more)	⊕⊕OO LOW		
								60%		150 more per 1000 (from 84 fewer to 486 more)			
Depression values)	on symptoma	tology - M	ild/moderate symp	otom severity (fo	illow-up mea	n 6 weeks; measu	red with: HAMD; end	dpoint so	core; complete	r analysis; Better indic	ated by lo	ower	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	36	25	-	MD 2.45 lower (4.39 to 0.51 lower)	⊕⊕OO LOW		

<sup>&</sup>lt;sup>1</sup> No attempt at blinding and high risk of attrition bias

# Acupuncture + SSRI versus SSRI

Quality assessment	No of patients	Effect	Quality Importance

<sup>&</sup>lt;sup>2</sup> Events<300

 <sup>&</sup>lt;sup>3</sup> 95% CI crosses a clinical decision threshold (RR 1.25) and events<300</li>
 <sup>4</sup> 95% CI crosses clinical decision threshold (SMD -0.5) and N<400</li>

No of studies	Design	Risk of bias	Inconsistency		<b>Imprecision</b>	considerations	Acupuncture + SSRI (fluoxetine/paroxetine) versus SSRI (fluoxetine/paroxetine)	Control	Relative (95% CI)	Absolute	
isconti	nuation due	to side ef	fects - Moderate	severe sympto	om severity (f	ollow-up mean 6	weeks)				
•	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	6/160 (3.8%)	4/95 (4.2%)	RR 0.95 (0.25 to 3.71)	2 fewer per 1000 (from 32 fewer to 114 more)	⊕OOO VERY LOW
								4.2%		2 fewer per 1000 (from 32 fewer to 114 more)	
isconti	nuation for a	ny reaso	n - Moderate/sev	ere symptom s	everity (follo	w-up mean 6 wee	ks)				
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	14/160 (8.8%)	8/95 (8.4%)	RR 0.92 (0.39 to 2.17)	7 fewer per 1000 (from 51 fewer to 99 more)	⊕OOO VERY LOW
								8.4%		7 fewer per 1000 (from 51 fewer to 98 more)	
Remissi	on - Moderate	e/severe	symptom severit	y (follow-up m	ean 6 weeks;	assessed with: H	IAMD endpoint score of 7 or below	<b>'</b> )			
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	28/109 (25.7%)	11/48 (22.9%)	RR 1.12 (0.61 to 2.06)	28 more per 1000 (from 89 fewer to 243 more)	⊕OOO VERY LOW
								22.9%		27 more per 1000 (from 89 fewer to 243 more)	
Respons	se - Moderate	/severe s	symptom severity	/ (follow-up me	ean 6 weeks;	assessed with: H	AMD reduction of at least 50% from	n the base	eline score	)	
	randomised trials	serious <sup>1</sup>	serious <sup>4</sup>	no serious indirectness	serious <sup>5</sup>	none	102/157 (65%)	43/95 (45.3%)	RR 1.37 (0.91 to 2.06)	167 more per 1000 (from 41 fewer to 480 more)	⊕000 VERY LOW
								45.3%		168 more per 1000 (from 41	

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#### Acupuncture + fluoxetine versus sham acupuncture + fluoxetine

			Quality asso	essment			No of patients			Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acupuncture + fluoxetine versus sham acupuncture + fluoxetine	Control	Relative (95% CI)	Absolute		
Discontin	nuation due to	side effe	ects - Mild/modera	ate symptom se	verity (follow	/-up mean 3 week	s)				•	
	randomised trials	serious <sup>1</sup>		no serious indirectness	very serious <sup>2</sup>	none	5/38 (13.2%)	2/35 (5.7%)	RR 2.3 (0.48 to 11.11)	74 more per 1000 (from 30 fewer to 578 more) 74 more per 1000 (from 30 fewer to 576 more)	⊕OOO VERY LOW	
Discontin	nuation for an	y reason	- Mild/moderate s	symptom severi	ty (follow-up	mean 3 weeks)					1	
1	randomised trials	serious <sup>1</sup>		no serious indirectness	very serious <sup>2</sup>	none	6/38 (15.8%)	3/35 (8.6%)	RR 1.84 (0.5 to 6.81)	72 more per 1000 (from 43 fewer to 498 more)		

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and both clinical decision thresholds (RR 0.8 and 1.25) and events<300

<sup>&</sup>lt;sup>3</sup> No attempt at blinding participants or personnel

<sup>&</sup>lt;sup>4</sup> I-squared is over 50%

<sup>&</sup>lt;sup>5</sup> 95% CI crosses both line of no effect and clinical decision threshold (RR 1.25) and events<300

<sup>&</sup>lt;sup>6</sup> 95% CI crosses clinical decision threshold (SMD -0.5) and N<400

# 6 Acupuncture + TAU versus TAU

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			Quality asse	essment			No of patients	5		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acupuncture + TAU versus TAU	Control	Relative (95% CI)	Absolute		
Discontin	uation due to	side effec	cts - Mild/moderate	e symptom sevel	rity (follow-u	p mean 13 weeks)						
1	randomised	serious <sup>1</sup>	no serious	no serious	very	none	7/302	3/151	RR 1.17	3 more per 1000 (from	$\oplus$ OOO	
	trials		inconsistency	indirectness	serious <sup>2</sup>		(2.3%)	(2%)	(0.31 to 4.45)	14 fewer to 69 more)	VERY	
											LOW	
								2%		3 more per 1000 (from		
								Z 70		14 fewer to 69 more)		
Discontin	uation for an	y reason -	Mild/moderate sy	mptom severity (	follow-up me	ean 13 weeks)						
1	randomised	serious1	no serious	no serious	very	none	53/302	21/151	RR 1.26	36 more per 1000 (from	⊕000	
	trials		inconsistency	indirectness	serious <sup>2</sup>		(17.5%)	(13.9%)	(0.79 to 2.01)	29 fewer to 140 more)	VERY	
			-							·	LOW	
								12.00/		36 more per 1000 (from		
								13.9%		29 fewer to 140 more)		
Depression	on symptoma	tology - M	ild/moderate symp	otom severity (fo	llow-up mea	n 13 weeks; meas	ured with: PHQ-9; end	dpoint s	core; complet	er analysis; Better indi	cated by	lower

<sup>&</sup>lt;sup>1</sup> Method of randomisation not reported and significant difference between groups at baseline in proportion of females (69.4% in intervention relative to 97.1% in control). Allocation concealment method is also not reported. Personnel also non-blind and blinding of outcome assessor not reported

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and both clinical decision thresholds (RR 0.8 and 1.25) and events<300

<sup>&</sup>lt;sup>3</sup> 95% CI crosses clinical decision threshold (SMD -0.5) and N<400

1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	249	128	-	MD 3.3 lower (4.67 to	⊕⊕00	
	trials		inconsistency	indirectness						1.93 lower)	LOW	

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# Acupuncture + TAU versus counselling + TAU

			Quality as	sessment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acupuncture + TAU versus Counselling + TAU	Control	Relative (95% CI)	Absolute		
Discontin	uation due to	side effe	ects - Mild/moder	ate symptom se	verity (follow-u	p mean 13 weeks	)					
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	7/302 (2.3%)	2/302 (0.7%)	RR 3.5 (0.73 to 16.71)	17 more per 1000 (from 2 fewer to 104 more)	⊕000 VERY LOW	
								0.7%		18 more per 1000 (from 2 fewer to 110 more)		
Discontin	uation for an	y reason	- Mild/moderate s	symptom severi	ty (follow-up m	ean 13 weeks)						
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	53/302 (17.5%)	65/302 (21.5%)	RR 0.82 (0.59 to 1.13)	39 fewer per 1000 (from 88 fewer to 28 more) 39 fewer per 1000 (from 88 fewer to 28		
Depression values)	on symptoma	atology - I	Mild/moderate sy	mptom severity	(follow-up mea	ın 13 weeks; meas	sured with: PHQ-9; endp		ore; complet	more)		lower
	randomised trials		no serious inconsistency	no serious indirectness	no serious imprecision	none	249	237	-	MD 1.5 lower (2.64 to 0.36 lower)	⊕⊕⊕O MODERATE	

<sup>&</sup>lt;sup>1</sup> No attempts at blinding
<sup>2</sup> 95% CI crosses line of no effect and both clinical decision thresholds (RR 0.8 and 1,25)
<sup>3</sup> 95% CI crosses clinical decision threshold (SMD -0.5) and N<400

No attempts at blinding
 95% CI crosses line of no effect and both clinical decision thresholds (RR 0.8 and 1.25)
 95% CI crosses both line of no effect and clinical decision threshold (RR 0.8)

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Pairwise comparisons: Behavioural couples therapy

Behavioural couples therapy versus CBT

			Quality asso	essment			No of patients			Effect	Quality	Importance		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Behavioural couples therapy versus CBT	Control	Relative (95% CI)	Absolute				
Depression	Depression symptomatology at endpoint (across severity) (follow-up 10-78 weeks; measured with: BDI/HAMD; Better indicated by lower values)													
4		very serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	serious <sup>3</sup>	none	67	68	-	SMD 0.03 higher (0.49 lower to 0.54 higher)	⊕000 VERY LOW	CRITICAL		
Treatmen	t discontinua	tion rates	(more severe dep	ression) (follow	-up mean 15	weeks; assessed	with: Number of partic	ipants d	iscontinuing t	for any reason)				
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	3/12 (25%)	3/12 (25%)	,	0 fewer per 1000 (from 188 fewer to 750 more)	⊕OOO VERY LOW			
								25%		0 fewer per 1000 (from 188 fewer to 750 more)				
Depression	on symptoma	tology at	endpoint (milder o	depression) (follo	ow-up 16-78	weeks; measured	with: BDI/HAMD; Bette	r indica	ted by lower v	ralues)				
3		very serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	very serious <sup>4</sup>	none	52	53	-	SMD 0.14 higher (0.49 lower to 0.78 higher)	⊕OOO VERY LOW	CRITICAL		
Depression	on symptoma	tology at	endpoint (more se	evere depression	n) (follow-up	mean 10 weeks; n	neasured with: BDI; Be	tter indi	cated by lowe	r values)				
1		- ,	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	15	15	-	SMD 0.34 lower (1.07 lower to 0.38 higher)	⊕OOO VERY LOW	CRITICAL		
Remissio	n (assessed v	with: BDI<	:10)											

1	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	13/19 (68.4%)	16/19 (84.2%)	RR 0.81 (0.57 to 1.17)	160 fewer per 1000 (from 362 fewer to 143 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Treatme	nt discontinua	tion rates	(across severity)	(follow-up 15-78	weeks; ass	essed with: Number	er of participants disc	ontinuino	for any reas	on)		
4	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	20/72 (27.8%)	9/70 (12.9%)	RR 1.97 (0.98 to 3.98)	125 more per 1000 (from 3 fewer to 383 more)	⊕⊕OO LOW	
								15.5%		150 more per 1000 (from 3 fewer to 462 more)		
Treatme	nt discontinua	tion rates	(milder depressi	on) (follow-up 16	5-78 weeks; a	ssessed with: Nur	nber of participants di	scontinu	ing for any re	ason)		
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	17/60 (28.3%)	6/58 (10.3%)	RR 2.49 (1.11 to 5.61)	154 more per 1000 (from 11 more to 477 more)	⊕⊕OO LOW	
								14.3%		213 more per 1000 (from 16 more to 659 more)		

<sup>&</sup>lt;sup>1</sup> High or unclear ROB in most domains

# Behavioural couples therapy versus waitlist

			Quality asse	essment			No of patients			Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Behavioural couples therapy versus waitlist control	Control	Relative (95% CI)	Absolute	_	
Depression	Depression symptomatology at endpoint (more severe depression) (follow-up mean 10 weeks; measured with: BDI; Better indicated by lower values)											

<sup>1</sup> 2 3 4 5 <sup>2</sup> I2 <80% but >50%

<sup>&</sup>lt;sup>3</sup> 95% confidence interval crosses one clinical decision threshold

<sup>&</sup>lt;sup>4</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>5</sup> Events<300

1	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	15	15	-	MD 12.07 lower (18.32 to 5.82 lower)	⊕OOO VERY LOW	CRITICAL		
Treatmen	eatment discontinuation rates (more severe depression) (follow-up mean 15 weeks; assessed with: Number of participants discontinuing for any reason)													
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	3/12 (25%)	0/12 (0%)	RR 7 (0.4 to 122.44)	-	⊕OOO VERY LOW			

<sup>&</sup>lt;sup>1</sup> High or unclear ROB in most domains

### Behavioural couples therapy versus interpersonal psychotherapy

			Quality asse	essment			No of patients			Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Behavioural couples therapy versus IPT	Control	(95% CI)			
Depression	on symptoma	tology at	endpoint (milder d	epression) (follo	w-up mean 7	'8 weeks; measure	ed with: BDI; Better indi	cated by	/ lower value	es)		
1	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	20	20	-	MD 1.56 higher (5.07 lower to 8.19 higher)	⊕OOO VERY LOW	
Treatmen	t discontinua	tion rates	(milder depressio	n) (follow-up me	an 78 weeks	; assessed with: N	umber of participants of	liscontir	nuing for any	reason)		
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious⁴	none	2/20 (10%)	2/20 (10%)	RR 1 (0.16 to 6.42)	0 fewer per 1000 (from 84 fewer to 542 more)	⊕OOO VERY LOW	
								10%		0 fewer per 1000 (from 84 fewer to 542 more)		

<sup>&</sup>lt;sup>1</sup> High or unclear ROB in most domains

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#### Behavioural couples therapy (BCT) versus combined BCT and CBT (individual) 9

<sup>&</sup>lt;sup>2</sup> OIS not met (<400 participants)

<sup>2</sup> 3 <sup>3</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>3</sup> Data not reported for all outcomes

<sup>&</sup>lt;sup>4</sup> 95% CI crosses two clinical decision thresholds

			Quality ass	essment			No of patients  Behavioural couples therapy		Effect			Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Behavioural couples therapy versus combined BCT and CBT (individual CBT for the depressed wife)	Control	Relative (95% CI)	Absolute	Quality	importance
Depressi	ion symptomatology at endpoint (milder depression) (measured with: HAMD						r indicated by lower values)					
		- ,	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	19	21	-	MD 4.12 higher (0.66 lower to 8.9 higher)	⊕OOO VERY LOW	
Remissio	on (milder de	pression	) (assessed with:	BDI<10)	!			•				
			no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	13/19 (68.4%)	12/21 (57.1%)		114 more per 1000 (from 149 fewer to 537 more)	⊕OOO VERY LOW	
								57.1%		114 more per 1000 (from 148 fewer to 537 more)		
Treatmer	nt discontinu	ation rate	es (milder depres	sion) (assesse	d with: Num	ber of participant	s discontinuing for any reason)					
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	8/27 (29.6%)	0/21 (0%)	RR 13.36 (0.81 to 218.99)	-	⊕⊕OO LOW	
								0%		-		

## Pairwise comparisons: Omega-3 fatty acids

#### Omega-3 fatty acids versus placebo 5

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Quality assessment	No of patients	Effect	Quality	Importance	
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<sup>&</sup>lt;sup>1</sup> High or unclear ROB in most domains <sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>3</sup> 95% CI crosses two clinical decision thresholds

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Omega-3 fatty acids versus placebo	Control	Relative (95% CI)	Absolute		
Remissio	n (milder dep	ression) (foll	ow-up 3-8 weeks;	assessed with:	BDI=>10 or F	IAMD <=7 at endp	oint)	1				
2		no serious risk of bias	serious <sup>1</sup>	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	44/143 (30.8%)	21/74 (28.4%)	RR 1.43 (0.48 to 4.29)	122 more per 1000 (from 148 fewer to 934 more)	⊕OOO VERY LOW	
								25.7%		111 more per 1000 (from 134 fewer to 846 more)		
Response	e (milder depr	ession) (follo	ow-up mean 8 wee	eks; assessed w	ith: HAMD re	duced by >50% at	endpoint)					
1		no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	52/131 (39.7%)	28/65 (43.1%)		34 fewer per 1000 (from 151 fewer to 134 more)	⊕OOO VERY LOW	
								43.1%		34 fewer per 1000 (from 151 fewer to 134 more)		
Treatmen	t discontinua	tion (milder	depression) (follow	w-up 3-8 weeks;	assessed wi	th: Number of part	icipants discontin	uing for	any reason)			
2		no serious risk of bias	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	16/144 (11.1%)	13/75 (17.3%)	RR 0.63 (0.32 to 1.24)	64 fewer per 1000 (from 118 fewer to 42 more)	⊕⊕OO LOW	
								14.2%		53 fewer per 1000 (from 97 fewer to 34 more)		
Discontin	uation due to	side effects	(milder depression	on) (follow-up me	ean 8 weeks;	assessed with: No	umber of participa	nts disco	ntinuing due	to side effects)	<u> </u>	
1		no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	1/131 (0.8%)	0/65 (0%)	RR 1.5 (0.06 to 36.32)	-	⊕OOO VERY LOW	
								0%		-		

<sup>&</sup>lt;sup>1</sup> I-squared >50%

### Omega-3 fatty acids plus SSRI/antidepressant versus placebo plus SSRI/antidepressant

Quality assessment	No of patients	Effect	Quality	Importance	
					1

<sup>&</sup>lt;sup>2</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>3</sup> Data not reported for all outcomes

<sup>&</sup>lt;sup>4</sup> 95% CI crosses one clinical decision threshold

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Omega-3 fatty acids + SSRI/antidepressants versus placebo + SSRI/antidepressants	Control	Relative (95% CI)	Absolute		
Remissio	on (more sev	ere depres	sion) (follow-up	mean 8 weeks;	assessed w	rith: HAMD <=7 at	t endpoint)					
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	8/18 (44.4%)	4/22 (18.2%)	RR 2.44 (0.88 to 6.82)	262 more per 1000 (from 22 fewer to 1000 more)	⊕OOO VERY LOW	
								18.2%		262 more per 1000 (from 22 fewer to 1000 more)		
Respons	e (more seve	ere depress	sion) (follow-up i	mean 8 weeks;	assessed wi	th: HAMD reduce	ed by >50% at endpoint)					
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	13/16 (81.3%)	8/16 (50%)	RR 1.62 (0.94 to 2.8)	310 more per 1000 (from 30 fewer to 900 more)	⊕OOO VERY LOW	
								50%		310 more per 1000 (from 30 fewer to 900 more)		
Treatmer	nt discontinu	ation (acro	ss severity) (foll	low-up 8-12 we	eks; assesse	ed with: Number	of participants discontinuing for an	ny reasor	)			
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	13/58 (22.4%)	16/59 (27.1%)	RR 0.85 (0.44 to 1.63)	41 fewer per 1000 (from 152 fewer to 171 more)	⊕OOO VERY LOW	
								29.4%		44 fewer per 1000 (from 165 fewer to 185 more)		
Treatmer	nt discontinu	ation (mild	er depression) (	follow-up mear	12 weeks; a	assessed with: N	umber of participants discontinuin	g for any	reason)			
		no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	6/18 (33.3%)	5/17 (29.4%)	RR 1.13 (0.42 to 3.03)	38 more per 1000 (from 171 fewer to 597 more)		

								29.4%		38 more per 1000 (from 171 fewer to 597 more)	⊕OOO VERY LOW	
Treatme	nt discontinu	iation (mor	e severe depres	sion) (follow-up	mean 8 wee	eks; assessed wi	th: Number of participants disconti	nuing fo	r any reaso	on)		
2	randomised trials	serious <sup>1</sup>		no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	7/40 (17.5%)	11/42 (26.2%)	RR 0.68 (0.29 to 1.62)	84 fewer per 1000 (from 186 fewer to 162 more)	⊕OOO VERY LOW	
Di di								25.9%		83 fewer per 1000 (from 184 fewer to 161 more)		
Disconti	nuation due	to side effe	ects (more severe	e depression) (	follow-up me	ean 8 weeks; asso	essed with: Number of participants	disconti	nuing due	to side effects)		
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	2/40 (5%)	1/42 (2.4%)		24 more per 1000 (from 19 fewer to 460 more)		
								2.5%		25 more per 1000 (from 20 fewer to 483 more)		

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# Pairwise comparisons: Psychosocial interventions (peer support)

### Peer support versus waitlist

			Quality asses	ssment			No of patients			Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peer support group versus waitlist	Control	Relative (95% CI)	Absolute	<b></b>	
Depression	n symptoms a	t endpoint	(milder depression	) (follow-up mear	4 weeks; me	easured with: BDI;	Better indicated by lo	wer valu	ies)			

<sup>&</sup>lt;sup>1</sup> High or unclear risk in multiple ROB domains <sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>3</sup> Data not reported for all outcomes

<sup>&</sup>lt;sup>4</sup> Unclear risk across multiple ROB domains

<sup>&</sup>lt;sup>5</sup> 95% CI crosses two clinical decision thresholds

			no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	19	67	-	MD 7.09 lower (9.77 to 4.41 lower)	⊕000 VERY	
	liiais	Serious	linconsistency	liturectress						to 4.41 lower)	LOW	

<sup>&</sup>lt;sup>1</sup> Unclear allocation concealment and non-blind participants, intervention administrators and outcome assessment

### 4 Peer support (online support group) versus attention-placebo control

			Quality asse	ssment			No of patients Effect  Peer support (online Balatice				Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peer support (online support group) versus attention control	Control	(95% CI)			
Treatmen	t discontinua	ition (milder	depression) (foll	ow-up mean 12	weeks; asse	ssed with: Numbe	r of participants who disc	ontinued	for any reas	son)		
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>1</sup>	reporting bias <sup>2</sup>	36/89 (40.4%)	11/82 (13.4%)	RR 3.02 (1.65 to 5.52)	271 more per 1000 (from 87 more to 606 more)	⊕⊕OO LOW	
								13.4%		271 more per 1000 (from 87 more to 606 more)		

<sup>&</sup>lt;sup>1</sup> Events<300

#### 7 Peer support group versus CBT group

			Quality asse	ssment			No of patients	•		Effect	Quality	Importance
No of studies	Design	Indirectness	Other considerations	Peer support group versus CBT group	Control	Relative (95% CI)	Absolute	quanty	importanie			
Depressio	n symptoms a	t endpoint	(milder depressio	n) (follow-up mea	an 4 weeks; r	neasured with: BD	l; Better indicated by I	ower va	lues)			

<sup>2</sup> N<400

<sup>3</sup> Data is not reported or cannot be extracted for all outcomes

<sup>&</sup>lt;sup>2</sup> Data is not reported or cannot be extracted for all outcomes

1	randomised	very	no serious	no serious	serious <sup>2</sup>	reporting bias3	19	50	-	MD 1.72 lower (4.8	⊕000	
	trials	serious <sup>1</sup>	inconsistency	indirectness						lower to 1.36 higher)	VERY	
											LOW	ļ

<sup>&</sup>lt;sup>1</sup> Unclear allocation concealment and non-blind participants, intervention administrators and outcome assessment

#### Peer support group versus self-help (without support)

			Quality asse	essment			No of patients			Effect	Quality	Importance
No of studies	studies Design bias		Inconsistency	Indirectness	Imprecision	Other considerations	Peer support group versus self-help (without support)		Relative (95% CI)	Absolute		
Depression	on symptoms	at endpoir	nt (milder depress	ion) (follow-up m	nean 4 weeks	; measured with:	BDI; Better indicated by lov	ver value	es)			
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	19	28	-	MD 2.87 lower (6.53 lower to 0.79 higher)	⊕OOO VERY LOW	

<sup>&</sup>lt;sup>1</sup> Unclear allocation concealment and non-blind participants, intervention administrators and outcome assessment

### Light therapy

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### Is bright light effective for depression with a seasonal pattern/SAD compared with waitlist control?

			Quality assess	sment					Summary	of findings		
				<del></del>			No of p	atients		Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	Waitlist	Relative (95% CI)	Absolute	Quality	
Leaving stu	ıdy early for an	y reason (overall)	(total number not	completing study)								

<sup>&</sup>lt;sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>2</sup> 3 <sup>3</sup> Data is not reported or cannot be extracted for all outcomes

<sup>&</sup>lt;sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>3</sup> Data is not reported or cannot be extracted for all outcomes

2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	3/42 (7.1%)	3/40 (7.5%) 8.7%	RR 0.95 (0.21 to 4.32)	0 fewer per 100 (from 6 fewer to 25 more)  0 fewer per 100 (from 7 fewer to 29 more)	⊕⊕OO LOW
Leaving st	udy early due to	o side effects - Lig	ht box vs waitlist co	ontrol							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/16 (0%)	0/15 (0%)	not pooled	not pooled	⊕⊕⊕O MODERATE
Leaving stu	udy early - Ligh	t room vs waitlist	control			l.		070		not pooled	
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	1/26 (3.8%)	1/25 (4%)	RR 0.96 (0.06 to 14.55)	0 fewer per 100 (from 4 fewer to 54 more)	⊕⊕⊕O MODERATE
								0%		0 fewer per 100 (from 0 fewer to 0 more)	
Mean self	rated SAD depi	ression scores at o	endpoint - Light roo	m vs waitlist contro	ol (measured with	: SIGH-SAD-SR; Bet	ter indicate	d by lower v	/alues)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	24	24	H	MD 12.8 lower (18.52 to 7.08 lower)	⊕⊕⊕O MODERATE
Mean clini	cian rated SAD	depression score	s at endpoint - Ligh	t box vs waitlist co	ntrol (measured w	rith: SIGH-SAD; Beti	ter indicated	d by lower v	alues)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	16	15	H	MD 10.4 lower (15.99 to 4.81 lower)	⊕⊕⊕O MODERATE
Mean clini	cian rated typic	cal depression sco	ores at endpoint - Li	ght box vs waitlist	control (measured	with: HRSD-21; Be	tter indicat	ed by lower	values)		,
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	16	15	H	MD 6.3 lower (10.34 to 2.26 lower)	⊕⊕⊕⊕ HIGH
Mean self-	rated depression	on score - overall	(Better indicated by	/ lower values)							
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	40	39	H	MD 1.15 lower (1.63 to 0.67 lower)	⊕⊕⊕⊕ HIGH
Mean self	rated depression	on scores at endp	oint - Light room vs	waitlist control (m	easured with: HRS	SD-21-SR; Better inc	dicated by lo	ower values	)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	24	24	H	MD 7.7 lower (11.58 to 3.82 lower)	⊕⊕⊕O MODERATE

Mean self	rated depression	on scores at endp	oint - Light box vs w	aitlist control (mea	asured with: BDI; I	Better indicated by	lower value	s)			
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	16	15	I	MD 10.9 lower (16.99 to 4.81 lower)	⊕⊕⊕O MODERATE
1ean clini	cian rated atyp	ical depression so	cores at endpoint - L	ight box vs waitlist	t control (measure	d with: SAD subsca	ile; Better in	dicated by	lower values)		
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	16	15	I	MD 4 lower (6.73 to 1.27 lower)	⊕⊕⊕O MODERATE
lean self	rated atypical o	depression scores	at endpoint - Light	room vs waitlist co	introl (measured v	vith: SAD-SR subsca	ale of SIGH-S	AD); Bette	er indicated by lov	ver values)	
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	24	24	ł	MD 5.2 lower (7.39 to 3.01 lower)	⊕⊕⊕O MODERATE
on remis	sion (SIGH-SAD	-SR) (overall)	-			<u> </u>					<b>!</b>
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/42 (47.6%)	36/40 (90%)	RR 0.53 (0.38 to 0.74)	42 fewer per 100 (from 23 fewer to 56 fewer)	⊕⊕⊕⊕ HIGH
lon vomic	sion (SICII SAD	CD) Light voom	ve vesitlist control					88%		41 fewer per 100 (from 23 fewer to 55 fewer)	
on remis	sion (SiGH-SAD	-SK) - Light room	vs waitlist control								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	12/26 (46.2%)	24/25 (96%)	RR 0.48 (0.31 to 0.73)	50 fewer per 100 (from 26 fewer to 66 fewer)	⊕⊕⊕O MODERATE
								96%		50 fewer per 100 (from 26 fewer to 66 fewer)	
on remis	sion (SIGH-SAD	-SR) - Light box v	s waitlist control								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	8/16 (50%)	12/15 (80%)	RR 0.62 (0.36 to 1.08)	30 fewer per 100 (from 51 fewer to 6 more)	⊕⊕⊕O MODERATE
								80%		30 fewer per 100 (from 51 fewer to 6 more)	
on respo	nse (SIGH-SAD)	- Light room vs v	vaitlist control								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	13/26 (50%)	25/25 (100%)	RR 0.50 (0.34 to 0.73)	50 fewer per 100 (from 27 fewer to 66 fewer)	⊕⊕⊕O MODERATE
								100%		50 fewer per 100 (from 27 fewer to 66 fewer)	

<sup>1</sup> Inconclusive effect size<sup>2</sup> Single study

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#### Is bright light effective for depression with a seasonal pattern/SAD compared with attentional control? 3

			Quality asses	sment					Summary of	findings		
							No o	f patients		Effect	- "	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	Attentional control	Relative (95% CI)	Absolute	Quality	
Leaving st	udy early for a	ny reason (overa	II)				<b>'</b>					•
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	18/134 (13.4%)	18/124 (14.5%)	RR 0.92 (0.51 to 1.64)	1 fewer per 100 (from 7 fewer to 9 more)	⊕⊕OO LOW	
								13.1%		1 fewer per 100 (from 6 fewer to 8 more)		
Leaving st	udy early for a	ny reason - Light	box vs deactivated	negative ion gene	rator							
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	8/41 (19.5%)	9/40 (22.5%)	RR 0.87 (0.37 to 2.02)	3 fewer per 100 (from 14 fewer to 23 more)	⊕⊕OO LOW	
								22.5%		3 fewer per 100 (from 14 fewer to 23 more)		
Leaving st	udy early for ar	ny reason - Low (	dose (<5000lux hou	rs/day) LED light v	rs negative ion ger	nerator						
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	1/15 (6.7%)	2/11 (18.2%)	RR 0.37 (0.04 to 3.55)	11 fewer per 100 (from 17 fewer to 46 more)	⊕⊕OO LOW	
								18.2%		11 fewer per 100 (from 17 fewer to 46 more)		
Leaving st	udy early for a	ny reason - Light	box vs high dose (>	300lux) dim red li	ght box							
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	6/33 (18.2%)	5/26 (19.2%)	RR 0.95 (0.32 to 2.76)	1 fewer per 100 (from 13 fewer to 34 more)	⊕⊕OO LOW	
								19.2%		1 fewer per 100 (from 13 fewer to 34 more)		
Leaving st	udy early for ar	ny reason - Light	box vs low-density	ionisation								

1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	2/23 (8.7%)	2/25 (8%)	RR 1.09 (0.17 to 7.1)	1 more per 100 (from 7 fewer to 49 more)	⊕⊕OO LOW	
								8%		1 more per 100 (from 7 fewer to 49 more)		
Leaving st	udy early for ar	ny reason - Low d	lose (<5000lux hou	rs/day) light box v	s no light box							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious²	none	1/10 (10%)	0/12 (0%)	RR 3.55 (0.16 to 78.56)	0 more per 100 (from 0 fewer to 0 more)	⊕⊕OO LOW	
								0%		0 more per 100 (from 0 fewer to 0 more)		
Leaving st	udy early for ar	ny reason - Low d	lose (<5000lux hou	rs/day) light visor	vs no light visor							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	0/12 (0%)	0/10 (0%)	not pooled	not pooled	⊕⊕⊕O MODERATE	
								0%		not pooled		
Leaving st	udy early due t	o lack of efficacy	- Low dose (<5000)	ux hours/day) LED	light vs negative	ion generator						
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	0/15 (0%)	1/11 (9.1%)	RR 0.25 (0.01 to 5.62)	7 fewer per 100 (from 9 fewer to 42 more)	⊕⊕OO LOW	
								9.1%	, , , , , , , , , , , , , , , , , , , ,	7 fewer per 100 (from 9 fewer to 42 more)		
Reported	side effects (ov	erall)	1				ļ				ļ <u> </u>	
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	25/45 (55.6%)	21/36 (58.3%)	RR 0.98 (0.73 to 1.32)	1 fewer per 100 (from 16 fewer to 19 more)	⊕⊕OO LOW	
								44.6%		1 fewer per 100 (from 12 fewer to 14 more)		
Reported	side effects - Lo	w dose (<5000lu	x hours/day) LED li	ght vs negative ior	generator	<b>'</b>			•		·	
1	randomised	no serious	no serious	no serious	serious <sup>2</sup>	none		4 /44 /0 45()		4 more per 100 (from 8		
	trials	limitations	inconsistency	indirectness			2/15 (13.3%)	1/11 (9.1%)	RR 1.47 (0.15 to 14.21)	fewer to 120 more)	⊕⊕⊕O MODERATE	
								9.1%		4 more per 100 (from 8 fewer to 120 more)		
Reported	side effects - Li	ght visor vs dim l	ight visor									
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious	none	23/30 (76.7%)	20/25 (80%)	RR 0.96 (0.73 to 1.27)	3 fewer per 100 (from 22 fewer to 22 more)		
	1	1	L	1	1	1	1		1	l .	l	

								80%		3 fewer per 100 (from 22 fewer to 22 more)	⊕⊕OO LOW
Mean clin	ician rated SAD	depression scor	es at endpoint (ove	rall) (measured wi	ith: SIGH-SAD; Be	tter indicated by lo	wer values)				
6	randomised trials	no serious limitations	serious³	no serious indirectness	serious¹	none	139	131	ŀ	MD 2.78 lower (6.81 lower to 1.26 higher)	⊕⊕OO LOW
Mean clin	ician rated SAD	depression scor	es at endpoint - Lov	v dose (<5000lux h	nours/day) LED lig	ht vs negative ion a	generator (n	neasured with: S	SIGH-SAD; Bette	r indicated by lower values	
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	14	9	ł	MD 4.7 lower (10.34 lower to 0.94 higher)	⊕⊕⊕O MODERATE
Mean clin	ician rated SAD	depression scor	es at endpoint - Ligl	nt visor vs dim ligh	nt visor (measured	with: SIGH-SAD; B	etter indica	ted by lower val	ues)		
2	randomised trials	no serious limitations	serious¹	no serious indirectness	serious <sup>3</sup>	none	64	58	ŀ	MD 0.86 higher (7.56 lower to 9.29 higher)	⊕⊕OO LOW
Mean clin	ician rated SAD	depression scor	es at endpoint - Ligl	nt box vs low-dens	sity ionisation (me	easured with: SIGH	-SAD; Better	indicated by lo	wer values)		
2	randomised trials	no serious limitations	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	40	42	ł	MD 8.56 lower (14.73 to 2.39 lower)	⊕⊕⊕O MODERATE
Mean clin	ician rated SAD	depression scor	es at endpoint - Lov	v dose (<5000lux h	nours/day) light b	ox vs no light box (	measured w	ith: SIGH-SAD; E	Better indicated	by lower values)	<u> </u>
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	9	12	ł	MD 1.4 higher (4.93 lower to 7.73 higher)	⊕⊕OO LOW
Mean clin	ician rated SAD	depression scor	es at endpoint - Lov	v dose (<5000lux h	nours/day) light vi	isor vs no light viso	r (measured	with: SIGH-SAD	); Better indicato	ed by lower values)	<u> </u>
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	12	10	ł	MD 0.2 lower (6.22 lower to 5.82 higher)	⊕⊕OO LOW
Mean clin	ician rated typi	cal depression so	cores at endpoint (n	neasured with: HA	MD-17/HRSD-21;	Better indicated b	y lower valu	es)	l .		<b>!</b>
5	randomised trials	no serious limitations	serious¹	no serious indirectness	serious¹	none	106	103	ł	SMD 0.07 lower (0.51 lower to 0.37 higher)	⊕⊕OO LOW
Mean clin	ician rated typi	cal depression so	cores at endpoint - I	ight visor vs dim l	ight visor (measu	red with: HAMD-17	//HRSD-21; I	Better indicated	by lower values	;)	<b>!</b>
2	randomised trials	no serious limitations	serious <sup>3</sup>	no serious indirectness	serious <sup>4</sup>	none	64	58	ł	SMD 0.05 higher (0.52 lower to 0.63 higher)	⊕⊕OO LOW

n cliniciai	n rated typic	al depression so	cores at endpoint -	Light box vs low-d	ensity ionisation	(measured with: HA	MD-17/HRS	D-21; Better ind	licated by lowe	er values)
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	21	23	H	SMD 0.81 lower (1.43 to 0.19 lower) ⊕⊕⊕O MODERATE
n clinicia:	n rated typic	al depression so	cores at endpoint -	Low dose (<5000li	ux hours/day) ligi	ht box vs no light bo	x (measured	with: HAMD-17	//HRSD-21; Be	tter indicated by lower values)
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	9	12	ł	SMD 0.26 higher (0.61 ⊕⊕⊕O lower to 1.13 higher) MODERATE
n clinicia:	n rated typic	al depression so	cores at endpoint -	Low dose (<5000li	ux hours/day) ligi	ht visor vs no light vi	isor (measur	ed with: HAMD-	17/HRSD-21; I	Better indicated by lower values)
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	12	10	H	SMD 0.2 higher (0.64 lower ⊕⊕⊕O to 1.04 higher) MODERATE
an clinicia:	n rated atypi	cal depression	scores at endpoint	measured with: S	AD subscale; Bet	ter indicated by low	er values)			· · · · · · · · · · · · · · · · · · ·
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	55	55	H	MD 1.25 lower (2.77 lower to 0.27 higher) ⊕⊕⊕⊕ HIGH
an clinicia	n rated atypi	cal depression	scores at endpoint	Light visor vs din	light visor (mea	sured with: SAD sub	scale; Better	indicated by lo	wer values)	,
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	34	33	ł	MD 2.1 lower (4.31 lower to 0.11 higher) MODERATE
an clinicia	n rated atypi	cal depression	scores at endpoint	- Low dose (<5000	lux hours/day) lig	ght box vs no light b	ox (measure	d with: SAD sub	scale; Better ii	ndicated by lower values)
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	9	12	ı	MD 1.2 higher (2.48 lower to 4.88 higher) ⊕⊕⊕O MODERATE
ean clinicia:	n rated atypi	cal depression	scores at endpoint	- Low dose (<5000	lux hours/day) lig	ght visor vs no light	visor (measu	red with: SAD s	ubscale; Bette	r indicated by lower values)
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	12	10	ł	MD 1.3 lower (3.84 lower to 1.24 higher) ⊕⊕⊕O MODERATE
ean self rati	ed depressio	n scores at end	point - Light box vs	deactivated nega	tive ion generato	r (measured with: B	DI; Better in	dicated by lowe	r values)	
ran tria		no serious imitations	no serious inconsistency	no serious indirectness	serious³	none	33	31	ł	MD 2.6 lower (6.72 lower to 1.52 higher) ⊕⊕⊕O MODERATE
			R or HDRS) (overall)							

6	randomised trials	no serious limitations	serious¹	no serious indirectness	serious <sup>3</sup>	none	99/176 (56.3%)	98/160 (61.3%)	RR 0.89 (0.66 to 1.2)	7 fewer per 100 (from 21 fewer to 12 more)	⊕⊕OO LOW	
								70.5%		8 fewer per 100 (from 24 fewer to 14 more)		
Non remis	sion (SIGH-SAD	or SIGH-SAD-SR	or HDRS) - Low dos	se (<5000lux hours	/day) LED light vs	negative ion gener	ator	•				
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	7/15 (46.7%)	10/11 (90.9%)	RR 0.51 (0.29 to 0.91)	45 fewer per 100 (from 8 fewer to 65 fewer)	⊕⊕⊕O MODERATE	
								90.9%		45 fewer per 100 (from 8 fewer to 65 fewer)		
Non remis	sion (SIGH-SAD	or SIGH-SAD-SR	or HDRS) - Light bo	x vs deactivated n	egative ion gener	ator				,		
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	21/41 (51.2%)	30/40 (75%)	RR 0.68 (0.48 to 0.97)	24 fewer per 100 (from 2 fewer to 39 fewer)	⊕⊕⊕O MODERATE	
							, ,	75%		24 fewer per 100 (from 2 fewer to 39 fewer)		
Non remis	sion (SIGH-SAD	or SIGH-SAD-SR	or HDRS) - Light vis	sor vs dim light vis	or							
2	randomised trials	no serious limitations	serious¹	no serious indirectness	serious <sup>4</sup>	none	33/64 (51.6%)	22/58 (37.9%)	RR 1.34 (0.79 to 2.27)	13 more per 100 (from 8 fewer to 48 more)	⊕⊕OO LOW	
								38.7%		13 more per 100 (from 8 fewer to 49 more)		
Non remis	sion (SIGH-SAD	or SIGH-SAD-SR	or HDRS) - Light bo	x vs high dose (>3	00lux) dim red lig	ht box						
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	25/33 (75.8%)	19/26 (73.1%)	RR 1.04 (0.77 to 1.4)	3 more per 100 (from 17 fewer to 29 more)	⊕⊕OO LOW	
								73.1%		3 more per 100 (from 17 fewer to 29 more)		
Non remis	sion (SIGH-SAD	or SIGH-SAD-SR	or HDRS) - Light bo	x vs low-density id	onisation							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	13/23 (56.5%)	17/25 (68%)	RR 0.83 (0.53 to 1.3)	12 fewer per 100 (from 32 fewer to 20 more)	⊕⊕OO LOW	
								68%		12 fewer per 100 (from 32 fewer to 20 more)		
Non respo	nse (SIGH-SAD)	) (overall)										

							1					
7	randomised trials	no serious limitations	serious³	no serious indirectness	serious¹	none	83/183 (45.4%)	92/171 (53.8%)	RR 0.86 (0.64 to 1.15)	8 fewer per 100 (from 19 fewer to 8 more)	⊕⊕OO LOW	
								58.3%		8 fewer per 100 (from 21 fewer to 9 more)		
Non respo	nse (SIGH-SAD)	) - Light box vs de	eactivated negative	ion generator								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	19/41 (46.3%)	25/40 (62.5%)	RR 0.74 (0.49 to 1.11)	16 fewer per 100 (from 32 fewer to 7 more)	⊕⊕⊕O MODERATE	
								62.5%		16 fewer per 100 (from 32 fewer to 7 more)		
Non respo	nse (SIGH-SAD)	) - Light visor vs o	lim light visor	,	'							
_	randomised trials	no serious limitations	serious³	no serious indirectness	serious <sup>4</sup>	none	30/64 (46.9%)	22/58 (37.9%)	RR 1.24 (0.56 to 2.75)	9 more per 100 (from 17 fewer to 66 more)	⊕⊕OO LOW	
							(	37.2%	,	9 more per 100 (from 16 fewer to 65 more)	_	
Non respo	nse (SIGH-SAD)	- Light box vs hi	gh dose (>300lux) o	lim red light box								
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious⁴	none	13/33 (39.4%)	14/26 (53.8%)	RR 0.73 (0.42 to 1.27)	15 fewer per 100 (from 31 fewer to 15 more)	⊕⊕⊕O MODERATE	
							,	53.9%		15 fewer per 100 (from 31 fewer to 15 more)		
Non respo	nse (SIGH-SAD)	) - Light box vs lo	w-density ionisatio	n							_	
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	9/23 (39.1%)	18/25 (72%)	RR 0.54 (0.31 to 0.96)	33 fewer per 100 (from 3 fewer to 50 fewer)	⊕⊕⊕O MODERATE	
								72%		33 fewer per 100 (from 3 fewer to 50 fewer)		
Non respo	nse (SIGH-SAD)	) - Low dose (<50	00lux hours/day) li	ght box vs no light	box							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	7/10 (70%)	7/12 (58.3%)	RR 1.2 (0.64 to 2.25)	12 more per 100 (from 21 fewer to 73 more)	⊕⊕⊕O MODERATE	
								58.3%		12 more per 100 (from 21 fewer to 73 more)		
Non respo	nse (SIGH-SAD)	) - Low dose (<50	00lux hours/day) li	ght visor vs no ligh	nt visor							

1	randomised trials	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	5/12 (41.7%)	6/10 (60%)	RR 0.69 (0.3 to	•	⊕⊕⊕O MODERATE	
						, ,	60%		19 fewer per 100 (from 42 fewer to 37 more)		

<sup>1</sup> Inconclusive effect size

### Is bright light effective for depression with a seasonal pattern/SAD compared with active treatments?

			Quality asses	sment					Summary of	findings		
							No	of patients		Effect	- "	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	Active treatment control	Relative (95% CI)	Absolute	Quality	
Leaving st	udy early for a	ny reason - Light	box vs group CBT			-						
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious¹	none	2/25 (8%)	4/24 (16.7%)	RR 0.53 (0.12 to 2.31)	8 fewer per 100 (from 15 fewer to 22 more)	⊕⊕⊕O MODERATE	
								17.8%		8 fewer per 100 (from 16 fewer to 23 more)		
Leaving st	udy early for a	ny reason - Light	box + placebo pill	vs dim light box +	fluoxetine							
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious¹	none	12/68 (17.6%)	8/68 (11.8%)	RR 1.5 (0.65 to 3.44)	6 more per 100 (from 4 fewer to 29 more)	⊕⊕⊕O MODERATE	
								9.8%		5 more per 100 (from 3 fewer to 24 more)		
Leaving st	udy early for a	ny reason - Light	box + hypericum v	s dim light + hype	ricum							
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/10 (0%)	0/10 (0%)	not pooled	not pooled	⊕⊕⊕⊕ HIGH	
Leaving st	udv early due t	to side effects - L	ight box + placebo	pill vs dim light be	ox + fluoxetine			0%		not pooled		
	,,		у			-						
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious²	none	1/48 (2.1%)	2/48 (4.2%)	RR 0.5 (0.05 to 5.33)	2 fewer per 100 (from 4 fewer to 18 more)		

<sup>2</sup> Single study; inconclusive effect size

<sup>&</sup>lt;sup>3</sup> Significant heterogeneity; random effects model used

<sup>4</sup> Single study

		1	1	1	1	1	1					
								4.2%		2 fewer per 100 (from 4 fewer to 18 more)	⊕⊕OO LOW	
Leaving stu	udy early due t	o side effects - L	Light box vs group C	BT								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious³	none	0/16 (0%)	0/15 (0%)	not pooled	not pooled	⊕⊕⊕O MODERATE	
			,					0%		not pooled		
Leaving stu	udy early due t	o lack of efficac	y - Light box + place	bo pill vs dim ligh	t box + fluoxetine							
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious²	none	2/43 (4.7%)	0/48 (0%)	RR 5.57 (0.27 to 112.85)	0 more per 100 (from 0 fewer to 0 more)		
								0%		0 more per 100 (from 0 fewer to 0 more)		
Reported s	side effects - Li	ght box + placeb	oo pill vs dim light b	ox + fluoxetine								
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious³	none	37/48 (77.1%)	75%	RR 1.03 (0.82 to 1.29)	22 more per 1000 (from 135 fewer to 217 more)		
Mean clini	cian rated SAD	depression sco	res at endpoint - Lig	ght box vs group C	BT (measured wit	th: SIGH-SAD; Bett	er indicated	by lower values)				
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	16	15	ł	MD 0.2 lower (6.5 lower to 6.1 higher)	⊕⊕OO LOW	
Mean clini	cian rated SAD	depression sco	res at endpoint - Lig	ght box + placebo	pill vs dim light bo	ox + fluoxetine (me	easured wit	h: SIGH-SAD; Bett	er indicated by l	lower values)		
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	68	68	ł	MD 0.49 lower (3.72 lower to 2.74 higher)	⊕⊕⊕⊕ HIGH	
Mean clini	cian rated typi	cal depression s	cores at endpoint -	Light box vs group	p CBT (measured	with: HAMD-17/HI	RSD-21; Bet	ter indicated by lo	ower values)			
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious²	none	16	15	ł	SMD 0.13 lower (0.83 lower to 0.58 higher)	⊕⊕OO LOW	
Mean clini	cian rated typi	cal depression s	cores at endpoint -	Light box + placel	oo pill vs dim light	: box + fluoxetine (	measured v	vith: HAMD-17/H	RSD-21; Better i	ndicated by lower values)		
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	68	68	ł	SMD 0.04 lower (0.38 lower to 0.29 higher)	⊕⊕⊕⊕ HIGH	
Mean clini	Mean clinician rated typical depression scores at endpoint - Light box + hypericum vs dim light + hypericum (measured with: HAMD-17/HRSD-21; Better indicated by lower values)											

1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	10	10	ł	SMD 0.32 lower (1.2 lower to 0.57 higher)	⊕⊕OO LOW	
Mean clin	ician rated aty	pical depression	scores at endpoint	- Light box vs gro	up CBT (measured	with: SAD subscal	e; Better in	dicated by lower	values)			
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious³	none	16	15	-	MD 0.4 higher (2.68 lower to 3.48 higher)	⊕⊕⊕O MODERATE	
Mean clin	ician rated aty	pical depression	scores at endpoint	- Light box + place	ebo pill vs dim ligh	nt box + fluoxetine	(measured	with: SAD subsca	le; Better indica	ted by lower values)		
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	68	68	ł	MD 0.3 lower (1.75 lower to 1.15 higher)	⊕⊕OO LOW	
Mean self	rated depress	ion scores at end	dpoint - Light box vs	group CBT (meas	ured with: BDI; B	etter indicated by I	ower value	es)				
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	16	15	ł	MD 0.7 lower (7.16 lower to 5.76 higher)		
Mean self	rated depress	ion scores at end	dpoint - Light box +	placebo pill vs din	n light box + fluox	etine (measured w	rith: BDI; Be	etter indicated by	lower values)			
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	48	48	ł	MD 1.6 lower (5.68 lower to 2.48 higher)	⊕⊕OO LOW	
Non remi	ssion - Light bo	x + placebo pill v	vs dim light box + flu	uoxetine								
2	randomised trials	no serious limitations	serious <sup>4</sup>	no serious indirectness	serious <sup>1</sup>	none	34/68 (50%)	37/68 (54.4%) 60.4%	RR 0.92 (0.67 to 1.27)	4 fewer per 100 (from 18 fewer to 15 more)  5 fewer per 100 (from 20	⊕⊕OO LOW	
Non remi	ssion - Light bo	x vs group CBT						00.470		fewer to 16 more)		
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/25 (48%)	15/24 (62.5%)	RR 0.77 (0.46 to 1.28)	14 fewer per 100 (from 34 fewer to 17 more)	⊕⊕⊕⊕ HIGH	
							(4070)	63.3%	10 1.20	15 fewer per 100 (from 34 fewer to 18 more)	Alloli	
Non respo	onse - Light box	c + placebo pill v	s dim light box + flu	oxetine								
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	22/68 (32.4%)	23/68 (33.8%)	RR 0.96 (0.59 to 1.54)	1 fewer per 100 (from 14 fewer to 18 more)		

								34.2%		1 fewer per 100 (from 14 fewer to 18 more)	⊕⊕OO LOW	
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<sup>&</sup>lt;sup>1</sup> Inconclusive effect size

#### 5 Is bright light effective for depression with a seasonal pattern/SAD compared with a combination of bright light and CBT?

			Quality asses	sment					Summary	of findings		
			Z,				No o	f patients		Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light	Light + CBT combo	Relative (95% CI)	Absolute	Quality	
Leaving st	udy early for ar	y reason										
randomised trials no serious no serious inconsistency indirectness no serious no serious indirectness no serious indirectness no serious indirectness no serious no												
								9.6%		1 fewer per 100 (from 8 fewer to 38 more)		
Leaving st	udy early due to	o side effects										
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	0/16 (0%)	1/15 (6.7%)	RR 0.31 (0.01 to 7.15)	5 fewer per 100 (from 7 fewer to 41 more)	⊕⊕OO LOW	
								6.7%		5 fewer per 100 (from 7 fewer to 41 more)		
Mean clini	cian rated SAD	depression score	es at endpoint (meas	ured with: SIGH-S	AD; Better indicate	ed by lower values)						
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	16	15	ł	MD 4.2 higher (0.52 lower to 8.92 higher)	⊕⊕⊕O MODERATE	
Mean clini	ician rated typic	cal depression sco	ores at endpoint (me	easured with: HAN	ID-17/HRSD-21; B	etter indicated by lo	wer value	es)				
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	16	15	I	SMD 0.46 higher (0.26 lower to 1.17 higher)	⊕⊕⊕O MODERATE	
Mean clini	Mean clinician rated atypical depression scores at endpoint (measured with: SAD subscale; Better indicated by lower values)											

<sup>&</sup>lt;sup>2</sup> Inconclusive effect size/single study

<sup>&</sup>lt;sup>3</sup> Single study

<sup>1</sup> 2 3 4 <sup>4</sup> Significant heterogeneity; random effects model used

<sup>1</sup> Inconclus	ivo of	ffact.	ciza
HICOHOUS	ive e	necii	SIZE

<sup>&</sup>lt;sup>2</sup> Inconclusive effect size; single study

randomised

randomised

randomised

trials

trials

Non remission (SIGH-SAD)

trials

no serious

limitations

no serious

limitations

no serious

limitations

#### 4 Does the time of day increase the effectiveness of bright light box therapy?

no serious

no serious

no serious

inconsistency

inconsistency

inconsistency

Mean self rated depression scores at endpoint (measured with: BDI; Better indicated by lower values)

no serious

no serious

no serious

indirectness

indirectness

indirectness

serious<sup>3</sup>

very serious<sup>2</sup>

no serious

imprecision

none

none

none

16

16

12/25

(48%)

15

15

5/23 (21.7%)

19.6%

RR 2.22 (0.92

to 5.32)

	Quality assessment							Sun	nmary of findir	ngs		
								No of patients		Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Morning	Afternoon/evening bright light box	Relative (95% CI)	Absolute	Quality	
Leaving st	udy early for a	ny reason (overa	all)									
3			no serious inconsistency	no serious indirectness	serious <sup>1</sup>	none	8/66 (12.1%)	8/64 (12.5%)	RR 0.98 (0.41 to 2.35)	0 fewer per 100 (from 7 fewer to 17 more)	⊕⊕⊕O MODERATE	
								0%		0 fewer per 100 (from 0 fewer to 0 more)		
Leaving st	udy early for a	ny reason - SAD										
2	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>1</sup>	none	8/50 (16%)	8/49 (16.3%)	RR 0.98 (0.41 to 2.35)	0 fewer per 100 (from 10 fewer to 22 more)	⊕⊕⊕O MODERATE	
								10%		0 fewer per 100 (from 6 fewer to 13 more)		

MD 2 higher (0.12 lower to

4.12 higher)

MD 2.3 higher (2.47 lower

to 7.07 higher)

27 more per 100 (from 2

fewer to 94 more)

24 more per 100 (from 2

fewer to 85 more)

 $\oplus \oplus \oplus O$ 

MODERATE

 $\oplus \oplus OO$ 

LOW

 $\oplus \oplus \oplus \oplus$ 

HIGH

<sup>3</sup> Single study

			an and an and CAD								
Leaving St	udy early for a	ny reason - Sui	osyndromal SAD								
Į.	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious²	none	0/16 (0%)	0/15 (0%)	not pooled	not pooled	⊕⊕⊕O MODERATE
								0%		not pooled	
eaving st	udy early due	to side effects	- Subsyndromal SAI								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/16 (0%)	0/15 (0%)	not pooled	not pooled	⊕⊕⊕O MODERATE
			,					0%		not pooled	
Reported	side effects - S	ubsyndromal S	AD								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	1/16 (6.3%)	2/15 (13.3%)	RR 0.47 (0.05 to 4.65)	7 fewer per 100 (from 13 fewer to 49 more)	⊕⊕OO LOW
								13.3%		7 fewer per 100 (from 13 fewer to 49 more)	
Mean clin	ician rated SAI	depression so	ores at endpoint (o	verall) (measured	d with: SIGH-	SAD; Better indicat	ed by lower	values)			
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	35	33	H	MD 1.38 lower (5.49 lower to 2.73 higher)	⊕⊕OO LOW
	criais	mmacions	meorisistemey	man cethess	3011003					lower to 2.73 mgnery	2000
Mean clin	ician rated SAI	depression so	ores at endpoint - S	Subsyndromal SA	D (measured	with: SIGH-SAD; Be	etter indicate	ed by lower values)			
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	16	14	ł	MD 0.6 higher (3.89 lower to 5.09 higher)	⊕⊕OO LOW
/lean clin	ician rated SAI	depression so	ores at endpoint - S	SAD (measured w	ith: SIGH-SAI	); Better indicated	by lower val	ues)			
	1			<u> </u>			1		T		
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	19	19	ł	MD 3.6 lower (8.5 lower to 1.3 higher)	⊕⊕OO LOW
/lean clin	ician rated typ	ical depression	scores at endpoint	(overall) (measu	red with: HA	 MD-17/HRSD-31; B	etter indicat	ed by lower values)			
							T				
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>1</sup>	none	25	22	H	SMD 0.05 lower (0.63 lower to 0.52 higher)	⊕⊕⊕O MODERATE
1ean clin	ician rated typ	ical depression	scores at endpoint	: - Subsyndromal	SAD (measure	ed with: HAMD-17,	/HRSD-21; B	etter indicated by lower va	alues)		
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	16	14	1	SMD 0.15 lower (0.87 lower to 0.57 higher)	⊕⊕OO LOW

Mean clini	cian rated typi	cal depression s	scores at endpoint	- SAD (HRSD-31) (	measured w	ith: HAMD-17/HRS	D-21; Better	r indicated by lower values			
		no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	9	8	·	SMD 0.12 higher (0.83 lower to 1.07 higher)	⊕⊕OO LOW
Mean clini	cian rated aty	oical depression	scores at endpoin	t - Subsyndromal	SAD (measur	ed with: SAD subsc	cale; Better	indicated by lower values)			
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	16	14	ł	MD 1 higher (1.72 lower to 3.72 higher)	⊕⊕OO LOW
Mean self	rated depressi	on scores at en	dpoint - SAD (meas	ured with: BDI; B	etter indicate	ed by lower values)					
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	33	32	ł	MD 0.9 lower (4.66 lower to 2.86 higher)	⊕⊕OO LOW
Non remis	sion - SAD			<del>!</del>	ļ						<del>'</del>
	randomised trials	no serious limitations	serious <sup>4</sup>	no serious indirectness	serious¹	none	27/50 (54%)	26/48 (54.2%)	RR 1.00 (0.69 to 1.45)	0 fewer per 100 (from 17 fewer to 24 more)	⊕⊕OO LOW
								42.5%		0 fewer per 100 (from 13 fewer to 19 more)	
Non respo	nse (overall)		•	•							·
_	randomised trials	no serious limitations	serious¹	no serious indirectness	serious¹	none	29/66 (43.9%)	27/63 (42.9%)	RR 1 (0.51 to 1.98)	0 fewer per 100 (from 21 fewer to 42 more)	⊕⊕OO LOW
								40%		0 fewer per 100 (from 20 fewer to 39 more)	
Non respo	nse - SAD		•	•							·
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious¹	none	24/50 (48%)	18/48 (37.5%)	RR 1.26 (0.78 to 2.01)	10 more per 100 (from 8 fewer to 38 more)	⊕⊕⊕O MODERATE
								32.5%		8 more per 100 (from 7 fewer to 33 more)	
Non respo	nse - Subsyndr	omal SAD	•								
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious³	none	5/16 (31.3%)	9/15 (60%)	RR 0.52 (0.23 to 1.2)	29 fewer per 100 (from 46 fewer to 12 more)	⊕⊕⊕O MODERATE
							,	60%		29 fewer per 100 (from 46 fewer to 12 more)	

- <sup>1</sup> Inconclusive effect size
- <sup>2</sup> Single study
- 1 2 3
- 3 Inconclusive effect size; single study
  4 Significant heterogeneity; random effects model used 4

### Is dawn simulation effective for depression with a seasonal pattern/SAD?

			Quality asses	sment					Summary of	findings		
			N				No of	patients		Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Dawn simulation	Attentional control	Relative (95% CI)	Absolute	Quality	
Leaving st	udy early for a	ny reason			1	1						
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	2/70 (2.9%)	10/71 (14.1%)	RR 0.33 (0.05 to 2.22)	9 fewer per 100 (from 13 fewer to 17 more)	⊕⊕OO LOW	
								19.4%		13 fewer per 100 (from 18 fewer to 24 more)	LOW	
Leaving st	udy early due	to side effects										
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	0/31 (0%)	1/31 (3.2%)	RR 0.33 (0.01 to 7.88)	2 fewer per 100 (from 3 fewer to 22 more)	⊕⊕OO LOW	
								3.2%		2 fewer per 100 (from 3 fewer to 22 more)		
Leaving st	udy early due	to lack of efficac	Y									
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>1</sup>	none	0/45 (0%)	6/44 (13.6%)	RR 0.14 (0.02 to 1.1)		⊕⊕⊕O MODERATE	
								11.9%		10 fewer per 100 (from 12 fewer to 1 more)		
Reported	side effects											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	6/14 (42.9%)	1/13 (7.7%)	RR 5.57 (0.77 to 40.26)	35 more per 100 (from 2 fewer to 302 more)	⊕⊕OO LOW	
								7.7%		35 more per 100 (from 2 fewer to 302 more)		

<sup>2</sup> Inconclusive	effect	size;	single	stud

randomised

randomised

randomised

randomised

trials

trials

Non remission (SIGH-SAD)

trials

Non response (SIGH-SAD)

trials

1 Inconclusive effect size

no serious

limitations

no serious

limitations

no serious

limitations

no serious

limitations

#### Is dawn simulation more effective than bright light box therapy for depression with a seasonal pattern/SAD?

Mean clinician rated typical depression scores at endpoint (measured with: HAMD-17/HRSD-21; Better indicated by lower values)

no serious

no serious

no serious

no serious

indirectness

indirectness

indirectness

Mean clinician rated atypical depression scores at endpoint (measured with: SAD subscale; Better indicated by lower values)

indirectness

serious<sup>3</sup>

serious<sup>3</sup>

serious<sup>3</sup>

no serious

inconsistency

			Quality asses	sment					Summary of	findings		
							No of	patients		Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Bright light Dawn Relative box simulation (95% CI)			Absolute	Quality	
Leaving st	udy early for ar	ny reason										
2	randomised no serious no serious no serious serious none inconsistency inconsistency inconsistency inconsistency							1/56 (1.8%)	RR 3.72 (0.62 to 22.22)	5 more per 100 (from 1 fewer to 38 more)		

none

none

none

none

no serious

imprecision

very serious<sup>2</sup>

serious1

serious1

SMD 0.53 lower (1.62

lower to 0.15 higher)

MD 2.20 lower (7.52 lower

to 3.11 higher)

5 fewer per 100 (from 27

fewer to 39 more)

5 fewer per 100 (from 27

fewer to 39 more)

11 fewer per 100 (from 17

more to 1195 more)

11 fewer per 100 (from 17

more to 1198 more)

36

36

29/58 (50%)

49.9%

21/58 (36.2%)

36.3%

RR 0.9 (0.46 to

1.78)

RR 0.71 (34 to

1.48)

37

37

25/56

(44.6%)

14/56 (25%)

 $\oplus \oplus \oplus O$ 

**MODERATE** 

**⊕**000

**VERY LOW** 

⊕⊕00

LOW

 $\oplus \oplus \oplus O$ 

MODERATE

<sup>&</sup>lt;sup>3</sup> Significant heterogeneity; random effects model used

								2%		5 more per 100 (from 1 fewer to 42 more)	⊕⊕⊕O MODERATE	
Leaving st	udy early due t	o side effects	•	•	•		•					
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	2/33 (6.1%)	0%	RR 4.71 (0.23 to 94.31)	0 more per 1000 (from 0 fewer to 0 more)		
Leaving st	udy early due t	o lack of efficacy	•		,	<b>'</b>	1	<u>'</u>	-		<del> </del>	
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/31 (0%)	0/31 (0%)	not pooled	not pooled	⊕⊕⊕⊕ HIGH	
Non remis	ssion (SIGH-SAD	)						070		not pooled		
2	randomised trials	no serious limitations	serious <sup>3</sup>	no serious indirectness	very serious <sup>1</sup>	none	30/56 (53.6%)	25/56 (44.6%)	RR 1.19 (0.7 to 2)	8 more per 100 (from 13 fewer to 45 more)	⊕OOO VERY LOW	
								46.1%		9 more per 100 (from 14 fewer to 46 more)		
Non respo	nse (SIGH-SAD)											
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious¹	none	20/56 (35.7%)	14/56 (25%) 26.1%	RR 1.45 (0.82 to 2.58)	11 more per 100 (from 5 fewer to 39 more)  12 more per 100 (from 5 fewer to 41 more)	⊕⊕⊕O MODERATE	
Depression	n: mean endpo	int scores (Better	r indicated by lower	values)						lewer to 41 more)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	21	24	ł	MD 0.9 lower (4 lower to 2.2 higher)	⊕⊕OO LOW	
SAD: mear	n endpoint scor	es (Better indica	ted by lower values	)	,	•	'	<u>'</u>	-		<del>,</del>	
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	21	24	I	MD 1.8 lower (6.98 lower to 3.38 higher)	⊕⊕OO LOW	
	sive effect size		1	1	1	•	1					

<sup>&</sup>lt;sup>1</sup> Inconclusive effect size

Inconclusive effect size; single study
 Significant effect size - random effects model used

# Non-light therapies for depression with a seasonal pattern/SAD

# Are antidepressants effective in depression with a seasonal pattern/SAD? (Acute phase efficacy data)

			Quality asse	ssment				Sum	mary of finding	gs		
							No of patients			Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Acute phase treatment :antidepressants	Control	Relative (95% CI)	Absolute	Quality	
Number n	ot achieving =	/> 50% reduction	on in SIGH-SAD sco	re at endpoint (o	verall)	'						
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	57/129 (44.2%)	68/126 (54%)	RR 0.82 (0.63 to 1.05)	10 fewer per 100 (from 20 fewer to 3 more)	⊕⊕⊕⊕ HIGH	
								57.8%		10 fewer per 100 (from 21 fewer to 3 more)		
Number n	ot achieving =	/> 50% reduction	on SIGH-SAD score									
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	41/93 (44.1%)	47/94 (50%)	RR 0.88 (0.65 to 1.2)	6 fewer per 100 (from 18 fewer to 10 more)	⊕⊕OO LOW	
								50%		6 fewer per 100 (from 18 fewer to 10 more)		
Number n	ot achieving =	/> 50% reduction	on in outcome scor	e at endpoint - Fl	uoxetine vs Plac	ebo						
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious¹	none	16/36 (44.4%)	21/32 (65.6%)	RR 0.68 (0.43 to 1.05)	21 fewer per 100 (from 37 fewer to 3 more)	⊕⊕OO LOW	
								65.6%		21 fewer per 100 (from 37 fewer to 3 more)		
Mean end	point SIGH-SA	D (clinician rate	ed) (antidepressan	ts) (Better indicat	ted by lower valu	ies)						
_	randomised trials	no serious limitations	serious <sup>2</sup>	no serious indirectness	serious	none	52	47	ł	SMD 0.11 lower (0.65 lower to 0.42 higher)	⊕⊕OO LOW	
Mean end	point (clinicia	n rated) (antide	pressants) - Mocio	bemide vs Placek	oo (Better indicat	ted by lower value	s)					
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	16	15	I	SMD 0.23 higher (0.48 lower to 0.94 higher)	⊕⊕OO LOW	

Mean end	Mean endpoint (clinician rated) (antidepressants) - Fluoxetine vs Placebo (Better indicated by lower values)														
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	none	36	32	ł	SMD 0.33 lower (0.81 lower to 0.15 higher)	⊕⊕OO LOW				
Mean end	dpoint BDI (sel	f rated) - Fluoxe	tine vs Placebo (B	etter indicated by	lower values)										
	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious¹	none	36	32	ł	MD 1.7 lower (6.53 lower to 3.13 higher)	⊕⊕OO LOW				
Mean cha	ınge (clinician ı	rated) - Sertralir	ne vs Placebo (Bet	ter indicated by lo	ower values)										
_	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	93	93	+	MD 4.51 lower (8.23 to 0.79 lower)	⊕⊕⊕O MODERATE				
Relapse P	revention - Nu	imber of patient	ts expriencing a re	currence											
_	randomised trials	no serious limitations	no serious inconsistency		no serious imprecision	none	92/542 (17%)	153/519 (29.5%)	RR 0.58 (0.46 to 0.72)	12 fewer per 100 (from 8 fewer to 16 fewer)	⊕⊕⊕⊕ HIGH				
								31.9%		13 fewer per 100 (from 9 fewer to 17 fewer)					

#### Are antidepressants effective in depression with a seasonal pattern/SAD? (Acute phase acceptability/tolerability data) 4

			Quality assess	ment				Summar	y of findings			
				_			No of patients			Effect		Importance
No of studies	ies Design Limitations Inconsistency Indirectness Imprecision consider						Acute phase acceptibility and tolerability (antidepressants)	Placebo	Relative (95% CI)	Absolute	Quality	
Number I	leaving the stu	dy early for any	reason (overall)	<u> </u>	!			-				
2		no serious limitations	serious <sup>1</sup>	no serious indirectness	very serious²	none	20/109 (18.3%)	23/112 (20.5%)	RR 0.7 (0.16 to 3.05)	6 fewer per 100 (from 17 fewer to 42 more)	⊕OOO VERY LOW	
								19%		6 fewer per 100 (from 16 fewer to 39 more)		

<sup>&</sup>lt;sup>1</sup> Single study; inconclusive effect size <sup>2</sup> Significant heterogeneity - random effects model used <sup>3</sup> Single study

Number l	eaving the stu	dy early for any	reason - Sertralin	e vs Placebo								
_		no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	20/93 (21.5%)	20/94 (21.3%) 21.3%	RR 1.01 (0.58 to 1.75)	0 more per 100 (from 9 fewer to 16 more) 0 more per 100 (from 9 fewer to 16 more)	⊕⊕OO LOW	
Number l	eaving the stu	dy early for any	reason - Moclobe	emide vs Placebo								
1		no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	0/16 (0%)	3/18 (16.7%)	RR 0.16 (0.01 to 2.87)	14 fewer per 100 (from 17 fewer to 31 more)	⊕⊕OO LOW	
								16.7%		(from 17 fewer to 31 more)		
Number l	eaving the stud	dy early due to	side effects	1						more		
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	12/145 (8.3%)	8/144 (5.6%)	RR 1.48 (0.63 to 3.47)	3 more per 100 (from 2 fewer to 14 more) 3 more per 100 (from	⊕⊕OO LOW	
Number l	eaving the stu	dy early due to	side effects - Serti	raline vs Placebo				3.3 /0		2 fewer to 13 more)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious²	none	10/93 (10.8%)	5/94 (5.3%) 5.3%	RR 2.02 (0.72 to 5.69)	5 more per 100 (from 1 fewer to 25 more) 5 more per 100 (from 1 fewer to 25 more)	⊕⊕OO LOW	
Number l	eaving the stu	dy early due to	side effects - Moc	lobemide vs Plac	ebo							
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	0/16 (0%)	2/18 (11.1%)	RR 0.22 (0.01 to 4.34)	9 fewer per 100 (from 11 fewer to 37 more) 9 fewer per 100 (from 11 fewer to 37 more)	⊕⊕OO LOW	
Number l	eaving the stu	dy early due to	side effects - Fluo	xetine vs Placebo	)	<u> </u>				11 10 (C)		
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious³	none	2/36 (5.6%)	1/32 (3.1%)	RR 1.78 (0.17 to 18.69)	2 more per 100 (from 3 fewer to 55 more)		

								3.1%		2 more per 100 (from 3 fewer to 55 more)	⊕⊕OO LOW	
Number r	reporting side	effects - Sertrali	ine vs Placebo									
				no serious indirectness	serious <sup>4</sup>	none	76/93 (81.7%)	47/94 (50%)	RR 1.63 (1.31 to 2.04)	•	⊕⊕⊕O MODERATE	
Number r	reporting side	effects - Fluoxet	tine vs Placebo								<u> </u>	
_				no serious indirectness	serious <sup>4</sup>	none	35/36 (97.2%)	29/32 (90.6%) 90.6%	RR 1.07 (0.95 to 1.21)	6 more per 100 (from 5 fewer to 19 more) 6 more per 100 (from 5 fewer to 19 more)	⊕⊕⊕O MODERATE	

<sup>&</sup>lt;sup>1</sup> Significant heterogeneity - random effects model used

#### Which antidepressant is more effective in depression with a seasonal pattern/SAD? 5

			Quality assessn	nent				Sum	mary of findi	ngs		
							No of patients			Effect		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Acute phase treatment: antidepressants	Active control	Relative (95% CI)	Absolute	Quality	
Number i	not achieving =/	'> 50% reduction	in SIGH-SAD score	at endpoint - Hig	h ion density	v Low ion density						
1		no serious limitations		no serious indirectness	serious¹	none	5/12 (41.7%)	11/13 (84.6%)	RR 0.49 (0.24 to 1)	43 fewer per 100 (from 64 fewer to 0 more)	⊕⊕⊕O MODERATE	
								84.6%		43 fewer per 100 (from 64 fewer to 0 more)		
Mean en	dpoint SIGH-SAI	D (clinician rated	l) - Moclobemide v	Fluoxetine (Bett	er indicated b	y lower values)						
1		no serious limitations	no serious inconsistency	no serious indirectness	very serious¹	none	11	18	ŀ	MD 1.6 lower (7.01 lower to 3.81 higher)	⊕⊕OO LOW	

<sup>1</sup> 2 3 4 <sup>2</sup> Inconclusive effect size

<sup>&</sup>lt;sup>3</sup> Single study; inconclusive effect size <sup>4</sup> Single study

<sup>1</sup> Single study; inconclusive effect size

### Is continuation treatment effective for depression with a seasonal pattern/SAD?

			Quality assessm	ent					Summary of f	indings				
			Z,				No of patier	nts		Effect		Importance		
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Continuation treatment Control (95% CI)			Absolute	Quality			
Mean end	ean endpoint HAMD-21 (clinician-rated) - Propanolol vs Placebo (Better indicated by lower values)													
1	randomised no serious no serious no serious serious none limitations inconsistency indirectness						12	11	ł	MD 7 lower (11.24 to 2.76 lower)	⊕⊕⊕O MODERATE			
Number le	eaving the study	y early for any rea	son - Propanolol vs	Placebo		•								
1	randomised trials	no serious limitations		no serious indirectness	very serious²	none	1/13 (7.7%)	0/11 (0%)	RR 2.57 (0.12 to 57.44)	0 more per 100 (from 0 fewer to 0 more)	⊕⊕OO LOW			
								0%		0 more per 100 (from 0 fewer to 0 more)				

<sup>1</sup> Single study

4 <sup>2</sup> Single study; inconclusive effect size

5

8

# 7 Further-line treatment (chapter 8)

Increasing the dose of antidepressant versus continuing with the antidepressant at the same dose

			Quality asse	ssment			No of	f patients		Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Increasing the dose of antidepressant	Continuing with the antidepressant at the same dose	Relative (95% CI)	Absolute	Quality	Importance

randomis s	d serious <sup>1</sup>	no serious	no serious	von	reporting bias <sup>3</sup>	50/165	51/162	RR 1.07	22 more per 1000	⊕000
trials	a serious.	inconsistency	indirectness	very serious <sup>2</sup>	reporting bias	(30.3%)	(31.5%)	(0.63 to	(from 116 fewer	₩
uiais		inconsistency	mairectriess	serious		(30.3%)	(31.5%)	1.83)	to 261 more)	
								1.03)	to 201 more)	LOW
									23 more per 1000	
							32.4%		(from 120 fewer	
							32. <del>4</del> /0		to 269 more)	
ponse (follow-	in 5-6 week	s: assessed with	: Number of pe	ople showin	g ≥50% improvem	ent on Hamilton Rat	ing Scale for Depres	sion (HAM-D)	,	
(	.,,	,		-	.g _00 /0p. 0 . 0		g ••••.•			
randomise	d serious <sup>1</sup>	no serious	no serious	serious4	reporting bias3	64/127	79/125	RR 0.8	126 fewer per	⊕000
trials		inconsistency	indirectness			(50.4%)	(63.2%)	(0.65 to	1000 (from 6	VERY
								0.99)	fewer to 221	LOW
								,	fewer)	
									107 fewer per	
							53.7%		1000 (from 5	
							0011 /0		fewer to 188	
				1					fewer)	
sponse (follow-l	ip 5-6 weeks	s; assessed with	: Number of pe	opie rated a	s much or very mu	ich improved on Cili	nical Global Impressi	ons scale (CC	žI-I))	
randomise	d serious <sup>1</sup>	very serious <sup>5</sup>	no serious	very	reporting bias <sup>3</sup>	96/135	105/135	RR 1.03	23 more per 1000	⊕000
trials		, , , , , , , ,	indirectness	serious <sup>2</sup>	3	(71.1%)	(77.8%)	(0.59 to	(from 319 fewer	VERY
						()	( 2.17)	1.8)	to 622 more)	LOW
								,	,	
									21 more per 1000	
							71.2%		(from 292 fewer	
									to 570 more)	
ression sympto	matology (f	ollow-up mean	6 weeks; meas	ared with: Ha	amilton Rating Sca	le for Depression (H	IAM-D; change score	); Better indic	cated by lower val	ues)
			no serious	serious <sup>7</sup>	reporting bias <sup>3</sup>	30	27		MD 1.7 higher	<b></b>
	d serious <sup>6</sup>		IIIO SCIIUUS	Sellous	reporting bias	30	21		(1.09 lower to	⊕OOO VERY
randomise	ed serious <sup>6</sup>	no serious								VERT
	d serious <sup>6</sup>	inconsistency	indirectness						`	1 0///
randomise	d serious <sup>6</sup>								4.49 higher)	LOW
randomise trials		inconsistency	indirectness	d with: Num	ber of participants	discontinuing for a	ny reason (including	adverse ever	4.49 higher)	LOW
randomise trials		inconsistency	indirectness	d with: Num	ber of participants	discontinuing for a	ny reason (including	adverse ever	4.49 higher)	LOW
randomise trials		inconsistency	indirectness	d with: Num		discontinuing for a	ny reason (including	adverse ever	4.49 higher)	LOW ⊕OOO
randomise trials	r any reason	inconsistency (follow-up 5-6 v	indirectness weeks; assesse		ber of participants		, ,		4.49 higher)	
randomise trials scontinuation for randomise	r any reason	inconsistency (follow-up 5-6 v	indirectness weeks; assesse	very		20/166	23/166	RR 0.7 (0.21 to	4.49 higher)  nts))  42 fewer per	⊕000
randomise trials continuation for randomise	r any reason	inconsistency (follow-up 5-6 v	indirectness weeks; assesse	very		20/166	23/166	RR 0.7	4.49 higher)  1000 (from 109	⊕000 VERY
randomise trials continuation for randomise	r any reason	inconsistency (follow-up 5-6 v	indirectness weeks; assesse	very		20/166	23/166	RR 0.7 (0.21 to	4.49 higher)  hts))  42 fewer per 1000 (from 109 fewer to 191	⊕000 VERY
randomise trials continuation for randomise	r any reason	inconsistency (follow-up 5-6 v	indirectness weeks; assesse	very		20/166	23/166	RR 0.7 (0.21 to	4.49 higher)  hts))  42 fewer per 1000 (from 109 fewer to 191	⊕000 VERY

										fewer to 186 more)		
Disconti	nuation due	to adverse	events (follow-u	p mean 6 week	s; assessed	with: Number of	participants discont	inuing due to adverse e	events)			
	randomised			no serious		reporting bias <sup>3</sup>	0/30	4/30	RR 0.11	119 fewer per	⊕000	
	trials	risk of bias	inconsistency	indirectness	serious <sup>9</sup>		(0%)	(13.3%)	(0.01 to 1.98)	1000 (from 132 fewer to 131	VERY LOW	
										more)	LOW	
										118 fewer per		
								13.3%		1000 (from 132 fewer to 130		
										more)		

<sup>&</sup>lt;sup>1</sup> Unclear blinding of intervention administrator and outcome assessor

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<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect, and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted/is not reported for all outcomes and study funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> Events<300

<sup>&</sup>lt;sup>5</sup> I-squared>80%

<sup>&</sup>lt;sup>6</sup> Unclear blinding of intervention administration and possible risk of attrition bias difference in drop-out between groups>20%) although ITT analysis used

<sup>&</sup>lt;sup>7</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (SMD 0.5) 8

<sup>8</sup> I-squared>50%

<sup>9 95%</sup> CI crosses line of no effect and both threshold for clinically important benefit (RR 0.75) and threshold for clinically important harm (RR 1.25)

Increasing the dose of antidepressant versus switching to another antidepressant

			Quality ass	essment			No of p	atients		Effect		
											Quality	Important
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Increasing the dose of antidepressant	Switching to another antidepressant	Relative (95% CI)	Absolute		
emissio	on (follow-up	mean 8 w	eeks; assessed v	vith: Number o	f people scorii	ng ≤10 on Montgo	omery Asberg Depres	sion Rating Scale (M	MADRS))			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	124/229 (54.1%)	102/243 (42%)	RR 1.29 (1.07 to 1.56)	122 more per 1000 (from 29 more to 235 more)	⊕000 VERY LOW	
								42%		122 more per 1000 (from 29 more to 235 more)		
espons	e (follow-up	mean 8 we	eks; assessed w	vith: Number of	people showi	ng ≥50% improve	ment on Montgomery	y Asberg Depressio	n Rating Sc	ale (MADRS))		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	167/229 (72.9%)	170/243 (70%)	RR 1.04 (0.93 to 1.17)	28 more per 1000 (from 49 fewer to 119 more)		
								70%		28 more per 1000 (from 49 fewer to 119 more)		
espons	e (follow-up	mean 8 we	eks; assessed w	ith: Number of	people rated	as much or very r	nuch improved on Cl	inical Global Impres	sions scale	e (CGI-I))		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	176/229 (76.9%)	182/243 (74.9%)	RR 1.03 (0.93 to 1.14)	22 more per 1000 (from 52 fewer to 105 more)		
								74.9%		22 more per 1000 (from 52 fewer to 105 more)		
epressi	on symptom	atology (fo	ollow-up mean 8	weeks; measur	ed with: Quick	Inventory of Dep	oressive Symptomato	ology (QIDS; change	score); Be	tter indicated by I	ower va	lues)
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	229	243	-	MD 0.9 lower (1.88 lower to	⊕⊕OO LOW	

randomi trials		no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>4</sup>	56/238 (23.5%)	53/246 (21.5%)	RR 1.09 (0.78 to 1.52)	19 more per 1000 (from 47 fewer to 112 more)	
								1.02)	,	
							21.5%		19 more per 1000 (from 47 fewer to 112 more)	
ontinuation	ue to adverse	events (follow-	ıp mean 8 weel	s; assessed w	ith: Number of pa	rticipants discontinu	ing due to adverse	events)		
randomi	ed no serious	no serious	no serious	very serious <sup>5</sup>	reporting bias <sup>3</sup>	13/238	13/246	RR 1.03	2 more per 1000	⊕OOO
randomi trials		no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	13/238 (5.5%)	13/246 (5.3%)		2 more per 1000 (from 27 fewer to 62 more)	
				very serious <sup>5</sup>	reporting bias <sup>3</sup>			(0.49 to	(from 27 fewer to 62 more)	VERY
				very serious⁵	reporting bias <sup>3</sup>			(0.49 to	(from 27 fewer to	VERY

<sup>&</sup>lt;sup>1</sup> Unclear blinding of outcome assessment and risk of attrition bias (drop-out>20% [23%]) although difference between groups<20% and ITT analysis

### Increasing the dose of antidepressant versus augmenting with another antidepressant/non-antidepressant agent

			Quality asse	essment			No	o of patients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Increasing the dose of antidepressant	Augmenting with another antidepressant/non-antidepressant agent	Relative (95% CI)	Absolute		
Remissi D))	on (increasir	ng dose of	SSRI versus TC	A augmentatio	on) (follow-u	p mean 4 weeks;	assessed with: Nu	mber of people scoring ≤7 or	n Hamilton	Rating Scale fo	r Depres	sion (HAM-
	randomised trials			no serious indirectness	serious <sup>1</sup>	reporting bias <sup>2</sup>	22/48 (45.8%)	13/46 (28.3%)	RR 1.6 (0.91 to	170 more per 1000 (from 25 fewer to 512	⊕000 VERY	
									2.81)	more)	LOW	
								27.2%		163 more per 1000 (from 24		

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted/is not reported for all outcomes and study funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>5</sup> 95% CI crosses line of no effect and both threshold for clinically important benefit (RR 0.75) and threshold for clinically important harm (RR 1.25)

_										more)	
si D)		ng dose of	SSRI versus li	thium augmen	tation) (folio	ow-up mean 4 weel	s; assessed with: N	umber of people scoring	g ≤7 on Hamilt	on Rating Scale	for Depress
	randomised ser trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>2</sup>	22/48 (45.8%)	12/48 (25%)	RR 1.83 (1.03 to 3.25)	208 more per 1000 (from 7 more to 562 more)	⊕OOO VERY LOW
								26.1%		217 more per 1000 (from 8 more to 587 more)	
	on (increasir ion (HAM-D)		SSRI versus T	eCA [mianseri	n] augment	ation) (follow-up m	ean 4 weeks; assess	ed with: Number of peo	pple scoring ≤7	on Hamilton Ra	ating Scale 1
	randomised trials	serious <sup>5</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>2</sup>	28/97 (28.9%)	43/98 (43.9%)	RR 0.66 (0.45 to 0.97)	149 fewer per 1000 (from 13 fewer to 241 fewer)	⊕OOO VERY LOW
								43.9%		149 fewer per 1000 (from 13 fewer to 241 fewer)	
	se (increasin Scale for Dep			eCA [mianserin	augmenta	ation) (follow-up me	ean 5 weeks; assess	ed with: Number of peo	ple showing ≥ŧ	/	nt on Hamil
	randomised trials	serious <sup>5</sup>	no serious inconsistency	no serious indirectness	serious <sup>6</sup>	reporting bias <sup>2</sup>	54/97 (55.7%)	66/98 (67.3%)	RR 0.83 (0.66 to 1.03)	114 fewer per 1000 (from 229 fewer to 20 more)	⊕000 VERY LOW
								67.4%		115 fewer per 1000 (from 229 fewer to 20 more)	
	se (increasin Global Impre			eCA [mianserir	i] augmenta	ation) (follow-up me	ean 5 weeks; assess	ed with: Number of peo	ple rated as m	uch or very muc	h improved
	randomised	serious <sup>5</sup>	no serious	no serious	serious <sup>6</sup>	reporting bias <sup>2</sup>	66/97	76/98		93 fewer per	

									RR 0.88	forwar to 21	0000	
									(0.74 to	fewer to 31 more)	⊕OOO VERY	
									1.04)	more)	LOW	
									1.04)	93 fewer per	LOVV	
										1000 (from 202		
								77.6%		fewer to 31		
										more)		
onrossio	on sympton	natology (	ilnereasing dos	o of SSRI vers	us TCA aug	mentation) (follow	-un maan 4 waaks:	measured with: Hamilton F	Pating Scale	/	(HAM-D:	change
	etter indica			or or oor word	uo ron uug	inontation) (ronow	up moun + wooks,	modulou with hamilton i	tuting Courc	TOT Depression	(IIIAIII D,	onunge
r	andomised	serious <sup>3</sup>	serious <sup>7</sup>	no serious	serious8	reporting bias <sup>2</sup>	48	46	-	MD 2.97 lower	⊕000	
t	rials			indirectness		, ,				(6.08 lower to	VERY	
										0.13 higher)	LOW	
										,		
	on sympton etter indica			e of SSRI vers	us lithium a	ugmentation) (foll	ow-up mean 4 week	s; measured with: Hamilto	n Rating Sca	ale for Depression	on (HAM-I	D; chan
	andomised	serious <sup>3</sup>	no serious	no serious	serious <sup>8</sup>	reporting bias <sup>2</sup>	48	48	-	MD 2 lower	⊕OOO	
t	rials		inconsistency	indirectness						(4.32 lower to	VERY	
										0.33 higher)	LOW	
	uation for a		n (increasing do	ose of SSRI ve	rsus TCA au	igmentation) (follo	w-up mean 4 weeks	; assessed with: Number of	f participant	ts discontinuing	for any r	reason
cluding	g adverse e	vents))	`									reason
r	adverse erandomised	vents))	no serious	no serious	very	reporting bias <sup>2</sup>	5/48	8/46	RR 0.58	73 fewer per	⊕000	reason
r	g adverse e	vents))	`						RR 0.58 (0.21 to	73 fewer per 1000 (from 137	⊕000 VERY	reason
r	adverse erandomised	vents))	no serious	no serious	very		5/48	8/46	RR 0.58	73 fewer per 1000 (from 137 fewer to 111	⊕000	reason
r	adverse erandomised	vents))	no serious	no serious	very		5/48	8/46	RR 0.58 (0.21 to	73 fewer per 1000 (from 137	⊕000 VERY	reason
rcluding	adverse erandomised	vents))	no serious	no serious	very		5/48	8/46	RR 0.58 (0.21 to	73 fewer per 1000 (from 137 fewer to 111 more)	⊕000 VERY	reason
r	adverse erandomised	vents))	no serious	no serious	very		5/48	8/46	RR 0.58 (0.21 to	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157	⊕000 VERY	reason
cluding r	adverse erandomised	vents))	no serious	no serious	very		5/48	8/46 (17.4%)	RR 0.58 (0.21 to	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127	⊕000 VERY	reason
r t	g adverse e randomised rials	vents)) serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>9</sup>	reporting bias <sup>2</sup>	5/48 (10.4%)	8/46 (17.4%)	RR 0.58 (0.21 to 1.64)	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127 more)	⊕OOO VERY LOW	
r t	g adverse e randomised rials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>9</sup>	reporting bias <sup>2</sup>	5/48 (10.4%)	8/46 (17.4%)	RR 0.58 (0.21 to 1.64)	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127 more)	⊕OOO VERY LOW	
sconting	randomised rials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%)	RR 0.58 (0.21 to 1.64)	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127 more) ants discontinui	⊕OOO VERY LOW	
sconting	randomised rials  uation for a gadverse e	serious <sup>3</sup>	no serious inconsistency	no serious indirectness  ose of SSRI vei	very serious <sup>9</sup>	reporting bias <sup>2</sup>	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Number	RR 0.58 (0.21 to 1.64)	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127 more) ants discontinui	⊕OOO VERY LOW	
sconting	randomised rials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Numbe	RR 0.58 (0.21 to 1.64) r of participal	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127 more) ants discontinui	⊕OOO VERY LOW	
sconting	randomised rials  uation for a gadverse e	serious <sup>3</sup>	no serious inconsistency	no serious indirectness  ose of SSRI vei	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Number	RR 0.58 (0.21 to 1.64)	73 fewer per 1000 (from 137 fewer to 111 more) 84 fewer per 1000 (from 157 fewer to 127 more) ants discontinui	⊕OOO VERY LOW	
sconting	randomised rials  uation for a gadverse e	serious <sup>3</sup>	no serious inconsistency	no serious indirectness  ose of SSRI vei	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Number	RR 0.58 (0.21 to 1.64) r of participal	73 fewer per 1000 (from 137 fewer to 111 more)  84 fewer per 1000 (from 157 fewer to 127 more)  ants discontinuit  41 fewer per 1000 (from 111 fewer to 162 more)	⊕OOO VERY LOW	
sconting	randomised rials  uation for a gadverse e	serious <sup>3</sup>	no serious inconsistency	no serious indirectness  ose of SSRI vei	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Number	RR 0.58 (0.21 to 1.64) r of participal	73 fewer per 1000 (from 137 fewer to 111 more)  84 fewer per 1000 (from 157 fewer to 127 more)  ants discontinuit  41 fewer per 1000 (from 111 fewer to 162 more)  41 fewer per	⊕OOO VERY LOW	
reluding t t secontin neluding	randomised rials  uation for a gadverse e	serious <sup>3</sup>	no serious inconsistency	no serious indirectness  ose of SSRI vei	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Number 7/48 (14.6%)	RR 0.58 (0.21 to 1.64) r of participal	73 fewer per 1000 (from 137 fewer to 111 more)  84 fewer per 1000 (from 157 fewer to 127 more)  ants discontinuit  41 fewer per 1000 (from 111 fewer to 162 more)  41 fewer per 1000 (from 110	⊕OOO VERY LOW	
r t t iscontin ncluding	randomised rials  uation for a gadverse e	serious <sup>3</sup>	no serious inconsistency	no serious indirectness  ose of SSRI vei	very serious <sup>9</sup>	reporting bias <sup>2</sup> augmentation) (fo	5/48 (10.4%)	8/46 (17.4%) 19.9% eks; assessed with: Number	RR 0.58 (0.21 to 1.64) r of participal	73 fewer per 1000 (from 137 fewer to 111 more)  84 fewer per 1000 (from 157 fewer to 127 more)  ants discontinuit  41 fewer per 1000 (from 111 fewer to 162 more)  41 fewer per	⊕OOO VERY LOW	

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<sup>195%</sup> CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>2</sup> Data cannot be extracted/is not reported for all outcomes and/or funding from pharmaceutical company

<sup>&</sup>lt;sup>3</sup> Unclear randomization method and allocation concealment and unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>4</sup> Events<300

<sup>&</sup>lt;sup>5</sup> Unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>&</sup>lt;sup>7</sup> I-squared>50%

<sup>&</sup>lt;sup>8</sup> 95% CI crosses both line of effect and threshold for clinically important benefit (SMD -0.5)

<sup>95%</sup> CI crosses line of no effect and both threshold for clinically important benefit (RR 0.75) and threshold for clinically important harm (RR 1.25)

Augmenting the antidepressant with another antidepressant or a non-antidepressant agent versus placebo 1 **Quality assessment** No of patients **Effect** Quality Importance Augmenting the No of Risk of Other antidepressant with another Relative Design Inconsistency Indirectness **Imprecision** Placebo **Absolute** studies bias considerations antidepressant or a non-(95% CI) antidepressant agent Remission (atypical antidepressant) (follow-up mean 4 weeks; assessed with: Number of people scoring ≤7 on Hamilton Rating Scale for Depression (HAM-D)) randomised serious1 no serious no serious serious<sup>2</sup> reporting bias<sup>3</sup> 23/41 9/45 RR 2.72 344 more per  $\oplus$ OOO 1000 (from 88 trials inconsistency indirectness (56.1%)(20%)(1.44 to **VERY** 5.14) more to 828 LOW more) 315 more per 1000 (from 81 18.3% more to 758 more) Remission (antipsychotic) (follow-up 4-8 weeks; assessed with: Number of people scoring <10/11 on Montgomery Asberg Depression Rating Scale (MADRS)/≤7 on Hamilton Rating Scale for Depression (HAM-D)) 226/1173 randomised serious4 no serious no serious reporting bias3 500/1408 RR 1.56 108 more per no serious ⊕⊕ОО trials inconsistency indirectness imprecision (35.5%)(19.3%) (1.36 to 1000 (from 69 LOW 1.78) more to 150 more) 96 more per 1000 17.2% (from 62 more to 134 more) Remission (lithium) (follow-up 2-6 weeks; assessed with: Number of people scoring ≤7 on Hamilton Rating Scale for Depression (HAM-D)) randomised serious1 serious<sup>2</sup> reporting bias3 24/54 12/56 RR 2.07 229 more per no serious no serious  $\oplus$ OOO trials inconsistency indirectness (44.4%) (21.4%)(1.16 to 1000 (from 34 **VERY** 3.69) more to 576 LOW more) 267 more per 1000 (from 40 25%

more to 673 more)

randomise	serious1	no serious	no serious	serious <sup>5</sup>	none	7/17	2/16	RR 3.29	286 more per	⊕⊕00
trials		inconsistency	indirectness	30040		(41.2%)	(12.5%)	(0.8 to	1000 (from 25	LOW
						(111=71)	(1210,10)	13.57)	fewer to 1000	2011
								, ,	more)	
									286 more per	
							12.5%		1000 (from 25	
							12.070		fewer to 1000	
-!	. 4 5 41 1				 		14 D-+i O-	-l- f D	more)	
sion (stimula	nt įmetnyip	nenidatej) (follov	v-up mean 4 we	eeks; assessed	with: Number of	people scoring ≤7 on Hamil	iton Rating Sc	ale for Dep	ression (HAM-D))	
randomise	serious <sup>1</sup>	no serious	no serious	very serious <sup>6</sup>	reporting bias <sup>3</sup>	4/30		RR 4 (0.47	100 more per	⊕OOO
trials		inconsistency	indirectness			(13.3%)	(3.3%)	to 33.73)	1000 (from 18	VERY
									fewer to 1000	LOW
									more)	
									99 more per 1000	
							3.3%		(from 17 fewer to	
onse (any aug	mentation a	agent) (follow-up	0 3-12 weeks:	assessed with	Number of people	e showing >50% improvem		on Rating S	` 1000 more)	on (HAM.
		gent) (follow-up sion Rating Scal		assessed with		e showing ≥50% improvem	ent on Hamilto		1000 more) cale for Depressi	on (HAM-
randomise	erg Depres	no serious	no serious	no serious	Number of people reporting bias <sup>3</sup>	759/1689	ent on Hamilton	RR 1.35	1000 more) cale for Depression 102 more per	on (HAM-
tgomery Asl	erg Depres	sion Rating Scal	e (MADRS))				ent on Hamilto	RR 1.35 (1.23 to	1000 more) cale for Depression 102 more per 1000 (from 67	,
randomise	erg Depres	no serious	no serious	no serious		759/1689	ent on Hamilton	RR 1.35	1000 more) cale for Depression 102 more per	⊕⊕OO
randomise	erg Depres	no serious	no serious	no serious		759/1689	ent on Hamilton	RR 1.35 (1.23 to	1000 more) cale for Depression 102 more per 1000 (from 67	⊕⊕OO
randomise	erg Depres	no serious	no serious	no serious		759/1689	ent on Hamilton	RR 1.35 (1.23 to	1000 more) cale for Depression 102 more per 1000 (from 67 more to 143 more)	⊕⊕OO
randomise	erg Depres	no serious	no serious	no serious		759/1689	ent on Hamilton	RR 1.35 (1.23 to	1000 more) cale for Depression 102 more per 1000 (from 67 more to 143	⊕⊕OO
randomise trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	759/1689 (44.9%)	416/1421 (29.3%) 25.3%	RR 1.35 (1.23 to 1.49)	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)	⊕⊕OO LOW
randomise trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	759/1689	416/1421 (29.3%) 25.3%	RR 1.35 (1.23 to 1.49)	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)	⊕⊕OO LOW
randomise trials	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness  nean 4 weeks;	no serious imprecision	reporting bias <sup>3</sup>	759/1689 (44.9%) le showing ≥50% improvem	416/1421 (29.3%) 25.3% nent on Hamilt	RR 1.35 (1.23 to 1.49) on Rating S	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  Scale for Depression	⊕⊕OO LOW
randomise trials	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup> : Number of peop	759/1689 (44.9%)	416/1421 (29.3%) 25.3%	RR 1.35 (1.23 to 1.49)	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  Scale for Depression	⊕⊕OO LOW
randomise trials  rase (atypical randomise)	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness  nean 4 weeks;	no serious imprecision	reporting bias <sup>3</sup> : Number of peop	759/1689 (44.9%) le showing ≥50% improvem	416/1421 (29.3%) 25.3% nent on Hamilt	RR 1.35 (1.23 to 1.49) on Rating S	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  Scale for Depression	⊕⊕OO LOW
randomise trials  nse (atypical randomise)	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness  nean 4 weeks;	no serious imprecision	reporting bias <sup>3</sup> : Number of peop	759/1689 (44.9%) le showing ≥50% improvem	416/1421 (29.3%) 25.3% nent on Hamilt	RR 1.35 (1.23 to 1.49) on Rating S RR 3.18 (1.05 to	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  Scale for Depression  436 more per 1000 (from 10	⊕⊕00 LOW ton (HAM ⊕000 VERY
randomise trials  nse (atypical randomise)	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness  nean 4 weeks;	no serious imprecision	reporting bias <sup>3</sup> : Number of peop	759/1689 (44.9%) le showing ≥50% improvem	416/1421 (29.3%) 25.3% nent on Hamilt	RR 1.35 (1.23 to 1.49) on Rating S RR 3.18 (1.05 to	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  Scale for Depression  436 more per 1000 (from 10 more to 1000	⊕⊕00 LOW ton (HAM ⊕000 VERY
randomise trials  nse (atypical randomise)	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness  nean 4 weeks;	no serious imprecision	reporting bias <sup>3</sup> : Number of peop	759/1689 (44.9%) le showing ≥50% improvem	25.3%  ent on Hamilto 25.3%  ent on Hamilto 3/15 (20%)	RR 1.35 (1.23 to 1.49) on Rating S RR 3.18 (1.05 to	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  6cale for Depression  436 more per 1000 (from 10 more to 1000 more)  436 more per 1000 (from 10 more)	⊕⊕00 LOW ton (HAM ⊕000 VERY
randomise trials  onse (atypical randomise)	serious <sup>4</sup>	no serious inconsistency sant) (follow-up r	no serious indirectness  nean 4 weeks;	no serious imprecision	reporting bias <sup>3</sup> : Number of peop	759/1689 (44.9%) le showing ≥50% improvem	416/1421 (29.3%) 25.3% nent on Hamilt	RR 1.35 (1.23 to 1.49) on Rating S RR 3.18 (1.05 to	1000 more) cale for Depression  102 more per 1000 (from 67 more to 143 more)  89 more per 1000 (from 58 more to 124 more)  6cale for Depression  436 more per 1000 (from 10 more to 1000 more)  436 more per	⊕⊕00 LOW ton (HAM ⊕000 VERY

l r	randomised	serious4	no serious	no serious	no serious	reporting bias3	660/1420	344/1184	RR 1.4	116 more per	⊕⊕00
	rials	5511545	inconsistency	indirectness	imprecision	roporting side	(46.5%)	(29.1%)	(1.25 to	1000 (from 73	LOW
			, , , , , , , ,				( = = = = ,	(	1.57)	more to 166	
									,	more)	
										,	
										114 more per	
								28.5%		1000 (from 71	
								20.570		more to 162	
		l		1	<u> </u>					more)	
sponse	e (lithium) (f	follow-up (	.3-6 weeks; asse	essed with: Nu	nber of people	showing ≥50% in	nprovement on Hamilton Ra	iting Scale for	Depression	n (HAM-D))	
r	randomised	serious4	no serious	no serious	very serious <sup>6</sup>	reporting bias <sup>3</sup>	9/38	6/38	RR 1.55	87 more per 1000	⊕000
t	rials		inconsistency	indirectness			(23.7%)	(15.8%)	(0.61 to	(from 62 fewer to	VERY
									3.91)	459 more)	LOW
								45 40/		83 more per 1000	
								15.1%		(from 59 fewer to 439 more)	
										439 111016)	
		ılsant [lam	otrigine]) (follow	-up 8-10 weeks	s; assessed wit	h: Number of pec	pple showing ≥50% improve	ment on Mont	gomery As	berg Depression	Rating So
r (r		very serious <sup>7</sup>	no serious inconsistency	no serious indirectness	very serious <sup>6</sup>	h: Number of peo	pple showing ≥50% improve  21/65  (32.3%)	22/65 (33.8%)	RR 0.96 (0.59 to	14 fewer per 1000 (from 139	⊕OOO VERY
r (r	randomised	very	no serious	no serious			21/65	22/65	RR 0.96	14 fewer per	⊕000
r (r	randomised	very	no serious	no serious			21/65	22/65	RR 0.96 (0.59 to	14 fewer per 1000 (from 139 fewer to 190 more)	⊕000 VERY
r (r	randomised	very	no serious	no serious			21/65	22/65 (33.8%)	RR 0.96 (0.59 to	14 fewer per 1000 (from 139 fewer to 190 more) 14 fewer per 1000 (from 141	⊕000 VERY
ADRS))	randomised	very	no serious	no serious			21/65	22/65	RR 0.96 (0.59 to	14 fewer per 1000 (from 139 fewer to 190 more) 14 fewer per 1000 (from 141 fewer to 192	⊕000 VERY
ADRS))	randomised trials	very serious <sup>7</sup>	no serious inconsistency	no serious indirectness	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65 (32.3%)	22/65 (33.8%) 34.3%	RR 0.96 (0.59 to 1.56)	14 fewer per 1000 (from 139 fewer to 190 more) 14 fewer per 1000 (from 141 fewer to 192 more)	⊕OOO VERY LOW
r t	randomised trials	very serious <sup>7</sup>	no serious inconsistency	no serious indirectness	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65	22/65 (33.8%) 34.3%	RR 0.96 (0.59 to 1.56)	14 fewer per 1000 (from 139 fewer to 190 more) 14 fewer per 1000 (from 141 fewer to 192 more)	⊕OOO VERY LOW
r t	randomised trials	very serious <sup>7</sup>	no serious inconsistency  (follow-up mean no serious	no serious indirectness  12 weeks; ass	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65 (32.3%) howing ≥50% improvement	22/65 (33.8%) 34.3% on Montgome	RR 0.96 (0.59 to 1.56) ry Asberg	14 fewer per 1000 (from 139 fewer to 190 more)  14 fewer per 1000 (from 141 fewer to 192 more)  Depression Rating	⊕OOO VERY LOW
r t esponse	randomised trials	very serious <sup>7</sup>	no serious inconsistency	no serious indirectness  12 weeks; ass	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65 (32.3%) howing ≥50% improvement	22/65 (33.8%) 34.3% on Montgome	RR 0.96 (0.59 to 1.56) ry Asberg  RR 1.31 (0.51 to	14 fewer per 1000 (from 139 fewer to 190 more)  14 fewer per 1000 (from 141 fewer to 192 more)  Depression Rating 73 more per 1000 (from 115 fewer	⊕OOO VERY LOW
r t	randomised trials  e (omega-3 randomised	very serious <sup>7</sup>	no serious inconsistency  (follow-up mean no serious	no serious indirectness  12 weeks; ass	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65 (32.3%) howing ≥50% improvement	22/65 (33.8%) 34.3% on Montgome	RR 0.96 (0.59 to 1.56) ry Asberg	14 fewer per 1000 (from 139 fewer to 190 more)  14 fewer per 1000 (from 141 fewer to 192 more)  Depression Rating	⊕OOO VERY LOW
r t esponse	randomised trials  e (omega-3 randomised	very serious <sup>7</sup>	no serious inconsistency  (follow-up mean no serious	no serious indirectness  12 weeks; ass	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65 (32.3%) howing ≥50% improvement	22/65 (33.8%) 34.3% on Montgome	RR 0.96 (0.59 to 1.56) ry Asberg  RR 1.31 (0.51 to	14 fewer per 1000 (from 139 fewer to 190 more)  14 fewer per 1000 (from 141 fewer to 192 more)  Depression Rating 73 more per 1000 (from 115 fewer to 560 more)	⊕OOO VERY LOW
r t esponse	randomised trials  e (omega-3 randomised	very serious <sup>7</sup>	no serious inconsistency  (follow-up mean no serious	no serious indirectness  12 weeks; ass	very serious <sup>6</sup>	reporting bias <sup>3</sup>	21/65 (32.3%) howing ≥50% improvement	22/65 (33.8%) 34.3% on Montgome	RR 0.96 (0.59 to 1.56) ry Asberg  RR 1.31 (0.51 to	14 fewer per 1000 (from 139 fewer to 190 more)  14 fewer per 1000 (from 141 fewer to 192 more)  Depression Rating 73 more per 1000 (from 115 fewer	⊕OOO VERY LOW

randomised		no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	46/103	37/102		76 more per 1000		
trials	serious <sup>7</sup>	inconsistency	indirectness			(44.7%)	(36.3%)	(0.87 to	(from 47 fewer to	VERY	
								1.68)	247 more)	LOW	
									68 more per 1000		
							32.5%		(from 42 fewer to		
									221 more)		
ponse (any augr	nentation a	gent) (follow-up	4-8 weeks; ass	essed with: Nu	mber of people ra	ated as much or very much in	mproved on	Clinical Glo	obal Impressions	scale (CGI	I <b>-I</b> ))
randomised	serious <sup>4</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	46/127	37/130	RR 1.29	83 more per 1000	⊕000	
trials		inconsistency	indirectness			(36.2%)	(28.5%)	(0.85 to	(from 43 fewer to	VERY	
						` ,	, ,	1.97)	276 more)	LOW	
									77 more per 1000		
							26.7%		(from 40 fewer to		
									259 more)		
ponse (atypical a	intidepress	ant) (follow-up n	nean 4 weeks; a	issessed with:	Number of peop	le rated as much or very much	ch improved	on Clinical	Global Impressio	ns scale (	CGI-
randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	7/11	3/15	RR 3.18	436 more per	⊕000	
trials		inconsistency	indirectness			(63.6%)	(20%)	(1.05 to	1000 (from 10	VERY	
								9.62)	more to 1000	LOW	
									more)		
									436 more per		
							20%		1000 (from 10		
							20 /0		more to 1000		
	·								more)		
(1141.1	r qu-wollot	nean 6 weeks: as	ssessed with: N	umber of peop	ole rated as much	or vary much improved on (	Clinical Globs	al Impressi	one ecala (CCILIV)		
ponse (lithium) (		o moono, ut				or very mach improved on c	Jiiiicai Glob		ons scale (col-i))		
randomised		no serious	no serious	very serious <sup>6</sup>	reporting bias <sup>3</sup>	5/18	4/17	RR 1.18	42 more per 1000		
		_		very serious <sup>6</sup>				RR 1.18 (0.38 to	42 more per 1000 (from 146 fewer	⊕000 VERY	
randomised		no serious	no serious	very serious <sup>6</sup>		5/18	4/17	RR 1.18	42 more per 1000		
randomised		no serious	no serious	very serious <sup>6</sup>		5/18	4/17	RR 1.18 (0.38 to	42 more per 1000 (from 146 fewer	VERY	
randomised		no serious	no serious	very serious <sup>6</sup>		5/18	4/17	RR 1.18 (0.38 to	42 more per 1000 (from 146 fewer to 628 more)	VERY	
randomised		no serious	no serious	very serious <sup>6</sup>		5/18	4/17 (23.5%)	RR 1.18 (0.38 to	42 more per 1000 (from 146 fewer to 628 more) 42 more per 1000	VERY	
randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	·	reporting bias <sup>3</sup>	5/18	4/17 (23.5%) 23.5%	RR 1.18 (0.38 to 3.67)	42 more per 1000 (from 146 fewer to 628 more) 42 more per 1000 (from 146 fewer to 627 more)	VERY LOW	cale (
randomised trials ponse (anticonv	serious <sup>1</sup>	no serious inconsistency otrigine]) (follow	no serious indirectness	eks; assessed	reporting bias <sup>3</sup> with: Number of p	5/18 (27.8%)	4/17 (23.5%) 23.5%	RR 1.18 (0.38 to 3.67)	42 more per 1000 (from 146 fewer to 628 more) 42 more per 1000 (from 146 fewer to 627 more) nical Global Impre	VERY LOW	cale ((
randomised trials  ponse (anticonv	serious <sup>1</sup>	no serious inconsistency otrigine]) (follow	no serious indirectness  y-up mean 8 wee	eks; assessed	reporting bias <sup>3</sup>	5/18 (27.8%) Deople rated as much or very	4/17 (23.5%) 23.5% y much impro	RR 1.18 (0.38 to 3.67)	42 more per 1000 (from 146 fewer to 628 more) 42 more per 1000 (from 146 fewer to 627 more) nical Global Impre	VERY LOW	cale (C
randomised trials ponse (anticonv	serious <sup>1</sup>	no serious inconsistency otrigine]) (follow	no serious indirectness	eks; assessed	reporting bias <sup>3</sup> with: Number of p	5/18 (27.8%)	4/17 (23.5%) 23.5%	RR 1.18 (0.38 to 3.67) oved on Cli RR 0.67 (0.23 to	42 more per 1000 (from 146 fewer to 628 more) 42 more per 1000 (from 146 fewer to 627 more) nical Global Impres	VERY LOW  essions so  OVERY	cale ((
randomised trials  ponse (anticonv	serious <sup>1</sup>	no serious inconsistency otrigine]) (follow	no serious indirectness  y-up mean 8 wee	eks; assessed	reporting bias <sup>3</sup> with: Number of p	5/18 (27.8%) Deople rated as much or very	4/17 (23.5%) 23.5% y much impro	RR 1.18 (0.38 to 3.67)	42 more per 1000 (from 146 fewer to 628 more) 42 more per 1000 (from 146 fewer to 627 more) nical Global Impre	VERY LOW	cale (

								35.3%		1000 (from 272 fewer to 335	
										more)	
ns	e (anxiolytic	) (follow-up	mean 6 weeks;	assessed with	n: Number of p	eople rated as mu	ich or very much improved o	on Clinical Gl	obal Impre	ssions scale (CGI	-I))
	randomised	serious <sup>10</sup>	no serious	no serious	very serious <sup>6</sup>	reporting bias <sup>3</sup>	17/51	16/51	RR 1.06	19 more per 1000	⊕000
	trials		inconsistency	indirectness	,	, ,	(33.3%)	(31.4%)	(0.61 to	(from 122 fewer	VERY
									1.86)	to 270 more)	LOW
										19 more per 1000	
								31.4%		(from 122 fewer	
						ļ	eople rated as much or ver			to 270 more)	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	13/30 (43.3%)	8/30 (26.7%)	RR 1.62 (0.79 to 3.34)	165 more per 1000 (from 56 fewer to 624	⊕000 VERY
									3.34)	more)	LOW
										166 more per 1000 (from 56	
								26.7%		fewer to 625	
/al	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>11</sup>	reporting bias <sup>3</sup>	th: Hamilton Rating Scale fo	r Depression	(HAM-D; c	SMD 1.12 lower	⊕000
	trials		inconsistency	indirectness						(1.96 to 0.27 lower)	VERY LOW
			ntipsychotic) (fol score); Better ind			l with: Hamilton R	ating Scale for Depression (	HAM-D; chan	ge score)/	Montgomery Asbe	rg Depres
	randomised	serious <sup>4</sup>	serious <sup>12</sup>	no serious	serious <sup>13</sup>	reporting bias <sup>3</sup>	172	290	-	SMD 0.4 lower	⊕OOO
	trials			indirectness						(0.86 lower to 0.06 higher)	VERY LOW
							cale for Depression (HAM-D				

	randomised	serious <sup>4</sup>	no serious	no serious	serious <sup>13</sup>	reporting bias <sup>3</sup>	41	42	_	SMD 0.23 lower	$\oplus$ OOO	
	trials	ocriodo	inconsistency	indirectness	ocilous	reporting bids	41	72		(0.86 lower to	VERY	
										0.39 higher)	LOW	
										5.55 mg.15.7	2011	
epress	ion sympton	natology (th	yroid hormone	[T3]) (follow-up	mean 2 weeks	s; measured with:	<b>Hamilton Rating Scale for Dep</b>	ression (H	AM-D; cha	nge score); Bette	r indicate	d by lowe
alues)												
										1		
		serious <sup>14</sup>	no serious	no serious	serious <sup>11</sup>	none	17	16	-	SMD 0.78 lower	⊕⊕00	
	trials		inconsistency	indirectness						(1.5 to 0.07	LOW	
										lower)		
onross	ion symptom	atology (a)	nticonvulsant [la	motriginal) (fo	llow-up 8-10 w	ooks, mossilled a	l vith: Montgomery Asberg Depre	ession Rat	ing Scale (	MADRS: change	score). B	ottor
	d by lower va		inticonvalsant pe	amoungme]) (10	110W-up 0-10 W	cons, measurea v	viiii. Monigomery Asserg Bepro	coolon ita	ing ocale (	inabito, change	score, D	ottoi
	,	,										
	randomised	very	no serious	no serious	serious <sup>13</sup>	reporting bias3	65	65	-	SMD 0.13 lower	⊕000	
	trials	serious15	inconsistency	indirectness		3				(0.54 lower to	VERY	
			,							0.27 higher)	LOW	
										<b>3</b> ,		
	ion symptom d by lower va		timulant [methyl	pnenidatej) (fo	now-up mean :	o weeks, illeasure	d with: Montgomery Asberg De	pression	Nating Sca	ile (MADICO, Chang	go 000.0,	, Detter
	d by lower va					· 			Rating Sca		go 000.0,	, Detter
	d by lower va	very	no serious	no serious	serious <sup>11</sup>	reporting bias <sup>3</sup>	72	72	-	SMD 0.06 higher	⊕000	, Detter
	d by lower va	lues)				· 			- -	SMD 0.06 higher (0.27 lower to	⊕000 VERY	, Detter
	d by lower va	very	no serious	no serious		· 			-	SMD 0.06 higher	⊕000	, Detter
dicate	randomised trials	very serious <sup>16</sup>	no serious inconsistency	no serious indirectness	serious <sup>11</sup>	reporting bias <sup>3</sup>		72	-	SMD 0.06 higher (0.27 lower to 0.38 higher)	⊕OOO VERY LOW	
dicate	randomised trials	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness pressant) (follow	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 scontinuin	- g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)	⊕OOO VERY LOW	
dicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> //eeks; assessed w	72 vith: Number of participants dis	72 Scontinuin	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher) eason (including a	⊕OOO VERY LOW	
dicate	randomised trials	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness pressant) (follow	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 scontinuin	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41	⊕OOO VERY LOW adverse e	
dicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 Scontinuin	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249	⊕OOO VERY LOW	
dicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 Scontinuin	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41	⊕OOO VERY LOW adverse e	
dicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 Scontinuin	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)	⊕OOO VERY LOW adverse e	
dicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 scontinuin 2/45 (4.4%)	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 fewer per 1000 fewer to 249 more)	⊕OOO VERY LOW adverse e	
dicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 Scontinuin	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 (from 62	⊕OOO VERY LOW adverse e	
ndicate	randomised trials inuation for a	very serious <sup>16</sup>	no serious inconsistency (atypical antider	no serious indirectness oressant) (follow no serious	serious <sup>11</sup> w-up mean 4 w	reporting bias <sup>3</sup> veeks; assessed w	72 vith: Number of participants dis	72 scontinuin 2/45 (4.4%)	g for any re	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 fewer per 1000 fewer to 249 more)	⊕OOO VERY LOW adverse e	
isconti	randomised trials  Inuation for a randomised trials	very serious 16  ny reason serious 1	no serious inconsistency  (atypical antider no serious inconsistency	no serious indirectness  pressant) (following serious indirectness	serious <sup>11</sup> w-up mean 4 w  very serious <sup>17</sup>	reporting bias <sup>3</sup> /eeks; assessed w	72 vith: Number of participants dis	72 scontinuin 2/45 (4.4%)	RR 0.68 (0.07 to 6.61)	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 (from 62 fewer to 376 more)	⊕OOO VERY LOW adverse e	
isconti	randomised trials  inuation for a randomised trials	very serious 16  ny reason  serious 1	no serious inconsistency  (atypical antider no serious inconsistency  (antipsychotic) (	no serious indirectness oressant) (followindirectness indirectness indirectness of the following the following 4-8 versions in	w-up mean 4 w very serious <sup>17</sup>	reporting bias <sup>3</sup> reeks; assessed was reporting bias <sup>3</sup>	vith: Number of participants dis	72 scontinuin 2/45 (4.4%)	RR 0.68 (0.07 to 6.61)	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 (from 62 fewer to 376 more)  ng adverse events	⊕OOO VERY LOW DOON VERY LOW LOW	
isconti	randomised trials inuation for a randomised trials inuation for a randomised trials	very serious 16  ny reason  serious 1	no serious inconsistency  (atypical antider no serious inconsistency  (antipsychotic) (antipsychotic) (no serious	no serious indirectness oressant) (followindirectness indirectness ind	very serious <sup>17</sup> veeks; assesse	reporting bias <sup>3</sup> /eeks; assessed w	72  vith: Number of participants dis  1/41 (2.4%)  f participants discontinuing for  265/1480	72 scontinuin 2/45 (4.4%) 6.7%	RR 0.68 (0.07 to 6.61)	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 (from 62 fewer to 376 more)  ng adverse events  32 more per 1000	⊕OOO VERY LOW adverse e ⊕OOO VERY LOW	
isconti	randomised trials  inuation for a randomised trials	very serious 16  ny reason  serious 1	no serious inconsistency  (atypical antider no serious inconsistency  (antipsychotic) (	no serious indirectness oressant) (followindirectness indirectness indirectness of the following the following 4-8 versions in	w-up mean 4 w very serious <sup>17</sup>	reporting bias <sup>3</sup> reeks; assessed was reporting bias <sup>3</sup>	vith: Number of participants dis	72 scontinuin 2/45 (4.4%)	RR 0.68 (0.07 to 6.61)	SMD 0.06 higher (0.27 lower to 0.38 higher)  eason (including a 14 fewer per 1000 (from 41 fewer to 249 more)  21 fewer per 1000 (from 62 fewer to 376 more)  ng adverse events	⊕OOO VERY LOW DOON VERY LOW LOW	

				1				14.1%		34 more per 1000 (from 3 more to		
								14.170		73 more)		
onti	nuation for a	nv reason (	(lithium) (follow-	up 2-6 weeks:	assessed with:	Number of parti	cipants discontinuing for any	reason (inc	luding adve			
			() (	тр = с посто,		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,	(	g	,,		
	randomised	serious <sup>1</sup>	no serious	no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup>	10/99	12/101	RR 0.87	15 fewer per	⊕000	
	trials		inconsistency	indirectness			(10.1%)	(11.9%)		1000 (from 70	VERY	
									1.84)	fewer to 100	LOW	
										more)		
										7 fewer per 1000		
								5.6%		(from 33 fewer to		
								0.070		47 more)		
cont	nuation for a	ny reason	(thyroid hormon	e [T3]) (follow-	up mean 2 wee	ks; assessed wit	h: Number of participants dis	scontinuing	for any reas	son (including adv	verse eve	ents)
		1 . 14			. 2		0.07	0/0/				
		serious <sup>14</sup>	no serious	no serious	serious <sup>2</sup>	none	0/27	0/24	not pooled	not pooled	⊕⊕OO	
	trials		inconsistency	indirectness			(0%)	(0%)			LOW	
								0%		not pooled		
scont	nuation for a	ny reason i	(anticonvulsant	[lamotrigine]) (	follow-up 8-10	weeks: assessed	with: Number of participant		ing for any		adverse	eve
scont	nuation for a	ny reason	(anticonvulsant	[lamotrigine]) (	follow-up 8-10	weeks; assessed	with: Number of participants		ing for any		adverse	eve
scont	randomised	very	no serious	[lamotrigine]) (		weeks; assessed reporting bias <sup>3</sup>	17/65	s discontinu	RR 0.81	reason (including	⊕OOO	eve
scont	randomised	very						s discontinu	RR 0.81 (0.48 to	reason (including 61 fewer per 1000 (from 168		eve
scont	randomised	very	no serious	no serious			17/65	s discontinu	RR 0.81	reason (including	⊕OOO	eve
scont	randomised	very	no serious	no serious			17/65	s discontinu	RR 0.81 (0.48 to	reason (including 61 fewer per 1000 (from 168	⊕000 VERY	eve
scont	randomised	very	no serious	no serious			17/65	s discontinu	RR 0.81 (0.48 to	reason (including 61 fewer per 1000 (from 168 fewer to 123 more)	⊕000 VERY	eve
scont	randomised	very	no serious	no serious			17/65	21/65 (32.3%)	RR 0.81 (0.48 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per	⊕000 VERY	eve
scont	randomised	very	no serious	no serious			17/65	s discontinu	RR 0.81 (0.48 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153	⊕000 VERY	eeve
scont	randomised	very	no serious	no serious			17/65	21/65 (32.3%)	RR 0.81 (0.48 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per	⊕000 VERY	eve
	randomised trials	very serious <sup>19</sup>	no serious inconsistency	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65	21/65 (32.3%) 29.5%	RR 0.81 (0.48 to 1.38)	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)	#OOO VERY LOW	eve
	randomised trials	very serious <sup>19</sup>	no serious inconsistency	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%)	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38)	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events	⊕OOO VERY LOW	e eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folice no serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38)	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events  78 fewer per	⊕000 VERY LOW	eve
	randomised trials	very serious <sup>19</sup>	no serious inconsistency	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%)	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38) con (includial RR 0.6 (0.24 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events  78 fewer per 1000 (from 149	⊕OOO VERY LOW	eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folice no serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38)	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events  78 fewer per	⊕000 VERY LOW	eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folice no serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38) con (includial RR 0.6 (0.24 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events  78 fewer per 1000 (from 149	⊕OOO VERY LOW	eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folicino serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38) con (includial RR 0.6 (0.24 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events  78 fewer per 1000 (from 149 fewer to 104 more)	⊕OOO VERY LOW	eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folicino serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38) con (includial RR 0.6 (0.24 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  78 fewer per 1000 (from 149 fewer to 104 more)  78 fewer per	⊕OOO VERY LOW	eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folicino serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38) con (includial RR 0.6 (0.24 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  ng adverse events  78 fewer per 1000 (from 149 fewer to 104 more)  78 fewer per 1000 (from 149	⊕OOO VERY LOW	eve
	randomised trials  nuation for a	very serious <sup>19</sup>	no serious inconsistency  (anxiolytic) (folicino serious	no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	17/65 (26.2%) of participants discontinuing	21/65 (32.3%) 29.5% for any reas	RR 0.81 (0.48 to 1.38) con (includial RR 0.6 (0.24 to	reason (including  61 fewer per 1000 (from 168 fewer to 123 more)  56 fewer per 1000 (from 153 fewer to 112 more)  78 fewer per 1000 (from 149 fewer to 104 more)  78 fewer per	⊕OOO VERY LOW	eve

	randomised	no serious	no serious	no serious	very serious 17	reporting bias3	6/52	4/18	RR 0.52	107 fewer per	⊕OOO
			inconsistency	indirectness	very serious	reporting blus	(11.5%)	(22.2%)	(0.17 to	1000 (from 184	VERY
ľ				in tail ooti 1000			(1.1.67%)	(==:= /5)	1.63)	fewer to 140	LOW
									1.00)	more)	2011
										moro)	
										107 fewer per	
								22.2%		1000 (from 184	
								22.2%		fewer to 140	
										more)	
scontir	uation for a	ny reason (	stimulant [meth	ylphenidate]) (1	follow-up meai	n 5 weeks; assess	sed with: Number of participan	ts discont	inuing for a	ny reason (includ	ing adverse
ents))											
		ı			. 21	2	11/70	1./=0	55.554		
		,	no serious	no serious	serious <sup>21</sup>	reporting bias <sup>3</sup>	11/73	4/72		95 more per 1000	
	trials	serious <sup>16</sup>	inconsistency	indirectness			(15.1%)	(5.6%)	(0.91 to	(from 5 fewer to	VERY
									8.12)	396 more)	LOW
										00 1000	
								5.6%		96 more per 1000 (from 5 fewer to	
								5.6%		399 more)	
o o o o o ti u	otion due	to odvorce	ovente (etypical	l antidan rassan	t) /fallow up m	aan 4 waaka saa	essed with: Number of particip	anta dia a	ntinuina di		nto\
COILLI	iuation due	to auverse	events (atypical	antidepressan	t) (Iollow-up III	ean 4 weeks; ass	essed with: Number of particip	Janus disco	munuing at	ie to adverse eve	nis)
	randomised	serious <sup>22</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	0/30	0/30	not pooled	not pooled	⊕000
	randomised trials			no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	5.00		not pooled	not pooled	⊕OOO VERY
			no serious inconsistency		serious <sup>2</sup>	reporting bias <sup>3</sup>	0/30 (0%)	0/30 (0%)	not pooled	not pooled	⊕OOO VERY LOW
					serious <sup>2</sup>	reporting bias <sup>3</sup>	5.00		not pooled	·	VERY
•	trials		inconsistency	indirectness			5.00	(0%)	•	not pooled	VERY
	trials	to adverse	inconsistency events (antipsyd	indirectness	up 4-8 weeks;	assessed with: No	(0%) umber of participants disconti	(0%) 0% nuing due	to adverse (	not pooled	VERY LOW
scontir	randomised	to adverse of serious 18	inconsistency events (antipsyo	indirectness			(0%) umber of participants disconti	0%) 0% nuing due	to adverse o	not pooled events) 37 more per 1000	VERY LOW
contir	trials	to adverse of serious 18	inconsistency events (antipsyd	indirectness	up 4-8 weeks;	assessed with: No	(0%) umber of participants disconti	(0%) 0% nuing due	RR 3.16 (1.97 to	not pooled events)  37 more per 1000 (from 17 more to	VERY LOW
scontir	randomised	to adverse of serious 18	inconsistency events (antipsyo	indirectness chotic) (follow-	up 4-8 weeks;	assessed with: No	(0%) umber of participants disconti	0%) 0% nuing due	to adverse o	not pooled events) 37 more per 1000	VERY LOW
scontir	randomised	to adverse of serious 18	inconsistency events (antipsyo	indirectness chotic) (follow-	up 4-8 weeks;	assessed with: No	(0%) umber of participants disconti	0%) 0% nuing due	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)	DOO VERY
scontir	randomised	to adverse of serious 18	inconsistency events (antipsyo	indirectness chotic) (follow-	up 4-8 weeks;	assessed with: No	(0%) umber of participants disconti	0%) 0% nuing due 21/1226 (1.7%)	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000	DOO VERY
scontir	randomised	to adverse of serious 18	inconsistency events (antipsyo	indirectness chotic) (follow-	up 4-8 weeks;	assessed with: No	(0%) umber of participants disconti	0%) 0% nuing due	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to	DOO VERY
scontir	ruation due randomised trials	to adverse of serious 18	events (antipsydnoserious inconsistency	indirectness  chotic) (follow-indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	(0%)  umber of participants disconti  120/1480 (8.1%)	(0%) 0% nuing due 21/1226 (1.7%) 2%	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)	DOO VERY
scontir	ruation due randomised trials	to adverse of serious 18	events (antipsydnoserious inconsistency	indirectness  chotic) (follow-indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	(0%) umber of participants disconti	(0%) 0% nuing due 21/1226 (1.7%) 2%	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)	DOO VERY
scontin	randomised trials	serious <sup>18</sup>	no serious inconsistency	no serious indirectness  (follow-up 2-6 v	serious <sup>2</sup> weeks; assess	reporting bias <sup>3</sup>	(0%)  umber of participants disconti  120/1480 (8.1%)  of participants discontinuing of	(0%) 0% nuing due 21/1226 (1.7%) 2% due to adve	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)	©OOO VERY LOW
scontin	randomised trials	serious <sup>18</sup>	no serious inconsistency	no serious indirectness  (follow-up 2-6 value)	serious <sup>2</sup> weeks; assess	reporting bias <sup>3</sup>	(0%)  umber of participants disconti  120/1480 (8.1%)  of participants discontinuing of	(0%) 0% nuing due 21/1226 (1.7%) 2% due to adve	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)	⊕OOO VERY LOW
scontir	randomised trials	serious <sup>18</sup>	no serious inconsistency	no serious indirectness  (follow-up 2-6 v	serious <sup>2</sup> weeks; assess	reporting bias <sup>3</sup>	(0%)  umber of participants disconti  120/1480 (8.1%)  of participants discontinuing of	(0%) 0% nuing due 21/1226 (1.7%) 2% due to adve	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)  11 more per 1000 (from 24 fewer to	DOOO VERY LOW
scontin	randomised trials	serious <sup>18</sup>	no serious inconsistency	no serious indirectness  (follow-up 2-6 value)	serious <sup>2</sup> weeks; assess	reporting bias <sup>3</sup>	(0%)  umber of participants disconti  120/1480 (8.1%)  of participants discontinuing of	(0%) 0% nuing due 21/1226 (1.7%) 2% due to adve	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)	⊕OOO VERY LOW
scontin	randomised trials	serious <sup>18</sup>	no serious inconsistency	no serious indirectness  (follow-up 2-6 value)	serious <sup>2</sup> weeks; assess	reporting bias <sup>3</sup>	(0%)  umber of participants disconti  120/1480 (8.1%)  of participants discontinuing of	(0%) 0% nuing due 21/1226 (1.7%) 2% due to adve	RR 3.16 (1.97 to 5.06)	not pooled events)  37 more per 1000 (from 17 more to 70 more)  43 more per 1000 (from 19 more to 81 more)  11 more per 1000 (from 24 fewer to	DOOO VERY LOW

	randomised	serious <sup>14</sup>	no serious	no serious	serious <sup>2</sup>	none	0/27	0/24	not pooled	not pooled	⊕⊕⊙⊙	
	trials		inconsistency	indirectness			(0%)	(0%)			LOW	
							(===)	()				
								0%		not pooled		
nt	inustion due		ovente (enticen	uulaant Ilamatu	iginal\ (fallaw	un 0 40 waaka a	accord with Number of part		continuina	•	ronto\	
conti	inuation due	to adverse	events (anticon	vuisant [iamotr	igine]) (follow-	up 8-10 weeks; as	ssessed with: Number of part	cipants dis	continuing	que to adverse e	vents)	
					_	1						
	randomised	very	no serious	no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup>	9/65	10/65	RR 1.12	18 more per 1000	⊕OOO	
	trials	serious <sup>19</sup>	inconsistency	indirectness			(13.8%)	(15.4%)	(0.21 to	(from 122 fewer	VERY	
			,				,	` ,	5.94)	to 760 more)	LOW	
									/	,		
									1	12 more per 1000		
								10.4%		(from 82 fewer to		
								10.4 /6		514 more)		
isconti	inuation due	to adverse	events (anxiolyt	iic) (follow-up n	nean 6 weeks;	assessed with: N	umber of participants discon	inuing due	to adverse	events)		
		20	no serious	no serious	serious <sup>2</sup>	reporting bias3	0/51	0/51	not pooled	not pooled	$\oplus$ OOO	
	randomised	serious	no senous	no senous				(00()	-		VERY	
	randomised trials	serious		indirectness	0011000		(0%)	(0%)				
		serious	inconsistency		5511545	, ,	(0%)	(0%)				
		serious					(0%)	,		not pooled	LOW	
	trials		inconsistency	indirectness				0%		not pooled	LOW	
isconti	trials		inconsistency	indirectness		12 weeks; assess	(0%) ed with: Number of participar	0%	nuing due to		LOW	
isconti	trials		inconsistency	indirectness	llow-up mean			0%			LOW	
isconti	trials inuation due		inconsistency events (omega-	indirectness	llow-up mean	12 weeks; assess		0%	nuing due to		LOW	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti	RR 0.35	36 fewer per	LOW ⊕OOO	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0%	RR 0.35 (0.02 to	36 fewer per 1000 (from 54	⊕OOO VERY	
sconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti	RR 0.35	36 fewer per 1000 (from 54 fewer to 236	LOW ⊕OOO	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti	RR 0.35 (0.02 to	36 fewer per 1000 (from 54	⊕OOO VERY	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti	RR 0.35 (0.02 to	36 fewer per 1000 (from 54 fewer to 236 more)	⊕OOO VERY	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti	RR 0.35 (0.02 to	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per	⊕OOO VERY	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti 1/18 (5.6%)	RR 0.35 (0.02 to	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per 1000 (from 55	⊕OOO VERY	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti	RR 0.35 (0.02 to	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per 1000 (from 55 fewer to 238	⊕OOO VERY	
isconti	trials inuation due	to adverse	inconsistency events (omega-	indirectness  3 fatty acid) (fo	llow-up mean		ed with: Number of participar	0% ts disconti 1/18 (5.6%)	RR 0.35 (0.02 to	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per 1000 (from 55	⊕OOO VERY	
	inuation due randomised trials	no serious risk of bias	events (omega-	indirectness  3 fatty acid) (fo  no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	ed with: Number of participar	0% ts disconti 1/18 (5.6%) 5.6%	RR 0.35 (0.02 to 5.25)	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per 1000 (from 55 fewer to 238 more)	+OOO VERY LOW	
	inuation due randomised trials	no serious risk of bias	events (omega-	indirectness  3 fatty acid) (fo  no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup>	ed with: Number of participar	0% ts disconti 1/18 (5.6%) 5.6%	RR 0.35 (0.02 to 5.25)	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per 1000 (from 55 fewer to 238 more)	+OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar 1/52 (1.9%)	0% ts disconti  1/18 (5.6%)  5.6%  ipants disconti	RR 0.35 (0.02 to 5.25)	36 fewer per 1000 (from 54 fewer to 236 more) 36 fewer per 1000 (from 55 fewer to 238 more) ue to adverse eve	⊕OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	events (omega-	indirectness  3 fatty acid) (fo  no serious indirectness  nt [methylphen no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup>	ed with: Number of participar  1/52 (1.9%)  sessed with: Number of partic	0% ts disconti  1/18 (5.6%)  5.6%  ipants disc	RR 0.35 (0.02 to 5.25)	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (38 more)	⊕OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar 1/52 (1.9%)	0% ts disconti  1/18 (5.6%)  5.6%  ipants disconti	RR 0.35 (0.02 to 5.25) ontinuing d RR 2.92 (0.21 to	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (from 15 fewer to 15	+OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness  nt [methylphen no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar  1/52 (1.9%)  sessed with: Number of partic	0% ts disconti  1/18 (5.6%)  5.6%  ipants disc	RR 0.35 (0.02 to 5.25)	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (38 more)	⊕OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness  nt [methylphen no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar  1/52 (1.9%)  sessed with: Number of partic	0% ts disconti  1/18 (5.6%)  5.6%  ipants disc	RR 0.35 (0.02 to 5.25) ontinuing d RR 2.92 (0.21 to	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (from 15 fewer to 15	+OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness  nt [methylphen no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar  1/52 (1.9%)  sessed with: Number of partic	0% ts disconti  1/18 (5.6%)  5.6%  ipants disc	RR 0.35 (0.02 to 5.25) continuing d RR 2.92 (0.21 to 40.65)	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (from 15 fewer to 777 more)	+OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness  nt [methylphen no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar  1/52 (1.9%)  sessed with: Number of partic	0% ts disconti  1/18 (5.6%)  5.6%  ipants disc  2/102 (2%)	RR 0.35 (0.02 to 5.25) continuing d RR 2.92 (0.21 to 40.65)	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (from 15 fewer to 777 more)  63 more per 1000	+OOO VERY LOW	
	randomised trials	no serious risk of bias to adverse	no serious inconsistency	indirectness  3 fatty acid) (fo  no serious indirectness  nt [methylphen no serious	very serious <sup>17</sup>	reporting bias <sup>3</sup> up 4-5 weeks; ass	ed with: Number of participar  1/52 (1.9%)  sessed with: Number of partic	0% ts disconti  1/18 (5.6%)  5.6%  ipants disc	RR 0.35 (0.02 to 5.25) continuing d RR 2.92 (0.21 to 40.65)	36 fewer per 1000 (from 54 fewer to 236 more)  36 fewer per 1000 (from 55 fewer to 238 more)  ue to adverse ever 1000 (from 15 fewer to 777 more)	+OOO VERY LOW	

<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and method for allocation concealment. Blinding of intervention administration and outcome assessment is also unclear

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted/is not reported for all outcomes and/or funding from pharmaceutical company

<sup>&</sup>lt;sup>4</sup> Unclear randomisation method and method for allocation concealment. Blinding of intervention administration and outcome assessment is also unclear for studies that make up >50% weighting in the analysis

- <sup>5</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)
- <sup>6</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)
- 7 Significant group differences in baseline demographics at baseline in studies contributing to>50% weighting in analysis and unclear blinding of intervention administration and outcome assessment
- <sup>8</sup> Unclear blinding of outcome assessment
- 9 Unclear blinding of outcome assessment and unclear risk of attrition bias (drop-out>20% [21%] but difference between groups<20% and ITT analysis)
- <sup>10</sup> Unclear randomisation method and method of allocation concealment. Blinding of outcome assessment is also unclear
- <sup>11</sup> N<400

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- <sup>12</sup> I-squared>50%
  - <sup>13</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD -0.5)
- <sup>14</sup> Unclear randomisation method and method of allocation concealment, and blinding of intervention administration unclear
- 15 High risk of bias associated with randomisation method as significant differences between groups at baseline in studies contributing >50% to weighting in analysis. Unclear blinding of outcome assessment and unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)
- <sup>16</sup> High risk of bias associated with randomisation method as significant difference between groups at baseline and method of allocation concealment is unclear. Blinding of intervention administration is also unclear
- <sup>17</sup> 95% CI crosses line of no effect and both threshold for clinically important benefit (RR 0.75) and threshold for clinically important harm (RR 1.25)
- 18 Unclear or high risk of bias associated with randomisation method, unclear method of allocation concealment, and unclear blinding of intervention administration in studies contributing to >50% of weighting in analysis
- 18 <sup>19</sup> High risk of bias associated with randomisation method as significant difference between groups at baseline
- 19 <sup>20</sup> Unclear randomisation method and method of allocation concealment
- 20 <sup>21</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25) 21
  - <sup>22</sup> Unclear randomisation method and method of allocation concealment, and blinding of intervention administration is unclear

## Augmenting the antidepressant with another antidepressant/non-antidepressant agent versus continuing with the antidepressant-only

			Quality ass	essment			No of patients		E	Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with another antidepressant/non-antidepressant agent versus continuing with the antidepressant-only	Control	Relative (95% CI)	Absolute	Quality	Importance
Remissi	on (TeCA [m	ianserin]	+ SSRI versus S	SRI-only) (follo	ow-up 5-6 wee	eks; assessed wi	th: Number of people scoring ≤7/8 on F	lamilton	Rating Sca	le for Depressi	on (HAM	-D))
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>3</sup>	reporting bias <sup>4</sup>	57/130 (43.8%)	44/136 (32.4%) 28.1%		168 more per 1000 (from 74 fewer to 650 more) 146 more per 1000 (from 65 fewer to 565 more)	⊕000 VERY LOW	

randomised	serious <sup>5</sup>	serious <sup>2</sup>	no serious	very serious <sup>6</sup>	reporting bias4	71/283	56/268	RR 1.12	25 more per	⊕OOO
trials			indirectness	1., 25525	,	(25.1%)	(20.9%)		1000 (from 113	
						(	(	2.75)	fewer to 366	LOW
								,	more)	
									20 more per	
							16.8%		1000 (from 91	
									fewer to 294 more)	
ion (anticonv	ulsant +	SSRI versus SS	RI-only) (follow	w-up mean 8 w	eeks; assessed	vith: Number of people scoring ≤7	on Hamilton	Rating Sca	/	on (HAM-D)
randomised	very	no serious	no serious	very serious <sup>6</sup>	reporting bias4	19/39	21/45	RR 1.04	19 more per	⊕000
trials	serious <sup>7</sup>	inconsistency	indirectness			(48.7%)	(46.7%)	(0.67 to	1000 (from 154	
								1.63)	fewer to 294	LOW
									more)	
									19 more per	
							46.7%		1000 (from 154	
							10.170		fewer to 294 more)	
ion (anxiolyti	c + SSRI	versus SSRI-or	nly) (follow-up	mean 8 weeks;	assessed with:	Number of people scoring ≤7 on H		g Scale fo	more)	AM-D))
randomised	very	no serious	no serious		assessed with: reporting bias <sup>4</sup>	15/46	lamilton Ratin	RR 0.7	more) r Depression (Ha	⊕000
							lamilton Ratin	RR 0.7 (0.42 to	more) r Depression (Hall) 140 fewer per 1000 (from 271	⊕OOO VERY
randomised	very	no serious	no serious			15/46	lamilton Ratin	RR 0.7	more) r Depression (Haral 140 fewer per 1000 (from 271 fewer to 84	⊕000
randomised	very	no serious	no serious			15/46	lamilton Ratin	RR 0.7 (0.42 to	more) r Depression (Hall) 140 fewer per 1000 (from 271	⊕OOO VERY
randomised	very	no serious	no serious			15/46	lamilton Ratin	RR 0.7 (0.42 to	more) r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per	⊕OOO VERY
randomised	very	no serious	no serious			15/46	lamilton Ratin	RR 0.7 (0.42 to	more) r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271	⊕OOO VERY
randomised	very	no serious	no serious			15/46	21/45 (46.7%)	RR 0.7 (0.42 to	more) r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per	⊕OOO VERY
randomised trials	very serious <sup>7</sup>	no serious inconsistency	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46	21/45 (46.7%)	RR 0.7 (0.42 to 1.18)	more) r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)	⊕OOO VERY LOW
randomised trials  ion (SARI + S	very serious <sup>7</sup>	no serious inconsistency us SSRI-only) (t	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46 (32.6%) ber of people scoring ≤7 on Hamilton	21/45 (46.7%) 46.7% ton Rating Sc.	RR 0.7 (0.42 to 1.18)	more) r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)  pression (HAM-D	⊕000 VERY LOW
randomised trials	very serious <sup>7</sup>	no serious inconsistency us SSRI-only) (t	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46 (32.6%) ber of people scoring ≤7 on Hamili	21/45 (46.7%) 46.7% ton Rating Sc.	RR 0.7 (0.42 to 1.18) ale for Dep RR 0.91 (0.58 to	more)  r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)  pression (HAM-D  42 fewer per 1000 (from 196	⊕OOO VERY LOW
randomised trials  ion (SARI + S	very serious <sup>7</sup>	no serious inconsistency us SSRI-only) (t	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46 (32.6%) ber of people scoring ≤7 on Hamilton	21/45 (46.7%) 46.7% ton Rating Sc.	RR 0.7 (0.42 to 1.18)	more) r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)  pression (HAM-D	⊕000 VERY LOW
randomised trials	very serious <sup>7</sup>	no serious inconsistency us SSRI-only) (t	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46 (32.6%) ber of people scoring ≤7 on Hamilton	21/45 (46.7%) 46.7% ton Rating Sc.	RR 0.7 (0.42 to 1.18) ale for Dep RR 0.91 (0.58 to	more)  r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)  pression (HAM-Dame 1000 (from 196 fewer to 205 more)	⊕OOO VERY LOW
randomised trials sion (SARI + S	very serious <sup>7</sup>	no serious inconsistency us SSRI-only) (t	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46 (32.6%) ber of people scoring ≤7 on Hamilton	21/45 (46.7%) 46.7% ton Rating Sc. 21/45 (46.7%)	RR 0.7 (0.42 to 1.18) ale for Dep RR 0.91 (0.58 to	more)  r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)  oression (HAM-Dame 1000 (from 196 fewer to 205 more)	⊕OOO VERY LOW
randomised trials sion (SARI + S	very serious <sup>7</sup>	no serious inconsistency us SSRI-only) (t	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>4</sup>	15/46 (32.6%) ber of people scoring ≤7 on Hamilton	21/45 (46.7%) 46.7% ton Rating Sc.	RR 0.7 (0.42 to 1.18) ale for Dep RR 0.91 (0.58 to	more)  r Depression (Hz  140 fewer per 1000 (from 271 fewer to 84 more)  140 fewer per 1000 (from 271 fewer to 84 more)  pression (HAM-Dame 1000 (from 196 fewer to 205 more)	⊕OOO VERY LOW

randomised	very	no serious	no serious	serious <sup>3</sup>	reporting bias4	18/48	12/45	RR 1.41	109 more per	⊕OOO
trials	serious <sup>7</sup>	inconsistency	indirectness			(37.5%)	(26.7%)	(0.77 to 2.58)	1000 (from 61 fewer to 421 more)	VERY LOW
							26.7%		109 more per 1000 (from 61 fewer to 422 more)	
onse (TeCA [m -D))	anserin]	+ SSRI versus S	SSRI-only) (foll	ow-up 5-6 wee	ks; assessed wit	th: Number of people showing ≥50% in	nproveme	nt on Ham	ilton Rating Sca	ale for Depi
randomised	serious1	serious <sup>2</sup>	no serious	very serious <sup>6</sup>	reporting bias4	86/130	83/136	RR 1.22	134 more per	⊕OOO
trials			indirectness		roporting state	(66.2%)	(61%)	(0.69 to 2.15)	1000 (from 189 fewer to 702 more)	
									118 more per	
							53.6%		1000 (from 166 fewer to 616	
									more)	
·				·		mber of people showing ≥50% improve			ating Scale for	
randomised trials		no serious inconsistency	no serious indirectness	serious <sup>10</sup>	reporting bias <sup>4</sup>	mber of people showing ≥50% improve  6/10  (60%)	2/14 (14.3%)	RR 4.2	/	Depression  OOO  VERY  LOW
randomised		no serious	no serious	·		6/10	2/14	RR 4.2 (1.06 to	457 more per 1000 (from 9 more to 1000 more)	⊕000 VERY
randomised		no serious	no serious	·		6/10	2/14	RR 4.2 (1.06 to	457 more per 1000 (from 9 more to 1000	⊕000 VERY
randomised trials	serious <sup>9</sup>	no serious inconsistency	no serious indirectness	serious <sup>10</sup>	reporting bias <sup>4</sup>	6/10 (60%)	2/14 (14.3%)	RR 4.2 (1.06 to 16.68)	457 more per 1000 (from 9 more to 1000 more) 458 more per 1000 (from 9 more to 1000 more)	⊕000 VERY LOW
randomised trials	serious <sup>9</sup>	no serious inconsistency	no serious indirectness	serious <sup>10</sup>	reporting bias <sup>4</sup>	6/10	2/14 (14.3%)	RR 4.2 (1.06 to 16.68)	457 more per 1000 (from 9 more to 1000 more) 458 more per 1000 (from 9 more to 1000 more)	⊕000 VERY LOW
randomised trials	serious <sup>9</sup> notic + Ssy Asberg	no serious inconsistency	no serious indirectness	serious <sup>10</sup>	reporting bias <sup>4</sup>	6/10 (60%)	2/14 (14.3%)	RR 4.2 (1.06 to 16.68)	457 more per 1000 (from 9 more to 1000 more) 458 more per 1000 (from 9 more to 1000 more)	⊕000 VERY LOW
randomised trials  conse (antipsyc M-D)/Montgomer	serious <sup>9</sup> notic + Ssy Asberg	no serious inconsistency SRI versus SSR Depression Ra	no serious indirectness  I-only) (follow-ting Scale (MA	serious <sup>10</sup> up mean 8 wee	reporting bias <sup>4</sup> eks; assessed wi	6/10 (60%) th: Number of people showing ≥50% in	2/14 (14.3%) 14.3% mproveme	RR 4.2 (1.06 to 16.68) ent on Ham RR 1.12 (0.61 to	457 more per 1000 (from 9 more to 1000 more)  458 more per 1000 (from 9 more to 1000 more)  ailton Rating Sca	#000 VERY LOW alle for Dep

										fewer to 317		
										more)		
spons (M-D)		ulsant + S	SRI versus SSI	RI-only) (follov	v-up mean 8 we	eks; assessed v	rith: Number of people showing ≥50%	improven	nent on Ha	milton Rating So	cale for D	epre
	randomised	very	no serious	no serious	very serious <sup>6</sup>	reporting bias4	24/39	30/45	RR 0.92	53 fewer per	⊕ООО	
	trials	serious <sup>7</sup>	inconsistency	indirectness	,	, ,	(61.5%)	(66.7%)	(0.67 to	1000 (from 220	VERY	
									1.27)	fewer to 180	LOW	
										more)		
										53 fewer per		
								66.7%		1000 (from 220		
								00 /0		fewer to 180		
	L						     Number of people showing ≥50% impr			more)		
IAM-D)		L	I					00/45	DD 0.05	100 5		
	randomised trials	,	no serious inconsistency	no serious	serious <sup>8</sup>	reporting bias4	26/46 (56,5%)	30/45	RR 0.85	100 fewer per	⊕000	
	ulais	serious <sup>7</sup>	inconsistency	indirectness			(56.5%)	(66.7%)	(0.61 to 1.18)	1000 (from 260 fewer to 120	VERY LOW	
									1.10)	more)	LOW	
										100 fewer per		
										1000 fewer per 1000 (from 260		
								66.7%		fewer to 120		
										more)		
espons	se (SARI + S	SRI versu	s SSRI-only) (fo	ollow-up mean	8 weeks; asse	ssed with: Numb	per of people showing ≥50% improven	nent on Ha	milton Ra	ting Scale for De	pression	(HA
	randomised	,	no serious	no serious	very serious <sup>6</sup>	reporting bias4	29/47	30/45	RR 0.93	47 fewer per	⊕000	
	trials	serious <sup>7</sup>	inconsistency	indirectness			(61.7%)	(66.7%)	(0.68 to	1000 (from 213		
									1.26)	fewer to 173	LOW	
										more)		
										47 fewer per		
								66.7%		1000 (from 213		
										fewer to 173		
										moro)	1	
	(4)		0001	ODI				0/ :		more)	01-6	
	se (thyroid h		· SSRI versus S	SRI-only) (folio	ow-up mean 8 v	veeks; assessed	   with: Number of people showing ≥50	% improve	ement on h	/	Scale for	
			oserious	SRI-only) (folio		veeks; assessed	with: Number of people showing ≥50	21/45	RR 1.25	lamilton Rating	Scale for	
	ion (HAM-D)	)								lamilton Rating  117 more per 1000 (from 75		
	randomised	very	no serious	no serious			28/48	21/45	RR 1.25	lamilton Rating	⊕000	
	randomised	very	no serious	no serious			28/48	21/45	RR 1.25 (0.84 to	lamilton Rating  117 more per 1000 (from 75	⊕OOO VERY	

										117 mara nar		
										117 more per 1000 (from 75		
								46.7%		fewer to 397		
										more)		
enone	o (ToCA Imi	ancorini -	L SSDI vorque S	SPI-only) (foll	OW-UD 5-6 WO	ke: accessed wit	th: Number of people rated as much or	vory mu	h improve	,	lohal Imn	rossio
ile (CC		ansemi	OSINI VEISUS S	ooki-only) (lon	ow-up 3-0 wee	rks, assessed wit	in. Number of people rated as much of	very muc	ii iiiipiove	d on Cillical G	iobai iiiip	1633101
10 (00	, i - i / j											
	andomised	serious <sup>1</sup>	verv serious <sup>11</sup>	no serious	very serious <sup>6</sup>	reporting bias4	99/130	101/136	RR 1.17	126 more per	⊕000	
	rials	Conodo	vory conodo	indirectness	vory concac	roporting blue	(76.2%)	(74.3%)	(0.65 to	1000 (from 260		
							(1.0.270)	(1.1070)	2.12)	fewer to 832	LOW	
									=: :=;	more)	LOVV	
										111 more per		
								CE 20/		1000 (from 228		
								65.2%		fewer to 730		
										more)		
pressi	on sympton	natology (	any augmentat	ion agent) (fol	low-up 6-8 we	eks; measured w	ith: Hamilton Rating Scale for Depress	ion (HAM	-D; change	score)/Montgo	mery As	berg
pressi	on Rating S	cale (MAI	ORS; change so	ore); Better in	dicated by low	ver values)						
	andomised	serious <sup>12</sup>	no serious	no serious	no serious	reporting bias4	270	261	-	SMD 0.37	$\oplus \oplus OO$	
		COMOGO	inconsistency	indirectness	imprecision	roporting blac	210			lower (0.55 to	LOW	
1	riais											
ľ	rials		inconsistency	indirectiness	Impredictor							
		a atala ay	,		·	) (fallow up mag	n C weeks were with Hemilton D	eting Coo	le fee Denn	0.2 lower)		22242
pressi tter ind	on sympton dicated by le	ower valu	(TeCA [mianser es)	in]) + SSRI ver	sus SSRI-only		n 6 weeks; measured with: Hamilton R		le for Depr	0.2 lower)		score)
pressi tter inc	on sympton dicated by lo	very	(TeCA [mianser es)	in]) + SSRI ver	·	reporting bias <sup>4</sup>	n 6 weeks; measured with: Hamilton R	ating Sca	le for Depr -	0.2 lower) ression (HAM-D	; change	score)
pressi tter inc	on sympton dicated by lo	very	(TeCA [mianser es)	in]) + SSRI ver	sus SSRI-only				le for Depr	0.2 lower)  ression (HAM-D  SMD 0.66 lower (1.14 to	⊕OOO VERY	score)
oressi ter ind	on sympton dicated by lo	very	(TeCA [mianser es)	in]) + SSRI ver	sus SSRI-only				le for Depr -	0.2 lower) ression (HAM-D	; change	score)
pressi tter ind	on sympton dicated by lo randomised rials	very serious <sup>13</sup>	(TeCA [mianser es) no serious inconsistency	no serious indirectness	serious <sup>14</sup>	reporting bias <sup>4</sup>	32	38	-	O.2 lower)  Pession (HAM-D  SMD 0.66 lower (1.14 to 0.17 lower)	⊕OOO VERY LOW	
pressi	on sympton dicated by lo randomised rials	very serious 13	(TeCA [mianser es)  no serious inconsistency  (antipsychotic 4	no serious indirectness	serious <sup>14</sup>	reporting bias <sup>4</sup>		38	-	O.2 lower)  Pession (HAM-D  SMD 0.66 lower (1.14 to 0.17 lower)	⊕OOO VERY LOW	
pressi tter ind pressi pressi	on sympton dicated by lo randomised rials on sympton	very serious <sup>13</sup> natology (	no serious inconsistency (antipsychotic -1 ver values)	no serious indirectness	serious <sup>14</sup>	reporting bias <sup>4</sup>	32	38	-	O.2 lower)  Pession (HAM-D  SMD 0.66 lower (1.14 to 0.17 lower)	⊕OOO VERY LOW	
pressi tter ind pressi pressi	on sympton dicated by lo randomised rials on sympton etter indica	very serious <sup>13</sup> natology (	no serious inconsistency (antipsychotic -1 ver values)	no serious indirectness	serious <sup>14</sup> SSRI-only) (fo	reporting bias <sup>4</sup>	32 veeks; measured with: Montgomery As	38 berg Dep	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)	⊕OOO VERY LOW	
pressi tter ind pressi pressi	on sympton dicated by lorandomised trials on sympton etter indicated and omised	very serious <sup>13</sup> natology (	no serious inconsistency (antipsychotic - ver values)	no serious indirectness  SSRI versus	serious <sup>14</sup> SSRI-only) (fo	reporting bias <sup>4</sup>	32 veeks; measured with: Montgomery As	38 berg Dep	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)	⊕OOO VERY LOW DRS; cha	
pressi tter ind pressi pressi	on sympton dicated by lorandomised trials on sympton etter indicated and omised	very serious <sup>13</sup> natology (	no serious inconsistency (antipsychotic - ver values)	no serious indirectness  SSRI versus	serious <sup>14</sup> SSRI-only) (fo	reporting bias <sup>4</sup>	32 veeks; measured with: Montgomery As	38 berg Dep	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)  ating Scale (MAI  SMD 0.33 lower (0.52 to	⊕OOO VERY LOW DRS; cha	
pressi tter ind pressi ore); B	on sympton dicated by lorandomised trials on sympton etter indicated trials	very serious <sup>13</sup> natology ( ted by lov serious <sup>15</sup>	no serious inconsistency  (antipsychotic + ver values)  no serious inconsistency	no serious indirectness  - SSRI versus  no serious indirectness	serious <sup>14</sup> SSRI-only) (fo	reporting bias <sup>4</sup> Illow-up mean 8 w reporting bias <sup>4</sup>	32 veeks; measured with: Montgomery As	38 berg Dep	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)  sting Scale (MAI  SMD 0.33 lower (0.52 to 0.15 lower)	⊕OOO VERY LOW DRS; cha	nnge
pressi pressi pressi pre); B	on sympton dicated by lorandomised trials andomised trials andomised trials	very serious <sup>13</sup> natology ( ted by lov serious <sup>15</sup>	no serious inconsistency  (antipsychotic + ver values)  no serious inconsistency	no serious indirectness  SSRI versus  no serious indirectness  ation agent) (f	serious <sup>14</sup> SSRI-only) (fo	reporting bias <sup>4</sup> llow-up mean 8 w reporting bias <sup>4</sup>	32 veeks; measured with: Montgomery As	38 berg Dep	ression Ra - - uny reason	SMD 0.66 lower (1.14 to 0.17 lower)  ating Scale (MAI  SMD 0.33 lower (0.52 to 0.15 lower)  (including adve	⊕OOO VERY LOW DRS; cha	nnge
pressi tter ind pressi ore); B	on sympton dicated by lorandomised rials andomised rials andomised rials	very serious <sup>13</sup> natology ( ted by lov serious <sup>15</sup>	no serious inconsistency  (antipsychotic + ver values)  no serious inconsistency  no serious inconsistency	no serious indirectness  - SSRI versus  no serious indirectness  ation agent) (f	serious <sup>14</sup> SSRI-only) (fo  no serious imprecision  follow-up 5-8 v	reporting bias <sup>4</sup> Illow-up mean 8 w reporting bias <sup>4</sup>	32  veeks; measured with: Montgomery As  238  with: Number of participants discontin  96/371	38 berg Dep  223 uing for a	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)  ating Scale (MAI  SMD 0.33 lower (0.52 to 0.15 lower)  (including adverting adv	⊕OOO VERY LOW DRS; cha	nnge
pressi tter ind pressi ore); B	on sympton dicated by lorandomised trials andomised trials andomised trials	very serious <sup>13</sup> natology ( ted by lov serious <sup>15</sup>	no serious inconsistency  (antipsychotic + ver values)  no serious inconsistency	no serious indirectness  SSRI versus  no serious indirectness  ation agent) (f	serious <sup>14</sup> SSRI-only) (fo  no serious imprecision  follow-up 5-8 v	reporting bias <sup>4</sup> llow-up mean 8 w reporting bias <sup>4</sup>	32 veeks; measured with: Montgomery As 238 with: Number of participants discontin	38 berg Dep 223 uing for a	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)  ating Scale (MAI  SMD 0.33 lower (0.52 to 0.15 lower)  (including advertion of the control of the contro	⊕OOO VERY LOW  DRS; cha  ⊕⊕OO LOW  erse even	nnge
pressi tter ind pressi ore); B	on sympton dicated by lorandomised rials andomised rials andomised rials	very serious <sup>13</sup> natology ( ted by lov serious <sup>15</sup>	no serious inconsistency  (antipsychotic + ver values)  no serious inconsistency  no serious inconsistency	no serious indirectness  - SSRI versus  no serious indirectness  ation agent) (f	serious <sup>14</sup> SSRI-only) (fo  no serious imprecision  follow-up 5-8 v	reporting bias <sup>4</sup> llow-up mean 8 w reporting bias <sup>4</sup>	32  veeks; measured with: Montgomery As  238  with: Number of participants discontin  96/371	38 berg Dep  223 uing for a	ression Ra	SMD 0.66 lower (1.14 to 0.17 lower)  ating Scale (MAI  SMD 0.33 lower (0.52 to 0.15 lower)  (including adverting adv	⊕OOO VERY LOW DRS; cha	nnge

										81 more per	
								18.9%		1000 (from 13	
										more to 172	
										more)	
		any reaso	n (TeCA [mians	erin] + SSRI ve	ersus SSRI-on	ly) (follow-up 5-6	weeks; assessed with: Number of par	ticipants	discontinui	ng for any reas	on (includin
erse	events))										
	randomised	serious <sup>17</sup>	no serious	no serious	serious <sup>18</sup>	reporting bias4	23/130	17/137	RR 1.43	53 more per	⊕000
	trials		inconsistency	indirectness		, ,	(17.7%)	(12.4%)	(0.79 to	1000 (from 26	VERY
			_				· ,	, ,	2.56)	fewer to 194	LOW
									<i>'</i>	more)	
										•	
										61 more per	
								14.3%		1000 (from 30	
								11.070		fewer to 223	
										more)	
		any reaso	n (antipsychotic	c + SSRI versu	s SSRI-only) (1	follow-up mean 8	3 weeks; assessed with: Number of pa	rticipants	discontinu	ing for any reas	son (includin
/erse	events))										
	randomised	serious <sup>19</sup>	no serious	no serious	serious <sup>10</sup>	reporting bias4	73/241	45/226	RR 1.44	88 more per	⊕000
	trials	00000	inconsistency	indirectness	00.1000	roporting side	(30.3%)		(1.03 to 2)	1000 (from 6	VERY
							(00000)	(1010,0)	(**************************************	more to 199	LOW
										more)	2011
										98 more per	
								22.2%		1000 (from 7	
								22.270		more to 222	
										more)	
conti	nuation due	to advers	se events (any a	ugmentation a	igent) (follow-u	up 6-8 weeks; as	sessed with: Number of participants d	iscontinu	ing due to a	dverse events	
	randomised	serious <sup>12</sup>	no serious	no serious	serious <sup>10</sup>	reporting bias4	45/273	5/264	RR 6.19	98 more per	⊕OOO
	trials	3003	inconsistency	indirectness	21,1000		(16.5%)	(1.9%)	(2.65 to	1000 (from 31	VERY
							(.0.070)	(,0)	14.47)	more to 255	LOW
									,	more)	2011
										,	
								0%		-	
conti	nuation due	to advers	e events (TeCA	(mianserin) +	SSRI versus S	SRI-only) (follow	w-up mean 6 weeks; assessed with: Nu	ımber of ı	participants	discontinuina	due to adve
ents)			(100)			, (.oo.				g	
	randomised	serious <sup>20</sup>		no serious	very serious <sup>21</sup>	reporting bias4	2/32	0/38	RR 5.91	-	⊕OOO
	trials		inconsistency	indirectness			(6.3%)	(0%)	(0.29 to		VERY
			1	1	1	I			118.78)		LOW
								0%	110.70)		LOVV

Discont	inuation due	to advers	se events (antip	sychotic + SSF	RI versus SSR	l-only) (follow-up	mean 8 weeks; assessed with: Numbe	r of part	icipants dis	scontinuing due	to adve	rse events)
2	randomised	serious <sup>19</sup>	no serious	no serious	serious <sup>10</sup>	reporting bias4	43/241	5/226	RR 6.22	115 more per	⊕000	
	trials		inconsistency	indirectness			(17.8%)	(2.2%)	(2.57 to	1000 (from 35	VERY	
									15.07)	more to 311	LOW	
										more)		
										·		
										63 more per		
								1.2%		1000 (from 19		
								1.270		more to 169		
										more)		

<sup>&</sup>lt;sup>1</sup> Unclear blinding of intervention administration, and unclear blinding or non-blind outcome assessment

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<sup>&</sup>lt;sup>2</sup> I-squared>50%

<sup>&</sup>lt;sup>3</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>4</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical company

<sup>&</sup>lt;sup>5</sup> Unclear or high risk of bias associated with randomisation method and unclear method of allocation concealment, unclear blinding of intervention administration and outcome assessment, and unclear risk of attrition bias (drop-out>20% and some differences between groups but ITT analysis used) in studies contributing>50% to weighting in analysis

<sup>&</sup>lt;sup>6</sup> 95% CI crosses line of no effect and both threshold for clinically important harm (RR 0.75) and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>7</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and unclear blinding of intervention administration and outcome assessment

<sup>8 95%</sup> CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>&</sup>lt;sup>9</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment

<sup>11</sup> <sup>10</sup> Events<300

<sup>12</sup> <sup>11</sup> I-squared>80%

<sup>12</sup> Unclear randomisation method and method of allocation concealment, unclear or non-blind intervention administration and outcome assessment, and unclear risk of attrition bias (drop-out>20% and some differences between groups but ITT analysis used), in studies contributing >50% to weighting in analysis

<sup>13</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administrator. Outcome assessment was non-blind. There was also an unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>14</sup> N<400

<sup>15</sup> Unclear randomisation method and method of allocation concealment, and unclear or non-blind intervention administration. There was also an unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used) in studies contributing >50% to weighing in analysis

<sup>16</sup> Unclear randomisation method and method of allocation concealment, and unclear or non-blind intervention administration, in studies contributing >50% to weighting in analysis

<sup>21</sup> <sup>17</sup> Unclear blinding of intervention administration

<sup>22</sup> <sup>18</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25) 23

<sup>&</sup>lt;sup>19</sup> Unclear randomisation method and method of allocation concealment, and unclear or non-blind intervention administration

<sup>&</sup>lt;sup>20</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administrator

<sup>&</sup>lt;sup>21</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

Augmenting the antidepressant with lithium compared to 'other' augmentation agents (head-to-head comparisons)

			Quality ass	essment			No of pati	ents		Effect		
											Quality	Importa
lo of udies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with lithium	'other' augmentation agent	Relative (95% CI)	Absolute		
							with: Number of people 50% improvement on H		amilton Rati	ng Scale for Depre	ssion (H	AM-D)/≤
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	95/382	123/392	RR 0.79	66 fewer per 1000	⊕000	
	trials		inconsistency	indirectness			(24.9%)	(31.4%)	(0.63 to	(from 3 fewer to	VERY	
			j					,	0.99)	116 fewer)	LOW	
									_	62 fewer per 1000		
								29.4%		(from 3 fewer to		
nissio	on (lithium ve	ersus TCA	) (follow-up mear	n 4 weeks; asse	essed with: N	umber of people	scoring ≤7 on Hamilton		Depression	109 fewer)		
nissio		serious <sup>4</sup>	no serious inconsistency	n 4 weeks; asse		umber of people s	scoring ≤7 on Hamilton 12/48 (25%)		RR 0.88 (0.45 to 1.74)	109 fewer)		
nissio	randomised		no serious	no serious			12/48	Rating Scale for	RR 0.88 (0.45 to	109 fewer) 1 (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)	VERY	
nissid	randomised		no serious	no serious			12/48	Rating Scale for	RR 0.88 (0.45 to	109 fewer)  (HAM-D))  34 fewer per 1000 (from 155 fewer to	VERY	
missic	randomised		no serious	no serious			12/48	13/46 (28.3%)	RR 0.88 (0.45 to	109 fewer)  (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000	VERY	
	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	12/48	13/46 (28.3%) 27.2%	RR 0.88 (0.45 to 1.74)	109 fewer)  1 (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000 (from 150 fewer to 201 more)	VERY LOW	
	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup> assessed wi	reporting bias <sup>3</sup>	12/48 (25%)	13/46 (28.3%) 27.2%	RR 0.88 (0.45 to 1.74)	109 fewer)  1 (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000 (from 150 fewer to 201 more)	VERY LOW	
	randomised trials	serious <sup>4</sup>	no serious inconsistency osychotic) (follow	no serious indirectness v-up 6-8 weeks;	very serious <sup>5</sup> assessed wi	reporting bias <sup>3</sup> th: Number of pe	12/48 (25%) ople scoring ≤8/<10 on	13/46 (28.3%) 27.2% Montgomery Asl	RR 0.88 (0.45 to 1.74)	109 fewer)  1 (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000 (from 150 fewer to 201 more)  sion Rating Scale (1997)	VERY LOW	
	randomised trials on (lithium ver	serious <sup>4</sup>	no serious inconsistency osychotic) (follow	no serious indirectness  v-up 6-8 weeks;	very serious <sup>5</sup> assessed wi	reporting bias <sup>3</sup> th: Number of pe	12/48 (25%) ople scoring ≤8/<10 on	13/46 (28.3%) 27.2% Montgomery Asi	RR 0.88 (0.45 to 1.74) Deerg Depres	109 fewer)  1 (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000 (from 150 fewer to 201 more)  sion Rating Scale (119 fewer per	VERY LOW	
	randomised trials on (lithium ver	serious <sup>4</sup>	no serious inconsistency osychotic) (follow	no serious indirectness  v-up 6-8 weeks;	very serious <sup>5</sup> assessed wi	reporting bias <sup>3</sup> th: Number of pe	12/48 (25%) ople scoring ≤8/<10 on	13/46 (28.3%) 27.2% Montgomery Asi	RR 0.88 (0.45 to 1.74) Deerg Depres	109 fewer)  (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000 (from 150 fewer to 201 more)  sion Rating Scale (1997)  119 fewer per 1000 (from 234 fewer to 132 more)	VERY LOW	
	randomised trials on (lithium ver	serious <sup>4</sup>	no serious inconsistency osychotic) (follow	no serious indirectness  v-up 6-8 weeks;	very serious <sup>5</sup> assessed wi	reporting bias <sup>3</sup> th: Number of pe	12/48 (25%) ople scoring ≤8/<10 on	13/46 (28.3%) 27.2% Montgomery Asi	RR 0.88 (0.45 to 1.74) Deerg Depres	109 fewer)  1 (HAM-D))  34 fewer per 1000 (from 155 fewer to 209 more)  33 fewer per 1000 (from 150 fewer to 201 more)  sion Rating Scale (1997)  119 fewer per 1000 (from 234 fewer to 132 more)	VERY LOW	

responding (≥50% improvement on HAM-D))

4	randomised	very	no serious	no serious	serious <sup>8</sup>	reporting bias3	17/86	25/90	RR 0.72	78 fewer per 1000	⊕000	
Į.	trials	serious <sup>7</sup>	inconsistency	indirectness		, ,	(19.8%)	(27.8%)	(0.42 to	(from 161 fewer to		
									1.22)	61 more)	LOW	
									-	92 fewer per 1000		
								32.9%		(from 191 fewer to		
										72 more)		
nissio	n (lithium ve	rsus anti	convulsant [lamo	trigine]) (follow	/-up mean 8 v	veeks; assessed	with: Number of people	e scoring ≤7 on H	amilton Rati	ng Scale for Depre	ssion (HA	AM-D))
r	randomised	serious <sup>4</sup>	no serious	no serious	very serious <sup>5</sup>	none	3/17	4/17	RR 0.75	59 fewer per 1000	⊕OOO	
t	trials		inconsistency	indirectness			(17.6%)	(23.5%)	(0.2 to 2.86)	(from 188 fewer to	VERY	
										438 more)	LOW	
									-	59 fewer per 1000		
								23.5%		(from 188 fewer to		
										` 437 more)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	135/317 (42.6%)	154/329 (46.8%)	RR 0.91 (0.78 to 1.08)	42 fewer per 1000 (from 103 fewer to 37 more)		
		00.1000			3311343	roperung side			(0.78 to	(from 103 fewer to	VERY	
									1.08)	37 more)	1 ( ) / / /	
									,	,	2011	
									_	,		
								52.7%		47 fewer per 1000 (from 116 fewer to		
									-	47 fewer per 1000 (from 116 fewer to 42 more)		
		rsus antip	sychotic) (follow	v-up 6-8 weeks;	assessed wit	h: Number of pec	ople showing ≥50% imp		ntgomery As	47 fewer per 1000 (from 116 fewer to 42 more)		ale
		rsus antip		v-up 6-8 weeks;	assessed wit	h: Number of pec	ople showing ≥50% imp		ntgomery As	47 fewer per 1000 (from 116 fewer to 42 more)		ale
ADRS))	·	rsus antip	no serious	no serious	assessed with	h: Number of peo	117/231	provement on Mo	RR 0.89	47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I	Rating Sc	ale
ADRS))	·							provement on Mo		47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I	Rating Sc	ale
ADRS))	randomised		no serious	no serious			117/231	provement on Mo	RR 0.89	47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I	Rating Sc	ale
ADRS))	randomised		no serious	no serious			117/231	provement on Mo	RR 0.89 (0.63 to	47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I 59 fewer per 1000 (from 198 fewer to 134 more)	⊕OOO VERY LOW	ale
ADRS))	randomised		no serious	no serious			117/231	provement on Mo	RR 0.89 (0.63 to	47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I 59 fewer per 1000 (from 198 fewer to 134 more) 73 fewer per 1000 (from 245 fewer to	⊕OOO VERY LOW	ale
ADRS))	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>3</sup>	117/231 (50.6%)	128/239 (53.6%)	RR 0.89 (0.63 to 1.25)	47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I 59 fewer per 1000 (from 198 fewer to 134 more) 73 fewer per 1000 (from 245 fewer to 165 more)	⊕OOO VERY LOW	
ADRS))	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>3</sup>	117/231	128/239 (53.6%)	RR 0.89 (0.63 to 1.25)	47 fewer per 1000 (from 116 fewer to 42 more) sberg Depression I 59 fewer per 1000 (from 198 fewer to 134 more) 73 fewer per 1000 (from 245 fewer to 165 more)	⊕OOO VERY LOW	
ADRS))	randomised trials e (lithium ver atology (QID	serious¹	no serious inconsistency oid hormone [T3]	no serious indirectness	serious <sup>8</sup> an 14 weeks;	reporting bias <sup>3</sup> assessed with: N	117/231 (50.6%)	128/239 (53.6%) 66.2%	RR 0.89 (0.63 to 1.25) ement on Qu	47 fewer per 1000 (from 116 fewer to 42 more)  sberg Depression I  59 fewer per 1000 (from 198 fewer to 134 more)  73 fewer per 1000 (from 245 fewer to 165 more)	⊕OOO VERY LOW	
ADRS))	randomised trials e (lithium ver atology (QIE	serious <sup>1</sup> rsus thyro OS))	no serious inconsistency  id hormone [T3]	no serious indirectness  (follow-up means)	serious <sup>8</sup> an 14 weeks;	reporting bias <sup>3</sup>	117/231 (50.6%)	128/239 (53.6%) 66.2% ring ≥50% improv	RR 0.89 (0.63 to 1.25) ement on Qu	47 fewer per 1000 (from 116 fewer to 42 more)  sberg Depression I  59 fewer per 1000 (from 198 fewer to 134 more)  73 fewer per 1000 (from 245 fewer to 165 more)  sick Inventory of D	⊕OOO VERY LOW	
ADRS))	randomised trials e (lithium ver atology (QIE	serious¹	no serious inconsistency oid hormone [T3]	no serious indirectness	serious <sup>8</sup> an 14 weeks;	reporting bias <sup>3</sup> assessed with: N	117/231 (50.6%)	128/239 (53.6%) 66.2%	RR 0.89 (0.63 to 1.25) ement on Qu	47 fewer per 1000 (from 116 fewer to 42 more)  sberg Depression I  59 fewer per 1000 (from 198 fewer to 134 more)  73 fewer per 1000 (from 245 fewer to 165 more)	⊕OOO VERY LOW	

								23.3%		75 fewer per 1000 (from 151 fewer to	⊕000 VERY
								20.070		84 more)	LOW
on	se (lithium ve	rsus antic	onvulsant [lame	otrigine]) (follov	v-up mean 8 w	eeks; assessed w	ith: Number of people	e showing ≥50% i	mprovement	on Hamilton Ratin	g Scale fo
ess	sion (HAM-D))										
	randomised	serious <sup>4</sup>	no serious	no serious	very serious <sup>5</sup>	none	7/17	9/17	RR 0.78	116 fewer per	⊕OOO
	trials		inconsistency	indirectness			(41.2%)	(52.9%)	(0.38 to 1.6)	`	VERY
										fewer to 318 more)	LOW
									+	116 fewer per	
								52.9%		1000 (from 328	
										fewer to 317 more)	
on	se (lithium ve	rsus antip	sychotic) (follo	w-up mean 6 we	eeks; assesse	d with: Number of	people rated as muc	h or very much in	proved on C	linical Global Impr	essions s
	randomised	serious <sup>10</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	133/221	153/229	RR 0.9	67 fewer per 1000	⊕OOO
	trials		inconsistency	indirectness			(60.2%)	(66.8%)	(0.78 to	(from 147 fewer to	VERY
									1.04)	27 more)	LOW
										67 fewer per 1000	
								66.8%		(from 147 fewer to	
										27 more)	
				•		•	weeks; measured with by lower values)	h: Hamilton Rating	g Scale for D	epression (HAM-D;	change
ore)/C	zuick invento	ry or Depre	essive Sympton	iatology (QIDS;	change score	e); better indicated	by lower values)				
	randomised	serious <sup>11</sup>	no serious	no serious	serious <sup>12</sup>	reporting bias <sup>3</sup>	151	153	-	SMD 0.14 higher	⊕ООО
	trials		inconsistency	indirectness						(0.14 lower to 0.42	
										higher)	LOW
							Jamilton Dating Cook	for Depression (	HAM-D: char	ge score): Better i	ndicated I
nress	sion symptom	atology (li	thium versus T	CA) (follow-up i	mean 4 weeks	measured with:	taminion Kanno Scar				
	sion symptom	atology (li	thium versus T	CA) (follow-up i	mean 4 weeks	measured with:	namilion Rating Scale	e ioi Depression (	u b, o	,,	
press ues)											
	randomised		no serious	no serious	serious <sup>12</sup>	reporting bias <sup>3</sup>	48	46	-	SMD 0.09 lower	⊕000
									-	SMD 0.09 lower (0.49 lower to 0.32	⊕OOO VERY
	randomised		no serious	no serious					-	SMD 0.09 lower	⊕000

	randomised	serious <sup>11</sup>	no serious	no serious	serious <sup>12</sup>	reporting bias <sup>3</sup>	86	90	-	SMD 0.15 higher	⊕OOO
	trials		inconsistency	indirectness						(0.14 lower to 0.45	
										higher)	LOW
nressi	on symptom	atology (li	 ithium versus ar	nticonvulsant []	amotriginel)	(follow-up mean 8	weeks; measured with	Hamilton Rating	Scale for D	enression (HAM-D	change sco
	dicated by lo			ilioonivaloant [i	umoungmo <sub>l</sub> ,	(lollow up illean o	moons, mousured with	i. Hammon Rating	, Could for D	cpression (IIIAIII B	, change see
		serious4	no serious	no serious	serious <sup>13</sup>	none	17	17	-	SMD 0.81 higher	⊕⊕ОО
	trials		inconsistency	indirectness						(0.11 to 1.51 higher)	LOW
scontin	nuation for a	ny reason	(lithium versus	any 'other' aug	ımentation a	gent) (follow-up 2-8	weeks; assessed with	: Number of part	icipants disc	continuing for any	reason (inclu
	events))										
	randomised	serious <sup>10</sup>	no serious	no serious	serious <sup>14</sup>	reporting bias <sup>3</sup>	60/331	45/331	RR 1.29	39 more per 1000	⊕000
	trials		inconsistency	indirectness			(18.1%)	(13.6%)	(0.91 to	(from 12 fewer to	VERY
			·				, ,		1.84)	114 more)	LOW
									4	0.4	
								44.00/		34 more per 1000	
iscontin	uation for a	av roason	(lithium vorsus	TCA) (follow u	n moan 4 wo	oks: assessed with	Number of participar	11.8%	for any roas	(from 11 fewer to 99 more)	rea avantell
							n: Number of participar	nts discontinuing		(from 11 fewer to 99 more) on (including adve	,
			no serious	no serious	p mean 4 we	eks; assessed with	7/48	nts discontinuing	RR 0.83	on (including adve	⊕000
	randomised				very			nts discontinuing		(from 11 fewer to 99 more) on (including adve	⊕000
	randomised		no serious	no serious	very		7/48	8/46 (17.4%)	RR 0.83 (0.33 to	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000	⊕OOO VERY
	randomised		no serious	no serious	very		7/48	nts discontinuing	RR 0.83 (0.33 to	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to	⊕OOO VERY
	randomised trials	serious <sup>15</sup>	no serious inconsistency	no serious indirectness	very serious <sup>16</sup>	reporting bias <sup>3</sup>	7/48 (14.6%)	8/46 (17.4%)	RR 0.83 (0.33 to 2.11)	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)	⊕OOO VERY LOW
	randomised trials	serious <sup>15</sup>	no serious inconsistency	no serious indirectness	very serious <sup>16</sup>	reporting bias <sup>3</sup>	7/48	8/46 (17.4%)	RR 0.83 (0.33 to 2.11)	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)	⊕OOO VERY LOW
iscontin	randomised trials	serious <sup>15</sup>	no serious inconsistency	no serious indirectness antipsychotic)	very serious <sup>16</sup> (follow-up 6-	reporting bias <sup>3</sup>	7/48 (14.6%)	8/46 (17.4%)  19.9%  cipants discontinuing	RR 0.83 (0.33 to 2.11) uing for any	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)  reason (including)	⊕OOO VERY LOW adverse even
viscontin	randomised trials	serious <sup>15</sup>	no serious inconsistency (lithium versus	no serious indirectness antipsychotic)	very serious <sup>16</sup>	reporting bias <sup>3</sup> -8 weeks; assessed	7/48 (14.6%)	8/46 (17.4%)	RR 0.83 (0.33 to 2.11) uing for any RR 1.66 (0.57 to	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)  reason (including)	⊕OOO VERY LOW
iscontin	randomised trials	serious <sup>15</sup>	no serious inconsistency  (lithium versus no serious	no serious indirectness antipsychotic)	very serious <sup>16</sup> (follow-up 6-	reporting bias <sup>3</sup> -8 weeks; assessed	7/48 (14.6%)	8/46 (17.4%)  19.9%  cipants discontinuing	RR 0.83 (0.33 to 2.11) uing for any	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)  reason (including)	⊕OOO VERY LOW adverse even
iscontin	randomised trials	serious <sup>15</sup>	no serious inconsistency  (lithium versus no serious	no serious indirectness antipsychotic)	very serious <sup>16</sup> (follow-up 6-	reporting bias <sup>3</sup> -8 weeks; assessed	7/48 (14.6%)	8/46 (17.4%) 19.9% cipants discontin	RR 0.83 (0.33 to 2.11) uing for any RR 1.66 (0.57 to	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)  reason (including)  96 more per 1000 (from 62 fewer to 550 more)  50 more per 1000	#000 VERY LOW  adverse ever
Discontin	randomised trials	serious <sup>15</sup>	no serious inconsistency  (lithium versus no serious	no serious indirectness antipsychotic)	very serious <sup>16</sup> (follow-up 6-	reporting bias <sup>3</sup> -8 weeks; assessed	7/48 (14.6%)	8/46 (17.4%)  19.9%  cipants discontinuing	RR 0.83 (0.33 to 2.11) uing for any RR 1.66 (0.57 to	(from 11 fewer to 99 more)  on (including adve)  30 fewer per 1000 (from 117 fewer to 193 more)  34 fewer per 1000 (from 133 fewer to 221 more)  reason (including)  96 more per 1000 (from 62 fewer to 550 more)	#000 VERY LOW  adverse ever

2	randomised	earioue <sup>15</sup>	no serious	no serious	very	none	1/27	0/27	RR 2.84		⊕000	
	trials	Scrious	inconsistency	indirectness	serious <sup>16</sup>	lione	(3.7%)	(0%)	(0.12 to	-	VERY	
	triaio		inconsistency	indirectiness	Scrious		(0.1 70)	(070)	65.34)		LOW	
								0%	00.04)	_	LOVV	
Discontin	ustion for a	N roscon	(lithium vorcus :	anticonvulcant	[lamotrigino]	/follow up moan	8 weeks; assessed wit		ticinante die	continuing for any	roscon	(including
adverse e		iy reason	(IIIIIIIIIIII Versus a	anticonvuisant	[iaiiiotrigiiie]	(tollow-up illean	o weeks, assessed wil	iii. Nuilibei oi pai	licipants uis	continuing for any	reason	(including
auverse e	events))											
1	randomised	serious <sup>15</sup>	no serious	no serious	very	none	2/17	2/17	RR 1 (0 16	0 fewer per 1000	⊕ООО	
	trials	3011003	inconsistency	indirectness	serious <sup>16</sup>	Horic	(11.8%)	(11.8%)	to 6.3)	(from 99 fewer to	VERY	
	indio		integricioterio	in an oothood	Conodo		(11.070)	(11.070)	10 0.0)	624 more)	LOW	
										024 more)	LOVV	
										0 fewer per 1000		
								11.8%		(from 99 fewer to		
										625 more)		
Discontir	nuation due t	o adverse	events (lithium	versus anv 'oth	er' augmenta	tion agent) (follow	/-up 2-14 weeks; asses	sed with: Numbe	r of particip	ants discontinuing	due to a	dverse
events)			,	•		3. , (	,		,			
,												
7	randomised	serious <sup>17</sup>	no serious	no serious	very	reporting bias <sup>3</sup>	37/366	32/370	RR 1.27	23 more per 1000	⊕000	
	trials		inconsistency	indirectness	serious <sup>16</sup>		(10.1%)	(8.6%)	(0.61 to	(from 34 fewer to	VERY	
									2.64)	142 more)	LOW	
								0%		-		
Discontir	nuation due t	o adverse	events (lithium	versus TCA) (fo	llow-up mea	n 4 weeks; assess	ed with: Number of pa	rticipants discont	inuing due	to adverse events)		
			·		·			•		·		
1	randomised	serious <sup>15</sup>	no serious	no serious	very	reporting bias3	1/14	2/12	RR 0.43	95 fewer per 1000	⊕000	
	trials		inconsistency	indirectness	serious <sup>16</sup>		(7.1%)	(16.7%)	(0.04 to	(from 160 fewer to	VERY	
									4.16)	527 more)	LOW	
										95 fewer per 1000		
								16.7%		(from 160 fewer to		
										528 more)		
Discontin	nuation due t	o adverse	events (lithium	versus antipsyo	chotic) (follow	v-up 6-8 weeks; as	ssessed with: Number	of participants di	scontinuing	due to adverse ev	ents)	
		serious <sup>1</sup>	no serious	no serious	very	reporting bias <sup>3</sup>	19/239	23/241		16 fewer per 1000		
	trials		inconsistency	indirectness	serious <sup>16</sup>		(7.9%)	(9.5%)	(0.46 to	(from 52 fewer to	VERY	
									1.48)	46 more)	LOW	
								=0/		9 fewer per 1000		
								5%		(from 27 fewer to		
		<u> </u>								24 more)		
Discontin	nuation due t	o adverse	events (lithium	versus thyroid	hormone [T3]	) (follow-up 2-14 v	veeks; assessed with:	Number of partic	pants disco	ontinuing due to ac	lverse ev	ents)

3	randomised	serious <sup>17</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	17/96	7/100	RR 2.44	101 more per	⊕000	
	trials		inconsistency	indirectness			(17.7%)	(7%)	(1.1 to 5.43)	1000 (from 7 more	VERY	
										to 310 more)	LOW	
								0%		-		
Disconti	nuation due t	o adverse	events (lithium	versus anticonv	ulsant [lamo	trigine]) (follow-u	p mean 8 weeks; asses	ssed with: Numbe	er of particip	ants discontinuing	due to a	dverse
events)												
1	randomised	serious <sup>15</sup>	no serious	no serious	serious <sup>2</sup>	none	0/17	0/17	not pooled	not pooled	$\oplus \oplus OO$	
	trials		inconsistency	indirectness			(0%)	(0%)			LOW	
								0%		not pooled		

<sup>&</sup>lt;sup>1</sup> Unclear method of allocation concealment and unclear or non-blind intervention administration in studies contributing >50% to weighting in analysis

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<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical company

<sup>&</sup>lt;sup>4</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>5</sup> 95% CI crosses line of no effect and threshold for clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>6</sup> I-squared>50%

<sup>&</sup>lt;sup>7</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline (in studies contributing >50% to weighting in analysis) and unclear method of allocation concealment and unclear blinding of intervention administration

<sup>&</sup>lt;sup>8</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>&</sup>lt;sup>9</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline and unclear method of allocation concealment and unclear blinding of intervention administration

<sup>&</sup>lt;sup>10</sup> Unclear method of allocation concealment and non-blind intervention administration

<sup>&</sup>lt;sup>11</sup> Risk associated with randomisation method is high or unclear, the method of allocation concealment is unclear, and blinding of intervention administration and outcome assessment is unclear, in studies contributing to >50% of weighting in analysis

<sup>&</sup>lt;sup>12</sup> N<400

<sup>&</sup>lt;sup>13</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (SMD 0.5)

<sup>&</sup>lt;sup>14</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>15</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration

<sup>&</sup>lt;sup>16</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>17</sup> Risk associated with randomisation method is high or unclear, the method of allocation concealment is unclear, and blinding of intervention administration is unclear, in studies contributing to >50% of weighting in analysis

Augmenting the antidepressant with an antipsychotic compared to 'other' augmentation agents (head-to-head comparisons)

			Quality ass	- Coolinging			No of patie	into		Effect	Quality	lmnorte
No of tudies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with an antipsychotic	Any 'other' augmentation agent	Relative (95% CI)	Absolute	Quanty	importa
missio	on (antipsych	notic vers	us anticonvulsa	nt) (follow-up n	nean 8 weeks	; assessed with:	Number of people scoring	ıg ≤7 on Hamilton	Rating Scal	le for Depression (	HAM-D))	
	randomised	very	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	12/45	19/39	RR 0.55	219 fewer per	⊕000	
	trials	serious <sup>1</sup>	inconsistency	indirectness		, 0	(26.7%)	(48.7%)	(0.31 to	1000 (from 10	VERY	
							,	, ,	0.98)	fewer to 336	LOW	
										fewer)		
										219 fewer per		
										1000 (from 10		
								48.7%		fewer to 336		
										fewer)		
		very serious <sup>1</sup>	no serious inconsistency	no serious indirectness		reporting bias <sup>3</sup>	ber of people scoring ≤7  12/45 (26.7%)	15/46 (32.6%)	RR 0.82 (0.43 to	59 fewer per 1000 (from 186 fewer to	⊕000	
									1.55)	179 more)	LOW	
											l I	
										59 fewer per 1000		
								32.6%		59 fewer per 1000 (from 186 fewer to		
								32.6%		59 fewer per 1000 (from 186 fewer to 179 more)		
missic	on (antipsych	notic vers	us thyroid horm	one) (follow-up	mean 8 wee	ks; assessed witl	n: Number of people scor		n Rating Sc	(from 186 fewer to 179 more)	n (HAM-D	))
missic	on (antipsych	very	us thyroid horm	one) (follow-up			n: Number of people scor		n Rating So	(from 186 fewer to 179 more)	1 (HAM-D ⊕000	))
missio				no serious		ks; assessed with reporting bias <sup>3</sup>		ring ≤7 on Hamilto		(from 186 fewer to 179 more) cale for Depression	⊕000	))
missio	randomised	very	no serious	no serious	very		12/45	ring ≤7 on Hamilto 18/48	RR 0.71	(from 186 fewer to 179 more) cale for Depression		))
missic	randomised	very	no serious	no serious	very		12/45	ring ≤7 on Hamilto 18/48	RR 0.71 (0.39 to	(from 186 fewer to 179 more) cale for Depression 109 fewer per 1000 (from 229	⊕000 VERY	))
missid	randomised	very	no serious	no serious	very		12/45	ring ≤7 on Hamilto 18/48	RR 0.71 (0.39 to	(from 186 fewer to 179 more) cale for Depression 109 fewer per 1000 (from 229 fewer to 112 more)	⊕000 VERY	))
missio	randomised	very	no serious	no serious	very		12/45	ring ≤ <b>7 on Hamilto</b> 18/48 (37.5%)	RR 0.71 (0.39 to	(from 186 fewer to 179 more) cale for Depression 109 fewer per 1000 (from 229 fewer to 112 more) 109 fewer per	⊕000 VERY	))
missio	randomised	very	no serious	no serious	very		12/45	ring ≤7 on Hamilto 18/48	RR 0.71 (0.39 to	(from 186 fewer to 179 more) cale for Depression 109 fewer per 1000 (from 229 fewer to 112 more)	⊕000 VERY	))

		very	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	12/45	20/47	RR 0.63	157 fewer per	⊕000	
	trials	serious <sup>1</sup>	inconsistency	indirectness			(26.7%)	(42.6%)	(0.35 to	1000 (from 277	VERY	
									1.13)	fewer to 55 more)	LOW	
									+	99 fewer per 1000		
								26.7%		(from 174 fewer to		
								20.7 /0		35 more)		
	. /4:	-41					November of manufactors	i>F00/ i		,	for Donn	!
M-D))	e (anupsych	ouc vers	us anticonvuisa	int) (iollow-up i	nean o weel	ks; assessed with:	Number of people show	wing 250% improve	ment on Hai	miton Rating Scale	e for Depre	essioi
(נט-ואו)												
	randomised	very	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	21/45	24/39	RR 0.76	148 fewer per	⊕ООО	
	trials	serious <sup>1</sup>	inconsistency	indirectness	0011000	roporting blac	(46.7%)	(61.5%)	(0.51 to	1000 (from 302	VERY	
ľ		0011040					(1011 /0)	(0.1070)	1.13)	fewer to 80 more)	LOW	
									,,,,	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	2011	
										148 fewer per		
								61.5%		1000 (from 301		
										fewer to 80 more)		
sponse	e (antipsych	otic vers	us anxiolytic) (f	ollow-up mean	8 weeks; as	sessed with: Numb	per of people showing	≥50% improvement	on Hamiltor	າ Rating Scale for I	Depressio	n (HA
ļ		very	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	21/45 (46.7%)	26/46 (56.5%)	RR 0.83 (0.55 to	96 fewer per 1000 (from 254 fewer to		
	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	21/45 (46.7%)	26/46 (56.5%)	RR 0.83 (0.55 to 1.23)	96 fewer per 1000 (from 254 fewer to 130 more)		
					serious <sup>5</sup>	reporting bias <sup>3</sup>			(0.55 to	(from 254 fewer to 130 more)	VERY	
					serious <sup>5</sup>	reporting bias <sup>3</sup>		(56.5%)	(0.55 to	(from 254 fewer to 130 more) 96 fewer per 1000	VERY	
					serious <sup>5</sup>	reporting bias <sup>3</sup>			(0.55 to	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to	VERY	
	trials	serious <sup>1</sup>	inconsistency	indirectness			(46.7%)	(56.5%)	(0.55 to 1.23)	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more)	VERY LOW	aross;
sponse	trials	serious <sup>1</sup>	inconsistency	indirectness				(56.5%)	(0.55 to 1.23)	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more)	VERY LOW	oressi
sponse	trials e (antipsych	serious <sup>1</sup>	inconsistency us thyroid horm	indirectness	p mean 8 we	eks; assessed with	(46.7%)	(56.5%) 56.5% owing ≥50% improv	(0.55 to 1.23)	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more)	VERY LOW	oressi
sponse	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up			(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% impro	(0.55 to 1.23)	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more) amilton Rating Sca	VERY LOW	oress
sponse	trials e (antipsych	serious <sup>1</sup>	inconsistency us thyroid horm	indirectness	p mean 8 we	eks; assessed with	(46.7%)	(56.5%) 56.5% owing ≥50% improv	(0.55 to 1.23)  vement on H  RR 0.8 (0.54 to	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more) amilton Rating Sca 117 fewer per 1000 (from 268	VERY LOW	oress
sponse	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up	p mean 8 we	eks; assessed with	(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% impro	(0.55 to 1.23)	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more) amilton Rating Sca 117 fewer per 1000 (from 268 fewer to 111	VERY LOW	oress
sponse	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up	p mean 8 we	eks; assessed with	(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% impro	(0.55 to 1.23)  vement on H  RR 0.8 (0.54 to	(from 254 fewer to 130 more) 96 fewer per 1000 (from 254 fewer to 130 more) amilton Rating Sca 117 fewer per 1000 (from 268	VERY LOW	oress
sponse	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up	p mean 8 we	eks; assessed with	(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% impro	(0.55 to 1.23)  vement on H  RR 0.8 (0.54 to	(from 254 fewer to 130 more)  96 fewer per 1000 (from 254 fewer to 130 more)  amilton Rating Sca  117 fewer per 1000 (from 268 fewer to 111 more)	VERY LOW	oressi
sponse AM-D))	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up	p mean 8 we	eks; assessed with	(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% improv  28/48 (58.3%)	(0.55 to 1.23)  vement on H  RR 0.8 (0.54 to	(from 254 fewer to 130 more)  96 fewer per 1000 (from 254 fewer to 130 more)  amilton Rating Sca  117 fewer per 1000 (from 268 fewer to 111 more)  117 fewer per	VERY LOW	pressi
sponse	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up	p mean 8 we	eks; assessed with	(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% impro	(0.55 to 1.23)  vement on H  RR 0.8 (0.54 to	(from 254 fewer to 130 more)  96 fewer per 1000 (from 254 fewer to 130 more)  amilton Rating Sca  117 fewer per 1000 (from 268 fewer to 111 more)  117 fewer per 1000 (from 268	VERY LOW	pressi
sponse (M-D))	e (antipsych	serious <sup>1</sup> otic vers	us thyroid horm	none) (follow-up	p mean 8 we	eks; assessed with	(46.7%)  a: Number of people sh	(56.5%)  56.5%  owing ≥50% improv  28/48 (58.3%)	(0.55 to 1.23)  vement on H  RR 0.8 (0.54 to	(from 254 fewer to 130 more)  96 fewer per 1000 (from 254 fewer to 130 more)  amilton Rating Sca  117 fewer per 1000 (from 268 fewer to 111 more)  117 fewer per	VERY LOW	press

1	randomised	very	no serious	no serious	serious <sup>5</sup>	reporting bias3	21/45	29/47	RR 0.76	148 fewer per	⊕000	
	trials	serious <sup>1</sup>	inconsistency	indirectness			(46.7%)	(61.7%)	(0.51 to	1000 (from 302	VERY	
									1.11)	fewer to 68 more)	LOW	
										112 fewer per		
								46.7%		1000 (from 229		
										fewer to 51 more)		

<sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and unclear blinding of intervention administration and outcome assessment

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## Augmenting the antidepressant with an anticonvulsant compared to 'other' augmentation agents (head-to-head comparisons)

			Quality ass	essment			No of patie	ents		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with an anticonvulsant	Any 'other' augmentation agent	Relative (95% CI)	Absolute		
Remissio	on (anticonvu	lsant ver	sus anxiolytic) (f	ollow-up mean	8 weeks; as	sessed with: Nur	nber of people scoring ≤7	on Hamilton Rati	ng Scale fo	r Depression (HAN	/I-D))	
				no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	19/39 (48.7%)	15/46 (32.6%) 32.6%	RR 1.49 (0.88 to 2.53)	160 more per 1000 (from 39 fewer to 499 more) 160 more per 1000 (from 39 fewer to 499	⊕OOO VERY LOW	
Remissio	on (anticonvu	ılsant ver	sus SARI) (follow	v-up mean 8 we	eeks; assess	ed with: Number	of people scoring ≤7 on h	Hamilton Rating S	cale for Dep	more) pression (HAM-D))		
				no serious indirectness	very serious <sup>4</sup>	reporting bias <sup>3</sup>	19/39 (48.7%)	20/47 (42.6%)	RR 1.14 (0.72 to 1.82)	60 more per 1000 (from 119 fewer to 349 more)		
								42.6%		60 more per 1000 (from 119 fewer to 349 more)		

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical company

<sup>&</sup>lt;sup>4</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>5</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

High risk of bias associated with randomisation method due to significant difference between groups at baseline, and unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>2</sup> 95% crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical company

<sup>4 95%</sup> CI crosses line of no effect and both threshold for clinically important harm (RR 0.75) and for clinically important benefit (RR 1.25)

1 Augmenting the antidepressant with an anxiolytic compared to 'other' augmentation agents (head-to-head comparisons)

			Quality as	sessment			No of patie	ents		Effect		
											Quality	Importar
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with an anxiolytic	Any 'other' augmentation agent	Relative (95% CI)	Absolute		
emissi	on (anxiolytic	versus a	typical antidepr	essant) (follow-	-up mean 6 we	eks; assessed w	ith: Number of people so	oring ≤7 on Hami	Iton Rating	Scale for Depress	ion (HAI	M-D))
		very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	86/286 (30.1%)	83/279 (29.7%)	RR 1.01 (0.79 to 1.3)	3 more per 1000 (from 62 fewer to 89 more)	⊕000 VERY LOW	
								29.8%		3 more per 1000 (from 63 fewer to 89 more)		
emissi	on (anxiolytic	versus S	SARI) (follow-up	mean 8 weeks;	assessed with	n: Number of peo	ple scoring ≤7 on Hamilt	ton Rating Scale f	or Depressi	on (HAM-D))		
		very serious <sup>4</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	15/46 (32.6%)	20/47 (42.6%)		98 fewer per 1000 (from 234 fewer to 128 more)		
								42.6%		98 fewer per 1000 (from 234 fewer to 128 more)		
		Warana 4	hyroid hormone	) (follow-up me	an 8 weeks; as	sessed with: Nu	mber of people scoring s	≦7 on Hamilton Ra	ating Scale 1	for Depression (H	AM-D))	
emissi	on (anxiolytic	versus i	nyroid normone									
emissi	randomised	very	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	15/46 (32.6%)	18/48 (37.5%)		49 fewer per 1000 (from 188 fewer to 191 more)		
	randomised trials	very serious <sup>4</sup>	no serious inconsistency	indirectness			(32.6%)	(37.5%)	(0.5 to 1.51)	(from 188 fewer to 191 more) 49 fewer per 1000 (from 188 fewer to 191 more)	VERY LOW	
espons	randomised trials	very serious <sup>4</sup>	no serious inconsistency	indirectness				(37.5%)	(0.5 to 1.51)	(from 188 fewer to 191 more) 49 fewer per 1000 (from 188 fewer to 191 more)	VERY LOW	ssive

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline and unclear method of allocation concealment, and unclear blinding of intervention administration

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical company

<sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

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## Augmenting the antidepressant with a thyroid hormone compared to 'other' augmentation agents (head-to-head comparisons)

			Quality ass	essment			No of patie	ents		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with a thyroid hormone	Any 'other' augmentation agent	Relative (95% CI)	Absolute		
Remissio	on (thyroid he	ormone v	ersus SARI) (foli	ow-up mean 8	weeks; asse	ssed with: Number	er of people scoring ≤7 or	n Hamilton Rating	Scale for D	epression (HAM-D	))	
			no serious inconsistency		very serious <sup>2</sup>	reporting bias <sup>3</sup>	18/48 (37.5%)	20/47 (42.6%)	RR 0.88 (0.54 to 1.44)	51 fewer per 1000 (from 196 fewer to 187 more)		
								42.6%		51 fewer per 1000 (from 196 fewer to		
Respons	e (thyroid ho	rmone ve	ersus SARI) (folio	ow-up mean 8 v	weeks; asses	ssed with: Numbe	r of people showing ≥50%	% improvement on	Hamilton F	187 more) Rating Scale for De	pression	ı (HAM-D))
1		- J	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	28/48 (58.3%)	29/47 (61.7%)	RR 0.95 (0.68 to 1.31)	31 fewer per 1000 (from 197 fewer to 191 more)		
								61.7%	1.01)	31 fewer per 1000 (from 197 fewer to 191 more)		

High risk of bias associated with randomisation method due to significant difference between groups at baseline, and unclear blinding of intervention administration and outcome assessment

## Augmenting the antidepressant with a psychological intervention compared to attention-placebo

Quality assessment	No of patients	Effect	Quality	Importance

<sup>&</sup>lt;sup>7</sup> Events<300

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and both threshold for clinically important harm (RR 0.75) and for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical company

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with a psych intervention	Attention- placebo	Relative (95% CI)	Absolute	
	on (Mindfulne ession (HAM-		cognitive therap	oy [MBCT] versu	us attention-p	placebo) (follow-u	p mean 8 weeks; assessed	with: Number	er of people	scoring ≤7 on Ham	ilton Rating S
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	19/87 (21.8%)	12/86 (14%)	RR 1.57 (0.81 to 3.02)	80 more per 1000 (from 27 fewer to 282 more)	⊕000 VERY LOW
								14%		80 more per 1000 (from 27 fewer to 283 more)	
			cognitive therap ression (HAM-D))		s attention-p	lacebo) (follow-u	o mean 8 weeks; assessed	with: Numbe	r of people	showing ≥50% impr	ovement on
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	27/87 (31%)	13/86 (15.1%)	RR 2.05 (1.14 to 3.71)	159 more per 1000 (from 21 more to 410 more)	⊕000 VERY LOW
								15.1%		159 more per 1000 (from 21 more to 409 more)	
•		<b>.</b> .	Mindfulness-base indicated by low	•	erapy [MBCT]	versus attention	-placebo) (follow-up mean 8	8 weeks; mea	sured with:	Hamilton Rating So	cale for Depre
	randomised trials	serious <sup>5</sup>	no serious inconsistency	no serious indirectness	serious <sup>6</sup>	none	23	20	-	MD 5.06 lower (7.78 to 2.34 lower)	⊕⊕OO LOW
			(Mindfulness-bancluding adverse		herapy [MBC	T] versus attention	n-placebo) (follow-up mea	n 8 weeks; as	ssessed wit	h: Number of partic	ipants
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>7</sup>	reporting bias <sup>3</sup>	15/113 (13.3%)	20/110 (18.2%)	RR 0.73 (0.39 to 1.34)	49 fewer per 1000 (from 111 fewer to 62 more)	⊕OOO VERY LOW
								20.6%		56 fewer per 1000 (from 126 fewer to 70 more)	

<sup>&</sup>lt;sup>1</sup> Unclear method of allocation concealment and non-blind intervention administration

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data cannot be extracted/is not reported for all outcomes

<sup>&</sup>lt;sup>4</sup> Events<300

<sup>5</sup> Non-blind intervention administration

<sup>6</sup> N<400

<sup>7</sup> 95% CI crosses line of no effect and both threshold for clinically important benefit (RR 0.75) and for clinically important harm (RR 1.25)

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Augmenting the antidepressant with a psychological intervention compared to continuing with the antidepressant-only

			Quality ass	sessment			No of pa	atients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with a psych intervention	Continuing with the antidepressant-only	Relative (95% CI)	Absolute		
			rersus any AD) (f nt on HAM-D))	follow-up mear	12 weeks; as	sessed with: Nur	mber of people scoring	<8 on Hamilton Ratin	g Scale for	Depression (HA	M-D) AN	D
1	randomised trials	serious <sup>1</sup>		no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	67/174 (38.5%)	30/76 (39.5%)	RR 0.98 (0.7 to 1.36)	8 fewer per 1000 (from 118 fewer to 142 more)	⊕000 VERY LOW	
Dominaia	on (CDT indi	sidual fav	or 45 occional	L TALL versus		20 27 weeke e	and with Number	39.5%		8 fewer per 1000 (from 119 fewer to 142 more)		oion (LIANA
			ventory (BDI))	F TAU Versus	(IOIIOW-u	ρ 20-27 weeks; as	ssessed with: Number o	or people scoring 57 (	on Hamilton	n Raung Scale ic	r Depres	SSION (HAIVI-
2	randomised	very	no serious	no serious	serious <sup>5</sup>	none	76/286	41/291	RR 1.89	125 more per	⊕000	
	trials	serious <sup>4</sup>	inconsistency	indirectness			(26.6%)	(14.1%)	(1.34 to 2.66)	1000 (from 48 more to 234 more)	VERY LOW	
								13.3%		118 more per 1000 (from 45 more to 221 more)		
Remission (HAM-D)	•	vidual [un	der 15 sessions	] + TAU versus	TAU) (follow-	up mean - weeks	; assessed with: Numb	er of people scoring s	7 on Hami	Iton Rating Scale	for Dep	ression
1	randomised trials	serious <sup>6</sup>		no serious indirectness	serious <sup>5</sup>	none	13/21 (61.9%)	4/21 (19%)		429 more per 1000 (from 51		

							•					
									RR 3.25	more to 1000	⊕⊕00	
									(1.27 to	more)	LOW	
									8.35)			
									,	430 more per		
										1000 (from 52		
								19.1%		more to 1000		
										more)		
	, ,,,,				1 1 12 .	AD/TALL	AD/TALL 1 X/S II	40.0=	<u> </u>	,		=
							any AD/TAU-only) (folio rement on HAM-D)/<10 o				eopie sco	oring ≤ <i>r</i> on
4	randomised	serious1	serious <sup>7</sup>	no serious	serious <sup>5</sup>	none	156/481	75/388	RR 1.68	131 more per	⊕000	
	trials			indirectness			(32.4%)	(19.3%)	(1.02 to	1000 (from 4	VERY	
							,	,	2.78)	more to 344	LOW	
									,	more)	2011	
									ĺ			
						1			1	116 more per		
									]	1000 (from 3		
								17%		more to 303		
						ļ				more)		
Remission					·		eople scoring ≤7 on Ham					
1	randomised	serious	no serious	no serious	very serious <sup>2</sup>	none	5/16	3/18	RR 1.88	147 more per	⊕000	
	trials		inconsistency	indirectness			(31.3%)	(16.7%)	(0.53 to	1000 (from 78	VERY	
									6.63)	fewer to 938	LOW	
										more)		
										147 more per		
										1000 (from 78		
								16.7%		`		
										fewer to 940		
										more)		
						TAU versus any % improvement o	AD/TAU) (follow-up 12-2 on HAM-D))	20 weeks; assessed	with: Numb	er of people sco	ring ≤7 o	n Hamilton
2	randomised	serious <sup>1</sup>	very serious9	no serious	very serious <sup>2</sup>	reporting bias10	63/198	31/106	RR 2.5	439 more per	$\oplus$ OOO	
2	randomised trials	serious <sup>1</sup>	very serious <sup>9</sup>	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>10</sup>	63/198 (31.8%)	31/106 (29.2%)	RR 2.5 (0.16 to	1000 (from 246	⊕OOO VERY	
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>						
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>			(0.16 to	1000 (from 246	VERY	
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>			(0.16 to	1000 (from 246 fewer to 1000	VERY	
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>			(0.16 to	1000 (from 246 fewer to 1000 more)	VERY	
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>		(29.2%)	(0.16 to	1000 (from 246 fewer to 1000 more)	VERY	
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>			(0.16 to	1000 (from 246 fewer to 1000 more)	VERY	
2		serious <sup>1</sup>	very serious <sup>9</sup>		very serious <sup>2</sup>	reporting bias <sup>10</sup>		(29.2%)	(0.16 to	1000 (from 246 fewer to 1000 more)  321 more per 1000 (from 180	VERY	

randomised	very	no serious	no serious	very serious <sup>2</sup>	reporting bias12	6/67	4/62	RR 1.39	25 more per	⊕ООО
trials	serious <sup>11</sup>	inconsistency	indirectness		repermig area	(9%)	(6.5%)	(0.41 to	1000 (from 38	VERY
		,				(2.22)	(2 2 2 2 )	4.69)	fewer to 238	LOW
								,	more)	
									,	
									25 more per	
							6.5%		1000 (from 38	
							0.570		fewer to 240	
									more)	
			/) (follow-up 19	-27 weeks; ass	essed with: Numl	per of people showing	≥50% improvement	on Hamilton	Rating Scale for	Depressi
k Depression	Inventory	(BDI))								
				1						
randomised		no serious	no serious	serious <sup>5</sup>	none	118/243	55/252	RR 2.22	266 more per	⊕OOO
trials	serious4	inconsistency	indirectness			(48.6%)	(21.8%)	(1.7 to 2.9)	1000 (from 153	VERY
									more to 415	LOW
									more)	
									074	
									271 more per	
							22.2%		1000 (from 155	
							22.2%		more to 422	
unsa (CRT indi	widual lov	or 15 sossions	+ TAll vareus	TAII) (fallow-u	maan 27 wooke	accessed with Number		og >50% impre	more to 422 more)	Donross
	vidual [ov	er 15 sessions]	+ TAU versus	TAU) (follow-u	o mean 27 weeks;	assessed with: Numb		ng ≥50% impro	more to 422 more)	C Depress
	very	no serious	+ TAU versus	rau) (follow-up	none	assessed with: Numb		RR 2.14	more to 422 more)	( Depress
ory (BDI))		no serious					per of people showing		more to 422 more)	
ory (BDI)) randomised	very	no serious	no serious			95/206	per of people showin	RR 2.14	more to 422 more) pyement on Beck 246 more per	⊕000
randomised	very	no serious	no serious			95/206	per of people showin	RR 2.14 (1.59 to	more to 422 more) ovement on Beck 246 more per 1000 (from 127	⊕000 VERY
randomised	very	no serious	no serious			95/206	per of people showin	RR 2.14 (1.59 to	more to 422 more) ovement on Beck 246 more per 1000 (from 127 more to 404 more)	⊕000 VERY
randomised	very	no serious	no serious			95/206	per of people showin	RR 2.14 (1.59 to	more to 422 more)  ovement on Beck  246 more per 1000 (from 127 more to 404 more)  246 more per	⊕000 VERY
randomised	very	no serious	no serious			95/206	46/213 (21.6%)	RR 2.14 (1.59 to	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127	⊕000 VERY
randomised	very	no serious	no serious			95/206	per of people showin	RR 2.14 (1.59 to	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404	⊕000 VERY
randomised trials	very serious <sup>13</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	95/206 (46.1%)	46/213 (21.6%)	RR 2.14 (1.59 to 2.87)	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)	⊕OOO VERY LOW
randomised trials	very serious <sup>13</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	95/206	46/213 (21.6%)	RR 2.14 (1.59 to 2.87)	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)	⊕OOO VERY LOW
randomised trials	very serious <sup>13</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	95/206 (46.1%)	46/213 (21.6%)	RR 2.14 (1.59 to 2.87)	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)	⊕OOO VERY LOW
randomised trials	very serious <sup>13</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	95/206 (46.1%)	46/213 (21.6%) 21.6%	RR 2.14 (1.59 to 2.87)	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)	⊕OOO VERY LOW
randomised trials	very serious <sup>13</sup> vidual [un	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	95/206 (46.1%)	46/213 (21.6%)	RR 2.14 (1.59 to 2.87)	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)  ovement on Hami	⊕OOO VERY LOW
randomised trials  onse (CBT indicepression (HAM)	very serious <sup>13</sup> vidual [un	no serious inconsistency der 15 sessions	no serious indirectness 	serious <sup>5</sup>	none up mean - weeks;	95/206 (46.1%)	46/213 (21.6%) 21.6%	RR 2.14 (1.59 to 2.87) g ≥50% impro	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)	⊕OOO VERY LOW
randomised trials  onse (CBT indiapression (HAM	very serious <sup>13</sup> vidual [un	no serious inconsistency  der 15 sessions	no serious indirectness  1 + TAU versus	serious <sup>5</sup>	none up mean - weeks;	95/206 (46.1%) assessed with: Numb	46/213 (21.6%) 21.6% per of people showin	RR 2.14 (1.59 to 2.87) g ≥50% impro	more to 422 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)  246 more per 1000 (from 127 more to 404 more)  ovement on Hami	⊕OOO VERY LOW

								23.8%		571 more per 1000 (from 129 more to 1000 more)	
pon	se (IPT + TAL	J versus 1	AU) (follow-up	mean 19 week	s; assessed w	vith: Number of pe	ople showing ≥50% im	provement on Hamil	ton Rating S	cale for Depress	ion (HAM-D)
	randomised trials	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	6/16 (37.5%)	4/18 (22.2%)	RR 1.69 (0.58 to 4.92)	153 more per 1000 (from 93 fewer to 871 more)	⊕OOO VERY LOW
								22.2%		153 more per 1000 (from 93 fewer to 870 more)	
								weeks; assessed wit	th: Number of	of people showin	g ≥50%
	randomised trials		no serious indirectness	serious <sup>5</sup>	none	112/227 (49.3%)	51/234 (21.8%)	RR 2.32 (1.64 to 3.27)	288 more per 1000 (from 139 more to 495 more)	⊕OOO VERY LOW	
								22.7%		300 more per 1000 (from 145 more to 515 more)	
	sion symptoned by lower va		CBASP + any A	D versus any i	AD) (follow-up	mean 12 weeks;	neasured with: Hamilto	on Rating Scale for D	epression (	HAM-D; change s	core); Bette
dicate		serious <sup>1</sup>	no serious	no serious	serious <sup>14</sup>	reporting bias <sup>3</sup>	174	76	-	SMD 0.36 lower	0000
dicate	randomised trials	Scrious	inconsistency	indirectness						(0.64 to 0.09 lower)	VERY LOW
epress	trials sion sympton	natology (	CBT individual	over 15 session			versus clinical manag je score); Better indica			lower)	LOW

			no serious	no serious	serious <sup>14</sup>	none	21	21	-	SMD 1.29 lower	0000	
trials	s		inconsistency	indirectness						(1.96 to 0.62	LOW	
										lower)		
ession sy	symptoma	atology (	l IPT + TAU versi	us TAU) (follow	v-up mean 19	weeks: measured	with: Hamilton Rating S	cale for Depression	(HAM-D: c	hange score): Bet	ter indica	ated by
r values)				, (	<b>up</b> o	,	g	ошо тот доргосотот	( 2, 0	go 000.0 <sub>/</sub> , _0.		
	<u>.</u>											
	domised		no serious	no serious	serious <sup>15</sup>	none	16	18	-	SMD 0.66 lower		
trials	s		inconsistency	indirectness						(1.35 lower to	LOW	
										0.04 higher)		
ession sy	symptoma	atology (s	short-term psyc	chodynamic ns	vchotherany	individual + any Al	versus any AD) (follow	w-up mean 12 weeks	s: measure	d with: Hamilton F	Rating Sc	ale fo
			core); Better inc			marriadar - any A	versus uny AB, (iono	w up mount 12 wooks	, incusure	a with hammon	tuting 00	uic 10.
(	( , -		,,		,							
rando	domised	serious <sup>1</sup>	no serious	no serious	serious <sup>14</sup>	reporting bias <sup>3</sup>	168	76	-	SMD 0.1 lower	⊕000	
trials	s		inconsistency	indirectness						(0.37 lower to	VERY	
										0.17 higher)	LOW	
			long-term psycl indicated by lo		chotherapy +	+ TAU versus TAU-	only) (follow-up mean 7	8 weeks; measured	with: Ham	ilton Rating Scale	for Depre	essior
rando	domised \	e); Better	no serious	no serious	serious <sup>15</sup>	reporting bias 12	only) (follow-up mean 7	8 weeks; measured	with: Ham	SMD 0.26 lower	⊕000	ession
M-D; chan	domised \	e); Better	indicated by lo	ower values)						SMD 0.26 lower (0.61 lower to	⊕000 VERY	ession
M-D; chan	domised \	e); Better	no serious	no serious						SMD 0.26 lower	⊕000	ession
rando trials	domised s	e); Better very serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>15</sup>	reporting bias 12		62	-	SMD 0.26 lower (0.61 lower to 0.09 higher)	⊕OOO VERY LOW	
rando trials	domised s	very serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>15</sup>	reporting bias 12	67	62	-	SMD 0.26 lower (0.61 lower to 0.09 higher)	⊕OOO VERY LOW	
rando trials pression sy rre); Better	domised s	very serious <sup>11</sup> atology (ed by low	no serious inconsistency cognitive biblio rer values)	no serious indirectness	serious <sup>15</sup> AD versus an	reporting bias 12	67	62	-	SMD 0.26 lower (0.61 lower to 0.09 higher) or Depression (HA	⊕OOO VERY LOW	
rando trials pression sy re); Better	domised s	very serious <sup>11</sup> atology (ed by low serious <sup>6</sup>	no serious inconsistency cognitive biblio er values)	no serious indirectness	serious <sup>15</sup>	reporting bias 12	67	62	-	SMD 0.26 lower (0.61 lower to 0.09 higher) or Depression (HA	⊕OOO VERY LOW M-D; cha	
rando trials ression sy re); Better	domised s symptomaer indicate domised s	very serious <sup>11</sup> atology (ed by low serious <sup>6</sup>	no serious inconsistency cognitive biblio rer values)	no serious indirectness therapy + any	serious <sup>15</sup> AD versus an	reporting bias <sup>12</sup> ny AD) (follow-up m	67 ean 6 weeks; measured	62 I with: Hamilton Rati	-	SMD 0.26 lower (0.61 lower to 0.09 higher) or Depression (HA	⊕OOO VERY LOW	
rando trials  pression syre); Better	domised s symptomaer indicate domised s	very serious <sup>11</sup> atology (ed by low serious <sup>6</sup>	no serious inconsistency cognitive biblio rer values)	no serious indirectness indirectness	serious <sup>15</sup> AD versus an	reporting bias <sup>12</sup> ny AD) (follow-up m	67 ean 6 weeks; measured	62 I with: Hamilton Rati	-	SMD 0.26 lower (0.61 lower to 0.09 higher) or Depression (HA	⊕OOO VERY LOW M-D; cha	
rando trials pression sy pre); Better rando trials	domised s symptoma er indicate domised s	very serious <sup>11</sup> atology (i ed by low serious <sup>6</sup>	no serious inconsistency cognitive biblio er values) no serious inconsistency	no serious indirectness  therapy + any and no serious indirectness	serious <sup>15</sup> AD versus an	reporting bias 12  By AD) (follow-up m	ean <b>6 weeks; measured</b> 49	62 I with: Hamilton Rati	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)	⊕OOO VERY LOW M-D; cha	inge
rando trials  pression syre); Better  rando trials  pression syre); Better	domised s symptoma er indicate domised s symptoma	very serious <sup>11</sup> atology (i ed by low serious <sup>6</sup>	no serious inconsistency cognitive biblio er values) no serious inconsistency	no serious indirectness  therapy + any and no serious indirectness	serious <sup>15</sup> AD versus an	reporting bias 12  By AD) (follow-up m	67 ean 6 weeks; measured	62 I with: Hamilton Rati	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)	⊕OOO VERY LOW M-D; cha	inge
rando trials  pression sylve); Better  rando trials  pression sylve); Better	domised s symptoma er indicate domised s symptoma	very serious <sup>11</sup> atology (i ed by low serious <sup>6</sup>	no serious inconsistency cognitive biblio er values) no serious inconsistency	no serious indirectness  therapy + any and no serious indirectness	serious <sup>15</sup> AD versus an	reporting bias 12  By AD) (follow-up m	ean <b>6 weeks; measured</b> 49	62 I with: Hamilton Rati	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)	⊕OOO VERY LOW M-D; cha	inge
rando trials pression sy pre); Better rando trials pression sy lower value	symptoma straight str	very serious <sup>11</sup> atology (i	no serious inconsistency cognitive biblio er values) no serious inconsistency	no serious indirectness  no serious indirectness  therapy + any A  no serious indirectness	serious <sup>15</sup> AD versus and serious <sup>15</sup> rsus TAU) (for	reporting bias 12  by AD) (follow-up m  none  pllow-up mean 24 w	ean 6 weeks; measured 49 eeks; measured with: E	62 d with: Hamilton Rati 41 Beck Depression Inv	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)  DI-II; change score	⊕OOO VERY LOW M-D; cha	inge
rando trials pression sy pre); Better rando trials pression sy lower value	symptoma ser indicate domised s symptoma ues)	very serious <sup>11</sup> satology (i ed by low serious <sup>6</sup> satology (i	no serious inconsistency  cognitive bibliouer values)  no serious inconsistency  mutual peer sup	no serious indirectness  therapy + any and no serious indirectness	serious <sup>15</sup> AD versus an	reporting bias 12  By AD) (follow-up m	ean <b>6 weeks; measured</b> 49	62 I with: Hamilton Rati	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)  DI-II; change score	⊕OOO VERY LOW  M-D; cha  ⊕⊕OO LOW  ⊕⊕OO LOW	inge
rando trials  pression sylvere; Better  rando trials  pression sylveression sylvere	symptoma ser indicate domised s symptoma ues)	very serious <sup>11</sup> satology (i ed by low serious <sup>6</sup> satology (i	no serious inconsistency cognitive biblio er values) no serious inconsistency	no serious indirectness  no serious indirectness  no serious indirectness  pport + TAU ve	serious <sup>15</sup> AD versus and serious <sup>15</sup> rsus TAU) (for	reporting bias 12  by AD) (follow-up m  none  pllow-up mean 24 w	ean 6 weeks; measured 49 eeks; measured with: E	62 d with: Hamilton Rati 41 Beck Depression Inv	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)  DI-II; change score  SMD 0.03 lower (0.25 lower to	⊕OOO VERY LOW  M-D; cha  ⊕⊕OO LOW  ; Better i	inge
rando trials  pression syore); Better  rando trials  pression sylverials  pression sylver value  rando	symptoma ser indicate domised s symptoma ues)	very serious <sup>11</sup> satology (i ed by low serious <sup>6</sup> satology (i	no serious inconsistency  cognitive bibliouer values)  no serious inconsistency  mutual peer sup	no serious indirectness  no serious indirectness  no serious indirectness  pport + TAU ve	serious <sup>15</sup> AD versus and serious <sup>15</sup> rsus TAU) (for	reporting bias 12  by AD) (follow-up m  none  pllow-up mean 24 w	ean 6 weeks; measured 49 eeks; measured with: E	62 d with: Hamilton Rati 41 Beck Depression Inv	ing Scale fo	SMD 0.26 lower (0.61 lower to 0.09 higher)  or Depression (HA  SMD 0.37 lower (0.79 lower to 0.05 higher)  DI-II; change score	⊕OOO VERY LOW  M-D; cha  ⊕⊕OO LOW  ⊕⊕OO LOW	inge

	randomised trials	serious'	serious'	no serious indirectness	no serious imprecision	none	481	388	-	SMD 0.52 lower (0.83 to 0.2		
	liidis			muneciness	imprecision					lower)	LOW	
	nuation for a	ny reasor	n (CBASP + any	AD versus any	(AD) (follow-u	up mean 12 weeks	; assessed with: Number	er of participants dis	scontinuing	for any reason (i	ncluding	advers
ents))												
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>18</sup>	reporting bias <sup>3</sup>	25/200 (12.5%)	16/96 (16.7%)	RR 0.75 (0.42 to	42 fewer per 1000 (from 97	⊕OOO VERY	
									1.34)	fewer to 57 more)	LOW	
										42 fewer per 1000 (from 97		
								16.7%		fewer to 57 more)		
						al management/T/	AU versus clinical mana	gement/TAU) (follow	w-up 20-27 v	,	with: Nu	mber of
rticipa	ınts discontii	nuing for	any reason (inc	luding adverse	events))							
				1	10		44/044	0.4/0.40	55.4.00			
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>19</sup>	none	44/314	34/313	RR 1.29	32 more per	$\oplus \oplus OO$	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious	none	(14%)	(10.9%)	(0.85 to 1.96)	1000 (from 16 fewer to 104	⊕⊕OO LOW	
		serious <sup>1</sup>			serious 19	none			(0.85 to	1000 (from 16		
		serious <sup>1</sup>			serious 19	none			(0.85 to	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119		
sconti	trials		inconsistency	indirectness			(14%)	(10.9%) 12.4%	(0.85 to 1.96)	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119 more)	LOW	erse
	trials		inconsistency	indirectness				(10.9%) 12.4%	(0.85 to 1.96)	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119 more)	LOW	erse
	trials	ny reasor	inconsistency	indirectness		versus TAU) (ass	(14%)	(10.9%) 12.4%	(0.85 to 1.96)	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119 more)	LOW	erse
	trials nuation for a	ny reasor	inconsistency	indirectness	ssions] + TAU	versus TAU) (ass	(14%) essed with: Number of	(10.9%)  12.4%  participants discon	(0.85 to 1.96) tinuing for a	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119 more)  ny reason (included)  48 fewer per 1000 (from 90	LOW  ding adve	erse
	trials  nuation for a	ny reasor	inconsistency  (CBT individua	indirectness  I [under 15 ses	ssions] + TAU	versus TAU) (ass	(14%) essed with: Number of	(10.9%)  12.4%  participants discon	(0.85 to 1.96)	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119 more)  ny reason (included)	LOW  ding adve	erse
isconti vents))	trials  nuation for a	ny reasor	inconsistency  (CBT individua	indirectness  I [under 15 ses	ssions] + TAU	versus TAU) (ass	(14%) essed with: Number of	(10.9%)  12.4%  participants discon	(0.85 to 1.96) tinuing for a	1000 (from 16 fewer to 104 more)  36 more per 1000 (from 19 fewer to 119 more)  ny reason (included)  48 fewer per 1000 (from 90 fewer to 390	LOW  ding adve	erse

	randomised	serious <sup>6</sup>	no serious	no serious	very serious <sup>18</sup>	none	5/17	2/23	RR 3.38	207 more per	⊕000	
	trials	3011003	inconsistency	indirectness	very serious	Horic	(29.4%)	(8.7%)	(0.74 to	1000 (from 23	VERY	
	triais		inconsistency	indirectricss			(23.470)	(0.7 70)	15.39)	fewer to 1000	LOW	
									15.39)		LOVV	
										more)		
										207 more per		
										1000 (from 23		
								8.7%		fewer to 1000		
										more)		
						individual + any	AD/TAU versus any AD	/TAU) (follow-up 12	-20 weeks; a	ssessed with: No	umber of	
rticipa	ants disconti	nuing for	any reason (inc	luding adverse	e events))							
	randomised	serious <sup>1</sup>	serious <sup>7</sup>	no serious	very serious <sup>18</sup>	reporting bias <sup>10</sup>	34/225	19/126	RR 1.19	29 more per	⊕000	
	trials			indirectness		,	(15.1%)	(15.1%)	(0.45 to	1000 (from 83	VERY	
							,	,	3.13)	fewer to 321	LOW	
									0.10)	more)	LOW	
										more		
										25 more per		
								13.3%		1000 (from 73		
								13.3%		fewer to 283		
	nuation for a			ychodynamic p	sychotherapy +	- TAU versus TAI	J-only) (follow-up mear	n 78 weeks; assesse	ed with: Num	more) ber of participan	nts discont	tinuing
y reas	randomised	yery	no serious	no serious		- TAU versus TAI reporting bias 12	10/67	8/62	RR 1.16	ber of participan	⊕OOO	tinuing
y reas	randomised	yery	no serious						RR 1.16 (0.49 to	21 more per 1000 (from 66	⊕000 VERY	tinuing
/ reas	randomised	yery	no serious	no serious			10/67	8/62	RR 1.16	21 more per 1000 (from 66 fewer to 225	⊕OOO	tinuinç
/ reas	randomised	yery	no serious	no serious			10/67	8/62	RR 1.16 (0.49 to	21 more per 1000 (from 66	⊕000 VERY	tinuing
/ reas	randomised	yery	no serious	no serious			10/67	8/62	RR 1.16 (0.49 to	21 more per 1000 (from 66 fewer to 225 more) 21 more per	⊕000 VERY	tinuing
/ reas	randomised	yery	no serious	no serious			10/67	8/62 (12.9%)	RR 1.16 (0.49 to	21 more per 1000 (from 66 fewer to 225 more)	⊕000 VERY	tinuing
reas	randomised	yery	no serious	no serious			10/67	8/62	RR 1.16 (0.49 to	21 more per 1000 (from 66 fewer to 225 more) 21 more per	⊕000 VERY	tinuing
/ reas	randomised	yery	no serious	no serious			10/67	8/62 (12.9%)	RR 1.16 (0.49 to	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66	⊕000 VERY	tinuinç
reas	randomised trials	very serious <sup>11</sup>	no serious inconsistency	no serious indirectness	very serious <sup>18</sup>	reporting bias <sup>12</sup>	10/67	8/62 (12.9%)	RR 1.16 (0.49 to 2.74)	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66 fewer to 224 more)	⊕OOO VERY LOW	
reas	randomised trials	very serious <sup>11</sup>	no serious inconsistency	no serious indirectness	very serious <sup>18</sup>	reporting bias <sup>12</sup> y AD) (follow-up	10/67 (14.9%)	8/62 (12.9%)	RR 1.16 (0.49 to 2.74)	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66 fewer to 224 more) discontinuing fo	⊕OOO VERY LOW	
y reas	randomised trials nuation for a	very serious <sup>11</sup>	no serious inconsistency	no serious indirectness	very serious <sup>18</sup> y AD versus an	reporting bias <sup>12</sup> y AD) (follow-up	10/67 (14.9%) mean 6 weeks; assess	8/62 (12.9%) 12.9% ed with: Number of	RR 1.16 (0.49 to 2.74)	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66 fewer to 224 more) discontinuing fo	⊕OOO VERY LOW	
reas	randomised trials  nuation for any adverse every randomised	very serious <sup>11</sup>	no serious inconsistency  n (cognitive bib	no serious indirectness	very serious <sup>18</sup> y AD versus an	reporting bias <sup>12</sup> y AD) (follow-up	10/67 (14.9%) mean 6 weeks; assess	8/62 (12.9%) 12.9% ed with: Number of	RR 1.16 (0.49 to 2.74) participants	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66 fewer to 224 more) discontinuing fo	⊕OOO VERY LOW	
y reas	randomised trials  nuation for any adverse every randomised	very serious <sup>11</sup>	no serious inconsistency  n (cognitive bib	no serious indirectness	very serious <sup>18</sup> y AD versus an	reporting bias <sup>12</sup> y AD) (follow-up	10/67 (14.9%) mean 6 weeks; assess	8/62 (12.9%) 12.9% ed with: Number of	RR 1.16 (0.49 to 2.74) participants	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66 fewer to 224 more) discontinuing fo	⊕OOO VERY LOW  r any reas	
y reas	randomised trials  nuation for any adverse every randomised	very serious <sup>11</sup>	no serious inconsistency  n (cognitive bib	no serious indirectness	very serious <sup>18</sup> y AD versus an	reporting bias <sup>12</sup> y AD) (follow-up	10/67 (14.9%) mean 6 weeks; assess	8/62 (12.9%) 12.9% ed with: Number of	RR 1.16 (0.49 to 2.74) participants	21 more per 1000 (from 66 fewer to 225 more) 21 more per 1000 (from 66 fewer to 224 more) discontinuing for 78 more per 1000 (from 56 fewer to 408	⊕OOO VERY LOW  r any reas	

continuation									fewer to 407	
									more)	
erse events	for any reaso	n (mutual peer s	support + TAU	versus TAU) (fo	ollow-up mean 24	weeks; assessed with	: Number of particip	ants discon	tinuing for any re	ason (includi
	))									
	nised serious <sup>1</sup>	no serious	no serious	very serious <sup>18</sup>	reporting bias <sup>16</sup>	15/144	26/243	RR 0.97	3 fewer per 1000	
trials		inconsistency	indirectness			(10.4%)	(10.7%)	(0.53 to	(from 50 fewer to	VERY
								1.78)	83 more)	LOW
								_	0.5 4000	
							10.7%		3 fewer per 1000	
							10.7%		(from 50 fewer to 83 more)	
		1 11				AD (TAIL	AD/TALL L \/C		/	1 1/1 1
					ies [combined] +	any AD/TAU versus ar	y AD/ I AU-only) (fol	low-up 12-2	/ weeks; assesse	d with: Numi
ticipants dis	continuing to	r any reason (inc	luding adverse	e events))						
randon	nised serious <sup>17</sup>	no serious	no serious	very serious <sup>18</sup>	nono	70/535	52/430	RR 1.06	7 more per 1000	0000
trials	iiseu serious	inconsistency	indirectness	very serious.	none	(13.1%)	(12.1%)	(0.75 to	(from 30 fewer to	
tilais		inconsistency	indirectiness			(13.170)	(12.170)	1.49)	59 more)	LOW
								1.49)	33 111016)	LOVV
									7 more per 1000	
							12.5%		(from 31 fewer to	
							12.070		61 more)	
continuation	due to adver	so events (CBAS	P + any AD yo	reue any AD) (fe	ollow-up mean 1	2 weeks; assessed with	· Number of partici	ante discor	,	verse events
Continuation	i due to duver	o crems (obac	i ally AD vo	ious uny Ab) (i	onow up mount	L WOOKS, assessed With	i. Hamber of partion	Junto diocor	itilianing add to do	voide evente
randon	nised serious <sup>1</sup>	no serious	no serious	very serious <sup>18</sup>	reporting bias <sup>3</sup>	2/200	2/96	RR 0.48	11 fewer per	⊕OOO
trials		inconsistency	indirectness		repermig area	(1%)	(2.1%)	(0.07 to	1000 (from 19	VERY
		,				(,	(,	3.36)	fewer to 49	LOW
								,	more)	
									,	
									11 fewer per	
							2.1%		1000 (from 20	
							2.170		fewer to 50	

								fewer to 35 more)		
1 Method of randomisation w 2 95% CI crosses line of no e 3 Drugs were supplied at no 4 High risk of bias associated outcome assessment, in studie Events<300 6 Non-blind participants and 7 I-squared>50% 8 Non-blind participants and 9 I-squared>80% 10 Data cannot be extracted companies 11 High risk of bias associate 12 Study partially funded by t 13 High risk of bias associate outcome assessment 14 N<400 15 95% CI crosses both line of Data cannot be extracted/ 7 High or unclear risk of ran 18 95% CI crosses line of no 19 95% CI crosses both line of Augmenting the antic	effect and threshold for cost by pharmaceutical with randomisation made of the secontributing >50% of the secontributing >50% of the secontributing >50% of the secontributing >50% of the second of t	r both clinically in all company and nethod due to sign of weighting in ator(s) and poter ator(s) and poter and method due to succeed an all control of the clinically outcomes and participants are poth clinically old for clinically old for clinically	mportant harm authors have fignificant differential risk of attribror drugs were dignificant differiation differial risk of attribror drugs were dignificant differial mortant beneated intervention differial rimportant beneated intervention differial mortant beneated at the mortant differial rimportant differial ri	(RR 0.75) and for inancial interests we note between ground ition bias (difference supplied at no concernce between ground effit (SMD -0.5) administrator(s) we fit (RR 0.75) and in (RR 1.25)	r clinically important benewith pharmaceutical compups at baseline, non-blind ce in drop-out between gost by pharmaceutical compups at baseline, non-blind pups at baseline, non-blind pups at baseline, non-blind clinically important harm	panies I participants and inter roups>20% but ITT a npany and authors ha d participants and inter d participants and inter (RR 1.25)	analysis used) ave financial ir ervention adm	nterests with phar ninistrator(s) ninistrator(s), and	maceutica	al
	Quality ass	essment			No of pati	ients	E	Effect		
No of Design Ris	Inconsistency	Indirectness	Improviolog	Other	Augmenting the	Augmenting with	Relative	Absolute	Quality	Importance

			Quality ass	essment			No of patie	ents		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with a psych intervention	Augmenting with a non-AD agent		Absolute		
	on (CBT indivion (HAM-D))	-	der 15 sessions]	+ AD versus li	thium + AD)	(follow-up mean	8 weeks; assessed with:	Number of people	scoring ≤7	on Hamilton Ratir	ng Scale	for
							0.100	0/04		400 farren man		
1	randomised trials				very serious²	none	6/23 (26.1%)	8/21 (38.1%)	RR 0.68 (0.28 to	122 fewer per 1000 (from 274	⊕000 VERY	

6	
7	

								38.1%		fewer to 248 more)	
229	ion symptom	atology (	CRT individual	lunder 15 sess	ions1 + AD v	ersus lithium + AD	) (follow-up mean 8 wee	eks: measured with	· Hamilton I	,	nression (l
	•	• • • •	d by lower valu	-	ionoj . Ab v		, (lonow up inicall o wee	ono, mododica mini	· manniton	tuting ocule for De	pression (i
				1		1		1 .			
		serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	23	21	-	SMD 0.7 higher	⊕⊕ОО
	trials		inconsistency	indirectness						(0.09 to 1.31	LOW
										higher)	
oonti	nuction for a	nv rocco	CPT individu	al fundor 15 co	osionol + AD	versus lithium + /	AD) (follow-up mean 8 w	vooko: aaaaaaad wiit	h. Number	of participants disc	ontinuina
	including adv	-	•	ai [uiiuei 15 Se	SSIUIIS] + AD	versus illillulii + /	(Ioliow-up illeali o w	reeks, assessed wit	ii. Nuilibei	oi participants disc	Jonana
i) iioes	including adv	CISC CVC	1113//								
	randomised	serious <sup>1</sup>	no serious	no serious	very	none	6/23	6/21	RR 0.91	26 fewer per 1000	⊕000
	trials		inconsistency	indirectness	serious4		(26.1%)	(28.6%)	(0.35 to	(from 186 fewer to	
			,				,	,	2.4)	400 more)	LOW
										26 fewer per 1000	
										the state of the s	
								28.6%		(from 186 fewer to	
								28.6%		(from 186 fewer to 400 more)	
sconti	nuation due t	o advers	e events (CBT i	ndividual [unde	er 15 session	ns] + AD versus litl	nium + AD) (follow-up m		ssed with: N	400 more)	ints discon
	nuation due t		e events (CBT i	ndividual [unde	er 15 session	ns] + AD versus litt	nium + AD) (follow-up m		ssed with: N	400 more)	ints discon
	dverse events	s)	· ·	-				nean 8 weeks; asses		400 more) Number of participa	
	randomised	s)	no serious	no serious	very	ns] + AD versus litt	0/23	nean 8 weeks; asses	RR 0.31	400 more) Number of participa  33 fewer per 1000	⊕000
	dverse events	s)	· ·	-				nean 8 weeks; asses	RR 0.31 (0.01 to	400 more)  Number of participa  33 fewer per 1000 (from 47 fewer to	⊕000 VERY
	randomised	s)	no serious	no serious	very		0/23	nean 8 weeks; asses	RR 0.31	400 more) Number of participa  33 fewer per 1000	⊕000
	randomised	s)	no serious	no serious	very		0/23	nean 8 weeks; asses	RR 0.31 (0.01 to	400 more)  Number of participa  33 fewer per 1000 (from 47 fewer to 291 more)	⊕000 VERY
	randomised	s)	no serious	no serious	very		0/23	nean 8 weeks; asses	RR 0.31 (0.01 to	400 more)  Number of participa  33 fewer per 1000 (from 47 fewer to	⊕000 VERY

# Augmenting the antidepressant with a psychological intervention compared to 'other' psychological intervention (head-to-head comparisons)

Quality assessment	No of patients	Effect	Quality Importance

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>4</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>1</sup> Method of randomisation was unclear, and non-blind participants and intervention administrator(s)

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

3

## Augmenting the antidepressant with a physical intervention compared to attention-placebo

			Quality ass	essment			No of patients			Effect		
							ito oi pationio					
						_		_			Quality	Importar
No of tudies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Augmenting the antidepressant with a physical intervention	Attention- placebo	Relative (95% CI)	Absolute		
	on (exercise ion (HAM-D))		y AD versus atte	ntion-placebo	SSRI/any A	D) (follow-up 10-1	2 weeks; assessed with: N	umber of peo	pple scoring	≤7/10 on Hamilton	Rating So	cale for
	randomised	serious <sup>1</sup>	no serious	no serious	very	none	39/55	28/47	RR 1.77	459 more per 1000	⊕000	
	trials		inconsistency	indirectness	serious <sup>2</sup>		(70.9%)	(59.6%)	(0.37 to	(from 375 fewer to	VERY	
			,				,	,	8.41)	1000 more)	LOW	
								07.00/		291 more per 1000		
								37.8%		(from 238 fewer to		
										4000 \		
-	e (exercise +	_	versus attention-	placebo + any A	AD) (follow-u	p mean 12 weeks;	; assessed with: Number o	f people show	wing ≥50% ii	1000 more) mprovement on Han	nilton Ra	ting Sca
-	randomised	very	no serious	no serious	very	p mean 12 weeks;	4/19	0/10	RR 4.95	,	⊕000	ting Sca
-	randomised	-D))								mprovement on Har		ting Sca
-	randomised	very	no serious	no serious	very		4/19	0/10	RR 4.95 (0.29 to	mprovement on Har	⊕000 VERY	ting Sca
r Depre	randomised trials fon symptom score); Better	very serious <sup>3</sup> atology (e	no serious inconsistency exercise + SSRI/a d by lower values	no serious indirectness any AD versus a	very serious <sup>2</sup> attention-pla	reporting bias <sup>4</sup> cebo + SSRI/any A	4/19 (21.1%) AD) (follow-up 10-12 weeks	0/10 (0%) 0% ; measured w	RR 4.95 (0.29 to 83.68)		⊕OOO VERY LOW	
r Depre	randomised trials fon symptom score); Better	very serious <sup>3</sup> atology (e	no serious inconsistency exercise + SSRI/a	no serious indirectness any AD versus a s)	very serious <sup>2</sup>	reporting bias <sup>4</sup>	4/19 (21.1%)	0/10 (0%)	RR 4.95 (0.29 to 83.68)		⊕OOO VERY LOW	
Pressi	randomised trials fon symptom score); Better	very serious <sup>3</sup> atology (e	no serious inconsistency exercise + SSRI/a d by lower values	no serious indirectness any AD versus a	very serious <sup>2</sup> attention-pla	reporting bias <sup>4</sup> cebo + SSRI/any A	4/19 (21.1%) AD) (follow-up 10-12 weeks	0/10 (0%) 0% ; measured w	RR 4.95 (0.29 to 83.68)		⊕OOO VERY LOW	
pressi ange s	randomised trials ion symptom score); Better randomised trials	very serious <sup>3</sup> atology (er indicated serious <sup>1</sup>	no serious inconsistency exercise + SSRI/a d by lower values very serious <sup>5</sup>	no serious indirectness any AD versus a s) no serious indirectness	very serious <sup>2</sup> attention-place serious <sup>6</sup>	reporting bias <sup>4</sup> cebo + SSRI/any A	4/19 (21.1%) AD) (follow-up 10-12 weeks	0/10 (0%) 0% ; measured w	RR 4.95 (0.29 to 83.68) vith: Hamilto		⊕OOO VERY LOW Depression	on (HAM
epressi ange s	randomised trials ion symptom score); Better randomised trials	very serious <sup>3</sup> atology (er indicated serious <sup>1</sup>	no serious inconsistency  exercise + SSRI/a by lower values  very serious <sup>5</sup> (exercise + SSR	no serious indirectness any AD versus a s) no serious indirectness	very serious <sup>2</sup> attention-place serious <sup>6</sup>	reporting bias <sup>4</sup> cebo + SSRI/any A	4/19 (21.1%) AD) (follow-up 10-12 weeks	0/10 (0%) 0% ; measured w	RR 4.95 (0.29 to 83.68) vith: Hamilto		⊕OOO VERY LOW Depression	on (HAN
pressi ange s	randomised trials  ion symptom score); Better randomised trials	very serious <sup>3</sup> atology (er indicated serious <sup>1</sup> ny reason verse ever	no serious inconsistency  exercise + SSRI/a by lower values  very serious <sup>5</sup> (exercise + SSR	no serious indirectness any AD versus a s) no serious indirectness	very serious <sup>2</sup> attention-place serious <sup>6</sup>	reporting bias <sup>4</sup> cebo + SSRI/any A	4/19 (21.1%) AD) (follow-up 10-12 weeks	0/10 (0%) 0% ; measured w	RR 4.95 (0.29 to 83.68) vith: Hamilto		⊕OOO VERY LOW Depression	on (HAN
epressi	randomised trials  ion symptom score); Better randomised trials	very serious <sup>3</sup> atology (er indicated serious <sup>1</sup> ny reason verse ever	no serious inconsistency exercise + SSRI/a d by lower values very serious <sup>5</sup> (exercise + SSR	no serious indirectness any AD versus as no serious indirectness	very serious <sup>2</sup> attention-place serious <sup>6</sup> s attention-p	reporting bias <sup>4</sup> cebo + SSRI/any A	4/19 (21.1%) AD) (follow-up 10-12 weeks 52 y AD) (follow-up 10-12 week	0/10 (0%) 0% ; measured w 45 ks; assessed	RR 4.95 (0.29 to 83.68) vith: Hamilto		⊕OOO VERY LOW Depression	on (HAM

					7.3%	39 more per 100 (from 44 fewer 355 more)		
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<sup>&</sup>lt;sup>1</sup> Non-blind intervention administration

9

### Switching to another antidepressant of a different class compared to placebo

			Quality asse	essment			No of patients			Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Switch to another antidepressant of different class	Placebo	Relative (95% CI)	Absolute	<b>Quanty</b>	
Remissio	n (SSRI to aty	pical ant	idepressant or pl	acebo) (follow-u	p mean 12 w	eeks; assessed w	vith: Number of people sco	ring ≤7 o	n Hamilton R	ating Scale for Depr	ession (F	IAM-D))
	randomised trials			no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	40/165 (24.2%)	39/157 (24.8%)	RR 0.98 (0.67 to 1.43)	5 fewer per 1000 (from 82 fewer to 107 more)	⊕000 VERY LOW	
								24.8%		5 fewer per 1000 (from 82 fewer to 107 more)		
•	e (SSRI to aty on (HAM-D))	pical anti	depressant or pla	cebo) (follow-u	o mean 12 w	eeks; assessed w	ith: Number of people show	ving ≥50%	% improveme	ent on Hamilton Rati	ng Scale	for
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	63/165 (38.2%)	58/157 (36.9%)	RR 1.03 (0.78 to 1.37)	11 more per 1000 (from 81 fewer to 137 more)	⊕000 VERY LOW	
								36.9%		11 more per 1000 (from 81 fewer to 137 more)	_	

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline and unclear method of allocation concealment. Intervention administration was non-blind

<sup>&</sup>lt;sup>4</sup> Study partially funded by pharmaceutical company

<sup>&</sup>lt;sup>5</sup> I-squared>80%

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD -0.5)

<sup>&</sup>lt;sup>7</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

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<sup>1</sup> Unclear randomisation method and method of allocation concealment, and unclear risk of attrition bias (drop-out>20% but difference between groups <20% and ITT analysis used)

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Study run and funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>5</sup> N<400

<sup>&</sup>lt;sup>6</sup> Events<300

<sup>&</sup>lt;sup>7</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

Switching to another antidepressant of a different class compared to continuing with the same antidepressant 1 **Quality assessment** No of patients **Effect** Quality Importance Switch to another No of Other Continuing with Relative Risk of Design Inconsistency Indirectness Imprecision antidepressant of a **Absolute** studies considerations the antidepressant (95% CI) bias different class Remission (any switch versus continuing with the antidepressant) (follow-up 6-12 weeks; assessed with: Number of people scoring ≤7/8 on Hamilton Rating Scale for Depression (HAM-D)/≤8 on Montgomery Asberg Depression Rating Scale (MADRS)) randomised serious1 no serious no serious very serious<sup>2</sup> reporting bias<sup>3</sup> 82/336 53/209 RR 0.93 18 fewer per  $\oplus$ OOO trials inconsistency indirectness (24.4%)(25.4%)(0.65 to 1000 (from 89 **VERY** 1.34) fewer to 86 LOW more) 14 fewer per 1000 (from 71 20.4% fewer to 69 more) Remission (switch to SSRI versus continuing TCA/SNRI) (follow-up 8-12 weeks; assessed with: Number of people scoring ≤8 on Montgomery Asberg Depression Rating Scale (MADRS)) randomised serious4 no serious no serious very serious<sup>2</sup> reporting bias<sup>3</sup> 29/198 25/126 RR 0.78 44 fewer per **⊕**000 trials indirectness 1000 (from 105 inconsistency (14.6%)(19.8%)(0.47 to **VERY** fewer to 54 1.27) LOW more) 44 fewer per 1000 (from 106 20% fewer to 54 more) Remission (switch to atypical AD/SNRI/TeCA [mianserin] versus continuing SSRI) (follow-up 6-8 weeks; assessed with: Number of people scoring ≤7/8 on Hamilton Rating Scale for Depression (HAM-D)) 53/138 28/83 RR 1.19 randomised very serious<sup>6</sup> no serious very serious<sup>2</sup> reporting bias<sup>3</sup> 64 more per  $\oplus$ OOO serious<sup>5</sup> indirectness (38.4%)(33.7%)(0.52 to 1000 (from 162 trials **VERY** 2.77) fewer to 597 LOW more) 62 more per 32.5%

1000 (from 156

									fewer to 575 more)	
		continuing with nery Asberg Dep				sessed with: Number o	of people showing ≥	50% improve	ement on Hamilto	n Rating Sca
randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>7</sup>	reporting bias <sup>3</sup>	140/336 (41.7%)	94/209 (45%)	RR 0.91 (0.74 to 1.12)	40 fewer per 1000 (from 117 fewer to 54 more)	⊕OOO VERY LOW
							43.4%		39 fewer per 1000 (from 113 fewer to 52 more)	
se (switch to Scale (MADRS		sus continuing	TCA/SNRI) (foli	ow-up 8-12 we	eks; assessed wi	th: Number of people s	showing ≥50% impr	ovement on	Montgomery Asb	erg Depressi
randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>7</sup>	reporting bias <sup>3</sup>	60/198 (30.3%)	50/126 (39.7%)	RR 0.8 (0.58 to 1.09)	79 fewer per 1000 (from 167 fewer to 36 more)	⊕000 VERY LOW
							40.4%		81 fewer per 1000 (from 170 fewer to 36 more)	
se (switch to Scale for Dep			mianserin] ver	sus continuing	SSRI) (follow-up	6-8 weeks; assessed v	with: Number of peo	pple showing	≥50% improveme	ent on Hamil
randomised trials	very serious <sup>5</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	80/138 (58%)	44/83 (53%)	RR 1.01 (0.73 to 1.41)	5 more per 1000 (from 143 fewer to 217 more)	⊕OOO VERY LOW
							51.8%		5 more per 1000 (from 140 fewer to 212 more)	
an /awitah ta		anserin] versus	continuing SS	SRI) (follow-up i	mean 6 weeks; as	sessed with: Number	of people rated as i	nuch or very	much improved	on Clinical G
sions scale (C	(GI-I))									

										100 mara par		
										188 more per 1000 (from 36		
								44.7%				
										fewer to 536		
										more)		
							-up 6-12 weeks; measur ed by lower values)	red with: Hamilton F	Rating Scale	for Depression (	HAM-D;	change
	randomised	serious <sup>10</sup>	no serious	no serious	no serious	reporting bias3	235	165	-	SMD 0.04 lower	⊕⊕ОО	
	trials		inconsistency	indirectness	imprecision					(0.3 lower to 0.23	LOW	
										higher)		
			switch to CCDI.		TO A (CNDI)	(fallow 0.42	en also e mana anoma al cosiste e N	4 - 10 4 - 10 - 10 - 10 - 10 - 10 - 10 -	Dommoodia	Detine Casla (M	ADDC: -	h
	Better indicat			ersus continu	ing ICA/SNRI)	(Iollow-up 6-12 w	eeks; measured with: N	nontgomery Asberg	Depression	i Rating Scale (W	ADRS; C	nange
	randomised	serious <sup>4</sup>	serious <sup>6</sup>	no serious	serious <sup>11</sup>	reporting bias <sup>3</sup>	202	127	_	SMD 0.03 higher	Φ000	
	trials	Scrious	Serious	indirectness	Serious	reporting bias	202	121	_	(0.31 lower to	VERY	
	tilais			indirectriess						0.38 higher)	LOW	
										0.36 Higher)	LOW	
	randomised	serious <sup>8</sup>	no serious	no porious	serious <sup>12</sup>			ı		I		
	randomised	serious <sup>8</sup>	no corious	no corious	12							
		ociloao	no senous	no serious	serious	reporting bias3	33	38	-	SMD 0.24 lower	$\oplus$ OOO	
	trials	Scrious	inconsistency	indirectness	serious	reporting bias	33	38	-	SMD 0.24 lower (0.71 lower to	⊕000 VERY	
			inconsistency	indirectness					-	(0.71 lower to 0.23 higher)	VERY LOW	
	nuation for a	ny reason	inconsistency	indirectness			71/341 (20.8%)		PR 1.23 (0.81 to 1.86)	(0.71 lower to 0.23 higher)	VERY LOW	reason
ncludi	nuation for ang adverse evandomised trials	iny reasor vents)) serious <sup>13</sup>	n (any switch ver	rsus continuin  no serious indirectness	g with the antic	reporting bias <sup>3</sup>	w-up 6-12 weeks; asses	38/210 (18.1%)	RR 1.23 (0.81 to 1.86)	(0.71 lower to 0.23 higher)  nts discontinuing  42 more per 1000 (from 34 fewer to 156 more)  42 more per 1000 (from 34 fewer to 156 more)	for any  OUT OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OUT OF THE PROPERTY OUT OF THE PROPERTY OUT	
scont	nuation for ang adverse evandomised trials	iny reasor vents)) serious <sup>13</sup>	n (any switch ver	rsus continuin  no serious indirectness	g with the antic	reporting bias <sup>3</sup>	w-up 6-12 weeks; asse:	38/210 (18.1%)	RR 1.23 (0.81 to 1.86)	(0.71 lower to 0.23 higher)  nts discontinuing  42 more per 1000 (from 34 fewer to 156 more)  42 more per 1000 (from 34 fewer to 156 more)	for any  OUT OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OUT OF THE PROPERTY OUT OF THE PROPERTY OUT	
scont	randomised trials	iny reasor vents)) serious <sup>13</sup>	n (any switch ver	rsus continuin  no serious indirectness	serious <sup>14</sup>	reporting bias <sup>3</sup>	w-up 6-12 weeks; asses	38/210 (18.1%)	RR 1.23 (0.81 to 1.86)	(0.71 lower to 0.23 higher)  nts discontinuing  42 more per 1000 (from 34 fewer to 156 more)  42 more per 1000 (from 34 fewer to 156 more)	for any  OUT OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OUT OF THE PROPERTY OUT OF THE PROPERTY OUT	
scont	randomised trials	serious <sup>13</sup>	n (any switch ver	no serious indirectness	serious <sup>14</sup>	reporting bias <sup>3</sup>	w-up 6-12 weeks; asses 71/341 (20.8%)	38/210 (18.1%)	RR 1.23 (0.81 to 1.86)	(0.71 lower to 0.23 higher)  nts discontinuing  42 more per 1000 (from 34 fewer to 156 more)  42 more per 1000 (from 34 fewer to 156 more)  41 more per 1000 (from 34 fewer to 156 more)	for any  OUT OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OUT OF THE PROPERTY OUT OF THE PROPERTY OUT	

									RR 1.13	fewer to 250	⊕OOO	
									(0.54 to	more)	VERY	
									2.38)		LOW	
										24 more per		
								18.6%		1000 (from 86		
								18.0%		fewer to 257		
										more)		
licconti	inuation for a	ny rosco	n (ewitch to atur	nical AD/SNDI/I	ToCA Imiansoriu	nl voreue continu	ing SSRI) (follow-up 6	8 wooks: assessed	Lwith: Numbe	,	discontin	uina foi
	son (includin			JICAI ADIONNII	reoz [illiansem	nj versus contine	ang com, (lonow-up c	-0 Weeks, assessed	With Name	or participants	uiscontii	iuiiig ioi
	randomised	serious <sup>17</sup>	no serious	no serious	verv serious16	reporting bias3	31/139	15/83	RR 1.37	67 more per	⊕000	
	trials		inconsistency	indirectness	, , , , , , , , , , , , , , , , , , , ,	repermigrans	(22.3%)	(18.1%)	(0.74 to	1000 (from 47	VERY	
	tiidio		inconsistency	in an comicoo			(22.070)	(10.170)	2.54)	fewer to 278	LOW	
									2.54)		LOVV	
										more)		
									4	07	1	
					1					67 more per		
					1			18.1%		1000 (from 47		
								10.170		fewer to 279		
		1	1	1	1	1	l			more)		
	e events)					·	nt) (follow-up 6-12 week	· 		articipants disco		lue to
	e events)	serious <sup>13</sup>		no serious indirectness		he antidepressar	15/336 (4.5%)	4/210 (1.9%)	RR 1.74 (0.32 to 9.6)	,	⊕OOO VERY LOW	lue to
	randomised			no serious		·	15/336	4/210	RR 1.74 (0.32 to	14 more per 1000 (from 13 fewer to 164 more)	⊕000 VERY	lue to
	randomised			no serious		·	15/336	4/210	RR 1.74 (0.32 to	14 more per 1000 (from 13 fewer to 164 more) 15 more per 1000 (from 14	⊕000 VERY	lue to
	randomised			no serious		·	15/336	4/210 (1.9%)	RR 1.74 (0.32 to	14 more per 1000 (from 13 fewer to 164 more) 15 more per 1000 (from 14 fewer to 172	⊕000 VERY	lue to
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup>	no serious indirectness	very serious <sup>16</sup>	reporting bias <sup>3</sup>	15/336 (4.5%)	4/210 (1.9%)	RR 1.74 (0.32 to 9.6)	14 more per 1000 (from 13 fewer to 164 more) 15 more per 1000 (from 14 fewer to 172 more)	⊕OOO VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup>	no serious indirectness	very serious <sup>16</sup>	reporting bias <sup>3</sup>	15/336	4/210 (1.9%)	RR 1.74 (0.32 to 9.6)	14 more per 1000 (from 13 fewer to 164 more) 15 more per 1000 (from 14 fewer to 172 more)	⊕OOO VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup>	no serious indirectness h to SSRI versu	very serious <sup>16</sup>	reporting bias <sup>3</sup> CA/SNRI) (follow-	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6)	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing descriptions	⊕OOO VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup> se events (switch	no serious indirectness h to SSRI versu	very serious <sup>16</sup>	reporting bias <sup>3</sup>	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6) f participants	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing d	⊕OOO VERY LOW	
sconti	randomised trials	serious <sup>13</sup>	serious <sup>6</sup>	no serious indirectness h to SSRI versu	very serious <sup>16</sup>	reporting bias <sup>3</sup> CA/SNRI) (follow-	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6) f participants	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing d	⊕000 VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup> se events (switch	no serious indirectness h to SSRI versu	very serious <sup>16</sup>	reporting bias <sup>3</sup> CA/SNRI) (follow-	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6) f participants	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing d	⊕OOO VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup> se events (switch	no serious indirectness h to SSRI versu	very serious <sup>16</sup>	reporting bias <sup>3</sup> CA/SNRI) (follow-	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6) f participants	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing d  10 more per 1000 (from 15 fewer to 106 more)	⊕000 VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup> se events (switch	no serious indirectness h to SSRI versu	very serious <sup>16</sup>	reporting bias <sup>3</sup> CA/SNRI) (follow-	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6) f participants	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing d  10 more per 1000 (from 15 fewer to 106 more)  10 more per 1000 (from 15	⊕000 VERY LOW	
dverse	randomised trials	serious <sup>13</sup>	serious <sup>6</sup> se events (switch	no serious indirectness h to SSRI versuno serious	very serious <sup>16</sup>	reporting bias <sup>3</sup> CA/SNRI) (follow-	15/336 (4.5%) -up 8-12 weeks; assess	4/210 (1.9%) 2% sed with: Number of	RR 1.74 (0.32 to 9.6) f participants	14 more per 1000 (from 13 fewer to 164 more)  15 more per 1000 (from 14 fewer to 172 more)  6 discontinuing d  10 more per 1000 (from 15 fewer to 106 more)	⊕000 VERY LOW	

nuation due to		•	to atypical AD	/SNRI/TeCA [m	ianserin] versus	continuing SSRI) (follo	w-up 6-8 weeks; ass	essed with	: Number of parti	icipants
	. 17	, 18		. 16	3	0/404	4/00	DD 4.0	40	
randomised	serious'	very serious <sup>18</sup>	no serious	very serious **	reporting bias <sup>3</sup>	8/134	1/83	RR 1.8	10 more per	⊕OOO
trials			indirectness			(6%)	(1.2%)	(0.01 to	1000 (from 12	VERY
								222.73)	fewer to 1000	LOW
									more)	
									9 more per 1000	
							1.1%		(from 11 fewer to	
									1000 more)	

<sup>&</sup>lt;sup>1</sup> Risk of randomisation method is high risk or unclear, method of allocation concealment is unclear, intervention administration is non-blind, risk of detection bias is high or unclear, in studies contributing>50% to weighting in analysis

#### 15 11 N<400 16 12 95% 0

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- <sup>12</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD -0.5)
- 17 13 Unclear or high risk of bias associated with randomisation method, method of allocation concealment is unclear and unclear blinding of intervention administration
  - <sup>14</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)
- 19 <sup>15</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration
- <sup>16</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)
  - <sup>17</sup> Risk of randomisation method is high or unclear and unclear blinding of intervention administration
- <sup>18</sup> I-squared>80%

Switching to a non-antidepressant agent compared to continuing with the antidepressant

Quality assessment	No of patients	Effect	Quality	Importance

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>5</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and unclear blinding of intervention administration and unclear blinding or non-blind outcome assessment, in studies contributing >50% to weighting in analysis

<sup>&</sup>lt;sup>6</sup> I-squared>50%

<sup>&</sup>lt;sup>7</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>&</sup>lt;sup>8</sup> Unclear randomisation method and method of allocation concealment, unclear blinding of intervention administration, non-blind outcome assessment and unclear risk of attrition bias (dropout>20% but difference between groups <20% and ITT analysis used)

<sup>&</sup>lt;sup>9</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>10</sup> Unclear randomisation method and method of allocation concealment, unclear blinding of intervention administration, unclear blinding or non-blind outcome assessment, and unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Switch to non- antidepressant agent	Continuing with the antidepressant	Relative (95% CI)	Absolute	
	on (switch to on Rating Sc			py versus cont	inuing SSRI/TO	CA/SNRI) (follow-u	up 8-12 weeks; asse	ssed with: Number of	f people sc	oring ≤8/10 on Moi	ntgomery Asbe
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	56/400 (14%)	59/329 (17.9%)	RR 0.79 (0.56 to 1.11)	38 fewer per 1000 (from 79 fewer to 20 more)	⊕000 VERY LOW
	vy (avritala ta	a a wala ina a	d autinovale tie	CODI		(CNDI) (fallow m	0.40	17.7% sed with: Number of		37 fewer per 1000 (from 78 fewer to 19 more)	
	on Rating So			r SSRI Versus (	continuing TCA	vanki) (lollow-up	o-12 weeks; asses	sea with: Number of p	beopie scoi	ing so on wontgo	nery Asberg
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	94/376 (25%)	25/126 (19.8%)	RR 1.17 (0.79 to 1.75)	34 more per 1000 (from 42 fewer to 149 more)	⊕OOO VERY LOW
								20%		34 more per 1000 (from 42 fewer to 150 more)	
			otic monotherar on Rating Scale (		nuing SSRI/TC	A/SNRI) (follow-u	p 8-12 weeks; asses	ssed with: Number of	people sho	owing ≥50% impro	vement on
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	94/400 (23.5%)	110/329 (33.4%)	RR 0.69 (0.49 to 0.96)	104 fewer per 1000 (from 13 fewer to 171 fewer)	OOO VERY LOW
								30.9%		96 fewer per 1000 (from 12 fewer to 158 fewer)	
			d antipsychotic + on Rating Scale (		ontinuing TCA	/SNRI) (follow-up	8-12 weeks; assess	sed with: Number of p	eople shov	ving ≥50% improve	ment on
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	140/376 (37.2%)	50/126 (39.7%)	RR 0.87 (0.68 to 1.12)	52 fewer per 1000 (from 127 fewer to 48 more)	

								40.4%		53 fewer per 1000 (from 129 fewer to	VERY	
								10.170		48 more)	LOW	
ress	ion symptom	atology (	switch to antino	sychotic monot	herany versus	continuing SSRI/T	│ ΓCA/SNRI) (follow-u	n 8-12 weeks: meas	sured with: Mo	ntgomery Asherg	Denressi	on R
			; Better indicate				i ozvortki) (ioliow-u	p 0-12 weeks, meas	sarea with in	onigoniery Asberg	Depressi	JII IX
		serious <sup>1</sup>	serious <sup>6</sup>	no serious	serious <sup>7</sup>	reporting bias <sup>3</sup>	403	330	-	SMD 0.22 higher	⊕OOO	
	trials			indirectness						(0.12 lower to 0.57		
										higher)	LOW	
nroce	ion symptom	atology (	switch to comb	ined antinevely	otic + SSPI vor	sus continuing TC	CA/SNRI) (follow-up	9 12 wooks: moasu	rod with: Mor	staomory Ashora F	lonrossion	n Dat
			; Better indicate			sus continuing 10	A/SNKI) (IOIIOW-up	o-12 weeks, illeasu	irea witti. Woi	itgomery Asberg L	epression	ı Kat
Juio (iii	, ibito, onan	90 000.0,	, Dottor maiout	ou by lottor valu	200,							
	randomised	serious <sup>1</sup>	no serious	no serious	no serious	reporting bias <sup>3</sup>	389	127	-	SMD 0.09 lower	⊕⊕ОО	
	trials		inconsistency	indirectness	imprecision					(0.29 lower to 0.11	LOW	
			_							higher)		
isconti	inuation for a	ny reaso	n (switch to ant	ipsychotic mon	otherapy versu	s continuing SSR	RI/TCA/SNRI) (follow	-up 8-12 weeks; as:	sessed with: I	Number of participa	ants disco	ontin
	inuation for a reason (inclu			ipsychotic mon	otherapy versu	s continuing SSR	RI/TCA/SNRI) (follow	-up 8-12 weeks; as:	sessed with: I	Number of particip	ants disco	ontin
				ipsychotic mon	otherapy versu	s continuing SSR	RI/TCA/SNRI) (follow	-up 8-12 weeks; ass	sessed with: I	Number of particip	ants disco	ontin
	reason (inclu	ding adve		no serious	otherapy versus	reporting bias <sup>3</sup>	122/405	63/333	RR 1.67	127 more per	⊕OOO	ontin
	reason (inclu	ding adve	erse events))			_				127 more per 1000 (from 49	⊕OOO VERY	ontin
	randomised	ding adve	no serious	no serious		_	122/405	63/333	RR 1.67	127 more per	⊕OOO VERY	ontin
	randomised	ding adve	no serious	no serious		_	122/405	63/333	RR 1.67 (1.26 to	127 more per 1000 (from 49 more to 233 more)	⊕OOO VERY	ontin
	randomised	ding adve	no serious	no serious		_	122/405	63/333 (18.9%)	RR 1.67 (1.26 to	127 more per 1000 (from 49 more to 233 more) 130 more per	⊕OOO VERY	ontin
	randomised	ding adve	no serious	no serious		_	122/405	63/333	RR 1.67 (1.26 to	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50	⊕OOO VERY	ontin
	randomised	ding adve	no serious	no serious		_	122/405	63/333 (18.9%)	RR 1.67 (1.26 to	127 more per 1000 (from 49 more to 233 more) 130 more per	⊕OOO VERY	ontin
or any r	reason (inclu randomised trials	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	122/405	63/333 (18.9%) 19.4%	RR 1.67 (1.26 to 2.23)	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more)	0000 VERY LOW	
or any r	reason (inclu randomised trials	serious <sup>6</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	122/405 (30.1%)	63/333 (18.9%) 19.4%	RR 1.67 (1.26 to 2.23)	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more)	0000 VERY LOW	
or any r	reason (inclu randomised trials	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency in (switch to conerse events))	no serious indirectness nbined antipsyc	serious <sup>5</sup>	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-u	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23)	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) umber of participar	0000 VERY LOW	
or any r	reason (inclu randomised trials	serious <sup>6</sup>	no serious inconsistency in (switch to conerse events))	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-L	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23)	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) umber of participar	0000 VERY LOW	
or any r	reason (inclu randomised trials	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency in (switch to conerse events))	no serious indirectness nbined antipsyc	serious <sup>5</sup>	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-u	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23)	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) Imber of participar 40 more per 1000 (from 56 fewer to	⊕OOO VERY LOW	
or any r	reason (inclu randomised trials inuation for a reason (inclu randomised	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency  n (switch to conerse events))	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-L	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23)	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) umber of participar	⊕OOO VERY LOW	
or any r	reason (inclu randomised trials inuation for a reason (inclu randomised	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency  n (switch to conerse events))	no serious indirectness	serious <sup>5</sup> chotic + SSRI v	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-L	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23) essed with: Nu	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) Imber of participar 40 more per 1000 (from 56 fewer to 210 more)	⊕OOO VERY LOW  ts discon	
or any r	reason (inclu randomised trials inuation for a reason (inclu randomised	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency  n (switch to conerse events))	no serious indirectness	serious <sup>5</sup> chotic + SSRI v	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-L	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23) essed with: Nu	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) Imber of participar 40 more per 1000 (from 56 fewer to	⊕OOO VERY LOW  ts discon	
or any r	reason (inclu randomised trials inuation for a reason (inclu randomised	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency  n (switch to conerse events))	no serious indirectness	serious <sup>5</sup> chotic + SSRI v	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-L	63/333 (18.9%) 19.4% up 8-12 weeks; asse	RR 1.67 (1.26 to 2.23) essed with: Nu	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) Imber of participar 40 more per 1000 (from 56 fewer to 210 more)	⊕OOO VERY LOW  ts discon	
or any r	reason (inclu randomised trials inuation for a reason (inclu randomised	serious <sup>8</sup> serious <sup>8</sup> ny reaso	no serious inconsistency  n (switch to conerse events))	no serious indirectness	serious <sup>5</sup> chotic + SSRI v	reporting bias <sup>3</sup>	122/405 (30.1%) TCA/SNRI) (follow-L	63/333 (18.9%) 19.4% up 8-12 weeks; asse 23/127 (18.1%)	RR 1.67 (1.26 to 2.23) essed with: Nu	127 more per 1000 (from 49 more to 233 more) 130 more per 1000 (from 50 more to 239 more) Imber of participar 40 more per 1000 (from 56 fewer to 210 more)	⊕OOO VERY LOW  ts discon	

3	randomised	serious <sup>8</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	51/405	8/333	RR 5.34	104 more per	⊕ООО	
	trials		inconsistency	indirectness			(12.6%)	(2.4%)	(2.57 to	1000 (from 38	VERY	
									11.09)	more to 242 more)	LOW	
										104 more per		
								2.4%		1000 (from 38		
										more to 242 more)		
Disconti	nuation due t	o advers	e events (switch	to combined a	ntipsychotic +	SSRI versus cont	inuing TCA/SNRI) (fo	ollow-up 8-12 weeks	; assessed	with: Number of pa	articipant	s
discontir	nuing due to	adverse (	events)									
2	randomised	serious <sup>8</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias3	39/389	3/127	RR 3.48	59 more per 1000	⊕000	
	trials		inconsistency	indirectness			(10%)	(2.4%)	(1.06 to	(from 1 more to	VERY	
			-						11.44)	247 more)	LOW	
										57 more per 1000		
								2.3%		(from 1 more to		
										240 more)		

Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment, and unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used) in studies contributing >50% to weighting in analysis

#### Switching to another antidepressant or non-antidepressant agent compared to augmenting with another antidepressant or non-antidepressant

#### 12 agent

1

7

10

11

	Quality ass	essment			No of <sub>l</sub>	patients	E	Effect		
Design	lisk of bias Inconsistency	Indirectness	Imprecision	Other considerations	Switch to another antidepressant/non-antidepressant agent	Augmentation with another antidepressant/non-antidepressant agent	Relative (95% CI)	Absolute	Quality	Importance

Remission (switch to TeCA versus augmentation with TeCA [mianserin]) (follow-up mean 6 weeks; assessed with: Number of people scoring ≤8 on Hamilton Rating Scale for Depression (HAM-D))

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>&</sup>lt;sup>3</sup> Funding from pharmaceutical companies

<sup>&</sup>lt;sup>4</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>5</sup> Events<300

<sup>&</sup>lt;sup>6</sup> I-squared>50%

<sup>&</sup>lt;sup>7</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (SMD 0.5)

<sup>&</sup>lt;sup>8</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration

<sup>&</sup>lt;sup>9</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

randomise	very	no serious	no serious	very serious <sup>2</sup>	reporting bias <sup>3</sup>	12/33	14/32	RR 0.83	74 fewer per	⊕OOO
trials	serious1	inconsistency	indirectness			(36.4%)	(43.8%)	(0.46 to	1000 (from	VERY
						, ,	· · · · · · · · · · · · · · · · · · ·	1.51)	236 fewer to	LOW
								,	223 more)	
									,	
									74 fewer per	
							43.8%		1000 (from	
							43.6%		237 fewer to	
									223 more)	
mission (switch pression Rating			augmentation v	with antipsych	notic) (follow-up	6-8 weeks; assessed with:	: Number of people sco	oring ≤10/<10	on Montgome	ry Asberg
randomise	serious <sup>4</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>6</sup>	82/422	127/427	RR 0.65	104 fewer per	⊕000
trials		inconsistency	indirectness			(19.4%)	(29.7%)	(0.48 to	1000 (from 36	
		,				,	,	0.88)	fewer to 155	LOW
									fewer)	2011
									101101)	
									104 fewer per	
							29.6%		1000 (from 36	
							/9 n%			
							20.070		fewer to 154	
		/chotic versus	augmentation	with lithium) (	follow-up mean 6	weeks; assessed with: N		ng <10 on Mo	fewer)	erg Depression
randomised	RS))	no serious	no serious	with lithium) (	follow-up mean 6	53/225	umber of people scorin	RR 0.87	fewer) ntgomery Asbo	⊕000
ting Scale (MAD	RS))		_				umber of people scoring	RR 0.87 (0.63 to	fewer) ntgomery Asbo 35 fewer per 1000 (from	⊕OOO VERY
randomised	RS))	no serious	no serious			53/225	umber of people scorin	RR 0.87	ntgomery Asbo 35 fewer per 1000 (from 100 fewer to	⊕000
randomised	RS))	no serious	no serious			53/225	umber of people scorin	RR 0.87 (0.63 to	fewer) ntgomery Asbo 35 fewer per 1000 (from	⊕OOO VERY
randomised	RS))	no serious	no serious			53/225	umber of people scorin	RR 0.87 (0.63 to	35 fewer per 1000 (from 100 fewer to 52 more)	⊕OOO VERY
randomised	RS))	no serious	no serious			53/225	60/221 (27.1%)	RR 0.87 (0.63 to	35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per	⊕OOO VERY
randomised	RS))	no serious	no serious			53/225	umber of people scorin	RR 0.87 (0.63 to	35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from	⊕OOO VERY
randomised	RS))	no serious	no serious			53/225	60/221 (27.1%)	RR 0.87 (0.63 to	35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per	⊕OOO VERY
randomised trials	d serious <sup>7</sup>	no serious inconsistency ersus augment	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>6</sup>	53/225	60/221 (27.1%)	RR 0.87 (0.63 to 1.19)	35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more)	⊕000 VERY LOW
randomised trials  sponse (switch ale for Depression randomised ra	d serious <sup>7</sup> d serious <sup>7</sup> to TeCA von (HAM-L	no serious inconsistency ersus augmenta D))	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>6</sup>	53/225 (23.6%) a 6 weeks; assessed with:	60/221 (27.1%)  27.2%  Number of people sho	RR 0.87 (0.63 to 1.19) wing ≥50% in	fewer) ntgomery Asbe 35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more) nprovement on	#000 VERY LOW Hamilton Ratin
randomised trials sponse (switch ale for Depression	serious <sup>7</sup> serious <sup>7</sup> to TeCA von (HAM-E	no serious inconsistency ersus augment	no serious indirectness ation with TeC	serious <sup>8</sup> A [mianserin]	reporting bias <sup>6</sup>	53/225 (23.6%)	60/221 (27.1%) 27.2%	RR 0.87 (0.63 to 1.19) wing ≥50% in	fewer) ntgomery Asbe 35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more) nprovement on	#000 VERY LOW
randomised trials  sponse (switch ale for Depression randomised ra	d serious <sup>7</sup> d serious <sup>7</sup> to TeCA von (HAM-L	no serious inconsistency ersus augmenta D))	no serious indirectness ation with TeC.	serious <sup>8</sup> A [mianserin]	reporting bias <sup>6</sup>	53/225 (23.6%) a 6 weeks; assessed with:	60/221 (27.1%)  27.2%  Number of people sho	RR 0.87 (0.63 to 1.19) wing ≥50% in	fewer) ntgomery Asbe 35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more) nprovement on	#000 VERY LOW Hamilton Ratin
randomised trials  sponse (switch ale for Depression randomised ra	d serious <sup>7</sup> d serious <sup>7</sup> to TeCA von (HAM-L	no serious inconsistency ersus augmenta D))	no serious indirectness ation with TeC.	serious <sup>8</sup> A [mianserin]	reporting bias <sup>6</sup>	53/225 (23.6%) a 6 weeks; assessed with:	60/221 (27.1%)  27.2%  Number of people sho	RR 0.87 (0.63 to 1.19) wing ≥50% in RR 0.78 (0.5 to	fewer) ntgomery Asbe 35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more) nprovement on	#000 VERY LOW  Hamilton Ratin
randomised trials  sponse (switch ale for Depression randomised ra	d serious <sup>7</sup> d serious <sup>7</sup> to TeCA von (HAM-L	no serious inconsistency ersus augmenta D))	no serious indirectness ation with TeC.	serious <sup>8</sup> A [mianserin]	reporting bias <sup>6</sup>	53/225 (23.6%) a 6 weeks; assessed with:	60/221 (27.1%)  27.2%  Number of people sho	RR 0.87 (0.63 to 1.19) wing ≥50% in RR 0.78 (0.5 to	fewer) ntgomery Asbe 35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more) nprovement on 138 fewer per 1000 (from 312 fewer to 131 more)	#000 VERY LOW  Hamilton Ratin
randomised trials sponse (switch ale for Depression randomised ran	d serious <sup>7</sup> d serious <sup>7</sup> to TeCA von (HAM-L	no serious inconsistency ersus augmenta D))	no serious indirectness ation with TeC.	serious <sup>8</sup> A [mianserin]	reporting bias <sup>6</sup>	53/225 (23.6%) a 6 weeks; assessed with:	60/221 (27.1%)  27.2%  Number of people sho	RR 0.87 (0.63 to 1.19) wing ≥50% in RR 0.78 (0.5 to	fewer) ntgomery Asbe 35 fewer per 1000 (from 100 fewer to 52 more) 35 fewer per 1000 (from 101 fewer to 52 more) nprovement on 138 fewer per 1000 (from 312 fewer to	#000 VERY LOW  Hamilton Ratin

										312 fewer to		
										131 more)		
			chotic versus a cale (MADRS))	ugmentation v	vith antipsy	chotic) (follow-up 6	6-8 weeks; assessed with:	Number of people sho	wing ≥50% in	nprovement or	n Montgoi	ner
	randomised	serious <sup>4</sup>	very serious9	no serious	serious <sup>8</sup>	reporting bias <sup>6</sup>	165/422	200/427	RR 0.8	94 fewer per	⊕OOO	
	trials		,	indirectness		, 0	(39.1%)	(46.8%)	(0.53 to	1000 (from	VERY	
									1.2)	220 fewer to	LOW	
										94 more)		
										93 fewer per		
								46.4%		1000 (from		
										218 fewer to 93 more)		
	randomised	serious <sup>7</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>6</sup>	114/225	112/221	RR 1	0 fewer per	⊕OOO	
	randomised	serious <sup>7</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>6</sup>	114/225	112/221	RR 1	0 fewer per	⊕000	
ľ	trials		inconsistency	indirectness			(50.7%)	(50.7%)	(0.83 to	1000 (from 86		
									1.2)	fewer to 101	LOW	
										more)		
										0 fewer per 1000 (from 86		
								50.7%				
										fewer to 101 more)		
obal In	npressions	scale (Co	GI-I))				6 weeks; assessed with:	Number of people rate		fewer to 101 more)	proved o	n Cl
lobal In	npressions randomised	very	no serious	no serious	A [mianserion serious8	n]) (follow-up mear reporting bias <sup>3</sup>	21/33	Number of people rate 23/32	RR 0.89	fewer to 101 more) very much im 79 fewer per	proved o	n CI
lobal In	npressions randomised	scale (Co	GI-I))					Number of people rate	RR 0.89 (0.63 to	revery much im  79 fewer per 1000 (from	⊕OOO VERY	n CI
lobal In	npressions randomised	very	no serious	no serious			21/33	Number of people rate 23/32	RR 0.89	rewer to 101 more) rewery much im rewery much im rewery fewer per 1000 (from 266 fewer to	proved o	n CI
lobal In	npressions randomised	very	no serious	no serious			21/33	Number of people rate 23/32	RR 0.89 (0.63 to	revery much im  79 fewer per 1000 (from	⊕OOO VERY	n Cl
lobal In	npressions randomised	very	no serious	no serious			21/33	Number of people rate 23/32	RR 0.89 (0.63 to	rewer to 101 more)  very much im  79 fewer per 1000 (from 266 fewer to 173 more)  79 fewer per	⊕OOO VERY	n CI
lobal In	npressions randomised	very	no serious	no serious			21/33	Number of people rate 23/32	RR 0.89 (0.63 to	rewer to 101 more)  very much im  79 fewer per 1000 (from 266 fewer to 173 more)  79 fewer per 1000 (from 1000 (from 1000 (from 1000 (from 1000 from 1000 fr	⊕OOO VERY	n CI
lobal In	npressions randomised	very	no serious	no serious			21/33	23/32 (71.9%)	RR 0.89 (0.63 to	79 fewer per 1000 (from 266 fewer to 173 more) 79 fewer per 1000 (from 266 fewer to 1700 (from 266 fewer to 166 fewer to 166 fewer to 166 fewer to 167 fewer to 168 fewer to 1	⊕OOO VERY	n Cl
lobal In	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>3</sup>	21/33 (63.6%)	23/32 (71.9%)	RR 0.89 (0.63 to 1.24)	79 fewer per 1000 (from 266 fewer to 173 more) 79 fewer per 1000 (from 266 fewer to 173 more)	⊕OOO VERY LOW	
espons	npressions randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>3</sup>	21/33	23/32 (71.9%)	RR 0.89 (0.63 to 1.24)	79 fewer per 1000 (from 266 fewer to 173 more) 79 fewer per 1000 (from 266 fewer to 173 more)	⊕OOO VERY LOW	
espons	randomised trials  e (switch to	very serious <sup>1</sup>	no serious inconsistency chotic versus a scale (CGI-I))	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>3</sup>	21/33 (63.6%)	23/32 (71.9%) 71.9%	RR 0.89 (0.63 to 1.24)	79 fewer per 1000 (from 266 fewer to 173 more) 79 fewer per 1000 (from 266 fewer to 173 more) 79 fewer per 1000 (from 266 fewer to 173 more) 26 fewer to 173 more) 26 fewer muce	⊕OOO VERY LOW	
espons	npressions randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>8</sup>	reporting bias <sup>3</sup>	21/33 (63.6%)	23/32 (71.9%)	RR 0.89 (0.63 to 1.24)	79 fewer per 1000 (from 266 fewer to 173 more) 79 fewer per 1000 (from 266 fewer to 173 more)	⊕OOO VERY LOW	

									RR 0.92	127 fewer to	⊕OOO
									(0.81 to	40 more)	VERY
									1.06)	40 111010)	LOW
									1.00)	53 fewer per	LOW
										1000 (from	
								66.8%		127 fewer to	
										40 more)	
cnonco	/ewitch to	antineve	hotic vorcus a	ugmontation v	vith lithium) (f	follow up moan 6	wooks: assessed with: N	lumber of people rated as	much or ve	,	oved on Clin
	pressions			uginientation v	viai nanami (i	onow-up mean o	weeks, assessed with it	idiliber of people rated as	much of ve	ery much impi	oved on onn
ra	andomised	serious <sup>7</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>6</sup>	139/225	133/221	RR 1.03	18 more per	⊕000
	rials		inconsistency	indirectness		, ,	(61.8%)	(60.2%)	(0.88 to	1000 (from 72	
							(= = = ,	(====,	1.19)	fewer to 114	LOW
									,	more)	
										,	
					1					18 more per	
								00.00/		1000 (from 72	
								60.2%		fewer to 114	
berg De	epression	Rating So	cale (MADRS; c	hange score);	Better indica	ted by lower valu	es)	on Rating Scale for Depre	1		
berg De		Rating So	cale (MADRS; c					on Rating Scale for Depres	ssion (HAM	,	⊕⊕OO
ra tri	epression andomised rials	serious <sup>10</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	230		-	SMD 0.39 higher (0.2 to 0.57 higher)	⊕⊕OO LOW
ra tri pressio ange sc	epression andomised rials on symptor core); Bette	serious <sup>10</sup> matology er indicat	no serious inconsistency (switch to TeC	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	230	230	-	SMD 0.39 higher (0.2 to 0.57 higher)	⊕⊕OO LOW  ression (HAI
ra tri pressio ange sc	epression andomised rials on symptor core); Bette	serious <sup>10</sup> matology or indicat	no serious inconsistency (switch to TeC ed by lower val	no serious indirectness A versus augr ues)	no serious imprecision nentation with	reporting bias <sup>3</sup> TeCA [mianseri	230 n]) (follow-up mean 6 wee	230 eks; measured with: Hami	- Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher)	⊕⊕OO LOW ression (HAI
ra tri pressio ange sc	epression andomised rials on symptor core); Bette	serious <sup>10</sup> matology er indicat	no serious inconsistency  (switch to TeC ed by lower value on serious	no serious indirectness  A versus augrues)	no serious imprecision nentation with	reporting bias <sup>3</sup> TeCA [mianseri	230 n]) (follow-up mean 6 wee	230 eks; measured with: Hami	- Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher) Scale for Dep	⊕⊕OO LOW  ression (HAI
ra tri pressio ange sc	epression andomised rials on symptor core); Bette	serious <sup>10</sup> matology er indicat	no serious inconsistency  (switch to TeC ed by lower value on serious	no serious indirectness  A versus augrues)	no serious imprecision nentation with	reporting bias <sup>3</sup> TeCA [mianseri	230 n]) (follow-up mean 6 wee	230 eks; measured with: Hami	- Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher) Scale for Dep SMD 0.41 higher (0.08	⊕⊕OO LOW  ression (HAI
ra tri pressio ange sc	epression andomised rials on symptor core); Bette andomised rials	serious <sup>10</sup> matology er indicat very serious <sup>1</sup>	no serious inconsistency  (switch to TeCed by lower value)  no serious inconsistency	no serious indirectness  A versus augrues)  no serious indirectness	no serious imprecision  nentation with	reporting bias <sup>3</sup> TeCA [mianserion reporting bias <sup>3</sup>	230 n]) (follow-up mean 6 wee	230 eks; measured with: Hami	- Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher) Scale for Dep SMD 0.41 higher (0.08 lower to 0.91 higher)	⊕⊕OO LOW  ression (HAI  ⊕OOO VERY LOW
ra tri	epression andomised rials on symptor core); Bette andomised rials on symptor	serious <sup>10</sup> matology er indicat very serious <sup>1</sup> matology	no serious inconsistency  (switch to TeCed by lower value)  no serious inconsistency	no serious indirectness  A versus augrues)  no serious indirectness	no serious imprecision  mentation with serious 11  serious 11  sus augmenta	reporting bias <sup>3</sup> TeCA [mianserion reporting bias <sup>3</sup>	230 n]) (follow-up mean 6 wee	230 eks; measured with: Hami	- Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher) Scale for Dep SMD 0.41 higher (0.08 lower to 0.91 higher)	⊕⊕OO LOW  ression (HAI  ⊕OOO VERY LOW
pressio ange sc tri	epression andomised rials on symptor core); Bette andomised rials on symptor ADRS; char	serious <sup>10</sup> matology er indicat very serious <sup>1</sup> matology nge score	no serious inconsistency  (switch to TeCed by lower value)  no serious inconsistency  (switch to antice); Better indicate	no serious indirectness  A versus augrues)  no serious indirectness  serious indirectness  cosychotic verseted by lower	no serious imprecision  mentation with serious 11  serious 11  sus augmentaralues)	reporting bias <sup>3</sup> TeCA [mianserion reporting bias <sup>3</sup> reporting bias <sup>3</sup>	230  n]) (follow-up mean 6 wee  33  chotic) (follow-up mean 8	230 eks; measured with: Hami	- Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher)  Scale for Dep  SMD 0.41 higher (0.08 lower to 0.91 higher)  y Asberg Depr	⊕⊕OO LOW  ression (HAI  ⊕OOO VERY LOW  ession Ratin
ra tri	epression andomised rials on symptor core); Bette andomised rials on symptor ADRS; char	serious <sup>10</sup> matology er indicat very serious <sup>1</sup> matology nge score	no serious inconsistency  (switch to TeCed by lower value)  no serious inconsistency  (switch to antiple); Better indications	no serious indirectness  A versus augrues)  no serious indirectness  serious indirectness  csychotic verseted by lower versus augrues	no serious imprecision  mentation with serious 11  serious 11  sus augmenta	reporting bias <sup>3</sup> TeCA [mianserion reporting bias <sup>3</sup>	230 n]) (follow-up mean 6 wee	230 eks; measured with: Hami 32 3 weeks; measured with: M	Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher)  Scale for Dep  SMD 0.41 higher (0.08 lower to 0.91 higher)  y Asberg Depr	⊕⊕OO LOW  ression (HAI  ⊕OOO VERY LOW  ession Ratin
ra tri	epression andomised rials on symptor core); Bette andomised rials on symptor ADRS; char	serious <sup>10</sup> matology er indicat very serious <sup>1</sup> matology nge score	no serious inconsistency  (switch to TeCed by lower value)  no serious inconsistency  (switch to antice); Better indicate	no serious indirectness  A versus augrues)  no serious indirectness  serious indirectness  cosychotic verseted by lower	no serious imprecision  mentation with serious 11  serious 11  sus augmentaralues)	reporting bias <sup>3</sup> TeCA [mianserion reporting bias <sup>3</sup> reporting bias <sup>3</sup>	230  n]) (follow-up mean 6 wee  33  chotic) (follow-up mean 8	230 eks; measured with: Hami 32 3 weeks; measured with: M	Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher)  Scale for Dep  SMD 0.41 higher (0.08 lower to 0.91 higher)  y Asberg Depr  SMD 0.38 higher (0.18	⊕⊕OO LOW  ression (HAI  ⊕OOO VERY LOW  ession Ratin  ⊕OOO VERY
ra tri	epression andomised rials on symptor core); Bette andomised rials on symptor ADRS; char	serious <sup>10</sup> matology er indicat very serious <sup>1</sup> matology nge score	no serious inconsistency  (switch to TeCed by lower value)  no serious inconsistency  (switch to antiple); Better indications	no serious indirectness  A versus augrues)  no serious indirectness  serious indirectness  csychotic verseted by lower versus augrues	no serious imprecision  mentation with serious 11  serious 11  sus augmentaralues)	reporting bias <sup>3</sup> TeCA [mianserion reporting bias <sup>3</sup> reporting bias <sup>3</sup>	230  n]) (follow-up mean 6 wee  33  chotic) (follow-up mean 8	230 eks; measured with: Hami 32 3 weeks; measured with: M	Iton Rating	SMD 0.39 higher (0.2 to 0.57 higher)  Scale for Dep  SMD 0.41 higher (0.08 lower to 0.91 higher)  y Asberg Depr	⊕⊕OO LOW  ression (HAI  ⊕OOO VERY LOW  ession Ratin

	randomised	serious14	no serious	no serious	serious15	reporting bias <sup>3</sup>	12/34	6/32	RR 1.88	165 more per	⊕000
	trials		inconsistency	indirectness		-	(35.3%)	(18.8%)	(0.8 to	1000 (from 37	
			,				,	,	4.42)	fewer to 641	LOW
									,	more)	
										165 more per	
								18.8%		1000 (from 38	
										fewer to 643	
										more)	
son (	including ac	lverse ev	ents))				sychotic) (follow-up 6-8 w				
	randomised	serious4	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>6</sup>	121/427	87/431	RR 1.4	81 more per	⊕OOO
	trials		inconsistency	indirectness			(28.3%)	(20.2%)	(1.11 to	1000 (from 22	
									1.78)	more to 157	LOW
										more)	
										82 more per	
								20.6%		1000 (from 23	
								20.6%		more to 161	
										more to 161 more)	
ason (	including ac	lverse ev	ents))				n) (follow-up mean 6 wee	ks; assessed with: Nu		more to 161 more) ipants discont	
ason (	including ac	lverse ev	ents)) no serious	no serious		ntation with lithiun	49/228	ks; assessed with: Nui 47/229	RR 1.05	more to 161 more) ipants discont	⊕000
ason (	including ac	lverse ev	ents))					ks; assessed with: Nu	RR 1.05 (0.73 to	more to 161 more) ipants discont	⊕000 VERY
ason (	including ac	lverse ev	ents)) no serious	no serious			49/228	ks; assessed with: Nui 47/229	RR 1.05	more to 161 more) ipants discont 10 more per 1000 (from 55 fewer to 101	⊕000
ason (	including ac	lverse ev	ents)) no serious	no serious			49/228	ks; assessed with: Nui 47/229	RR 1.05 (0.73 to	more to 161 more) ipants discont	⊕000 VERY
ason (	including ac	lverse ev	ents)) no serious	no serious			49/228	ks; assessed with: Nui 47/229	RR 1.05 (0.73 to	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per	⊕000 VERY
ason (	including ac	lverse ev	ents)) no serious	no serious			49/228	47/229 (20.5%)	RR 1.05 (0.73 to	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55	⊕000 VERY
ason (	including ac	lverse ev	ents)) no serious	no serious			49/228	ks; assessed with: Nui 47/229	RR 1.05 (0.73 to	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 fewer to 100	⊕000 VERY
eason (	including ac randomised trials	lverse ev	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	<sup>6</sup> reporting bias <sup>6</sup>	49/228 (21.5%)	47/229 (20.5%)	RR 1.05 (0.73 to 1.49)	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 more)	⊕000 VERY LOW
eason (	including acrandomised trials	serious <sup>7</sup>	no serious inconsistency	no serious indirectness	very serious <sup>1</sup>	<sup>6</sup> reporting bias <sup>6</sup>	49/228	47/229 (20.5%)	RR 1.05 (0.73 to 1.49)	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 more)	⊕000 VERY LOW
isconti ue to a	including ac randomised trials nuation due dverse even	serious <sup>7</sup> to adverts)	ents)) no serious inconsistency se events (swit	no serious indirectness	very serious <sup>1</sup>	<sup>6</sup> reporting bias <sup>6</sup> tation with TeCA	49/228 (21.5%)	47/229 (20.5%) 20.5%	RR 1.05 (0.73 to 1.49)	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 more) er of participan	⊕000 VERY LOW
ason (	randomised trials  nuation due dverse even	serious <sup>7</sup> to adverts)	no serious inconsistency se events (swit	no serious indirectness cch to TeCA ve	very serious <sup>1</sup>	<sup>6</sup> reporting bias <sup>6</sup>	49/228 (21.5%) [mianserin]) (follow-up m	47/229 (20.5%) 20.5%	RR 1.05 (0.73 to 1.49)	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 more) er of participan	⊕000 VERY LOW
isconti	including ac randomised trials nuation due dverse even	serious <sup>7</sup> to adverts)	ents)) no serious inconsistency se events (swit	no serious indirectness	very serious <sup>1</sup>	<sup>6</sup> reporting bias <sup>6</sup> tation with TeCA	49/228 (21.5%)	47/229 (20.5%) 20.5%	RR 1.05 (0.73 to 1.49)	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 more) er of participan  172 more per 1000 (from 9	⊕000 VERY LOW tts disconti
isconti	randomised trials  nuation due dverse even	serious <sup>7</sup> to adverts)	no serious inconsistency se events (swit	no serious indirectness cch to TeCA ve	very serious <sup>1</sup>	<sup>6</sup> reporting bias <sup>6</sup> tation with TeCA	49/228 (21.5%) [mianserin]) (follow-up m	47/229 (20.5%) 20.5%	RR 1.05 (0.73 to 1.49)	more to 161 more) ipants discont  10 more per 1000 (from 55 fewer to 101 more)  10 more per 1000 (from 55 fewer to 100 more) er of participan	⊕000 VERY LOW

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<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and method of allocation concealment and unclear blinding of intervention administration. Risk of attrition bias was also unclear (drop-out>20% but difference between groups<20% and ITT analysis used). Outcome assessment was non-blind

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Funding from pharmaceutical companies

<sup>&</sup>lt;sup>4</sup> Unclear method of allocation concealment and unclear blinding of, or non-blind, intervention administrator(s)

<sup>&</sup>lt;sup>5</sup> Events<300

<sup>&</sup>lt;sup>6</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical companies

<sup>&</sup>lt;sup>7</sup> Unclear method of allocation concealment and non-blind intervention administrator(s)

<sup>&</sup>lt;sup>8</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>9</sup> I-squared>80%

<sup>&</sup>lt;sup>10</sup> Unclear randomisation method and method of allocation concealment, unclear blinding of intervention administrator(s), unclear blinding of (or non-blind) outcome assessment, and unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>&</sup>lt;sup>11</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (SMD 0.5)

<sup>&</sup>lt;sup>12</sup> Unclear randomisation method and method of allocation concealment, unclear blinding of intervention administrator(s) and outcome assessment, and unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>16 &</sup>lt;sup>13</sup> N<400

2 3 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)
 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

Switching to another antidepressant of the same class compared to switching to another antidepressant of a different class 4

			Quality as	sessment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Switch to another antidepressant of the same class versus switch to another antidepressant of a different class	Control	(95% CI)	Absolute		
Remissio	on (switch to	another	SSRI versus swi	tch to SNRI) (fo	ollow-up 12-14	weeks; assesse	d with: Number of people scoring ≤	4/7 on Ha	milton Rati	ing Scale for Dep	ression	(HAM-D))
	randomised trials			no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	75/440 (17%)	123/444 (27.7%)	RR 0.61 (0.45 to 0.83)	108 fewer per 1000 (from 47 fewer to 152 fewer)	⊕OOO VERY LOW	
								28.1%		110 fewer per 1000 (from 48 fewer to 155 fewer)		
Remissio (HAM-D))		another	SSRI versus swi	tch to an atypi	cal AD) (follow	-up mean 14 wee	ks; assessed with: Number of peop	ole scorir	ng ≤7 on Ha	milton Rating Sc	ale for D	epression
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	42/238 (17.6%)	51/239 (21.3%)	RR 0.83 (0.57 to 1.19)	36 fewer per 1000 (from 92 fewer to 41 more)	⊕OOO VERY LOW	
								21.3%		36 fewer per 1000 (from 92 fewer to 40 more)		
	e (switch to natology (QII		SSRI versus swit	ch to SNRI) (fo	llow-up mean	14 weeks; asses	sed with: Number of people showin	g ≥50% i	mprovemei	nt on Quick Inver	itory of E	epressive
	randomised trials			no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	63/238 (26.5%)	70/250 (28%)		14 fewer per 1000 (from 81		

									RR 0.95	fewer to 73	⊕OOO	
									(0.71 to	more)	VERY	
									1.26)		LOW	
										18 fewer per		
								36.5%		1000 (from 106		
								30.5%		fewer to 95		
										more)		
				itch to an atypi	ical AD) (follow	-up mean 14 wee	ks; assessed with: Number of peo	ple showii	ng ≥50% im	provement on Q	uick Inven	ntory
epress	ive Sympton	iatology	(QID3))									
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>6</sup>	reporting bias3	63/238	62/239	RR 1.02	5 more per 1000	⊕OOO	
	trials		inconsistency	indirectness			(26.5%)	(25.9%)	(0.76 to	(from 62 fewer to	VERY	
			,				,	,	1.38)	` 99 more)	LOW	
										5 more per 1000		
								25.9%		(from 62 fewer to		
										) 98 more)		
nress	ion sympton	natology	(switch to anot)	ner SSRI versus	s switch to SNI	RI) (follow-up mea	an 14 weeks; measured with: Quic	k Inventor	of Denres	sive Symptomate	ology (OIF	าร
.ugo (	,, <u>Dono</u>	· maiout	ed by lower valu	.00,								
	randomised	corious <sup>1</sup>	no serious	no serious	no serious	reporting hige <sup>3</sup>	238	250	_	SMD 0.08 lower	$\Phi\Phi\Theta$	
		serious <sup>1</sup>	no serious	no serious	no serious	reporting bias <sup>3</sup>	238	250	-	SMD 0.08 lower	⊕⊕00	
	trials		inconsistency	indirectness	imprecision				-	(0.26 lower to 0.09 higher)	LOW	
	trials ion sympton	natology	inconsistency	indirectness	imprecision		238 w-up mean 14 weeks; measured v		- Inventory	(0.26 lower to 0.09 higher)	LOW	ology
IDS; c	trials ion sympton	natology ); Better	inconsistency (switch to anotlindicated by low	indirectness	imprecision				-	(0.26 lower to 0.09 higher) of Depressive Sy	LOW mptomate	ology
IDS; c	trials ion sympton hange score	natology ); Better	inconsistency (switch to anotl indicated by lov	indirectness ner SSRI versus ver values)	imprecision s switch to an a	atypical AD) (follo	w-up mean 14 weeks; measured v	with: Quick	-	(0.26 lower to 0.09 higher) of Depressive Sy	LOW mptomate	ology
IDS; c	trials ion sympton hange score	natology ); Better	inconsistency (switch to anotlindicated by low	indirectness ner SSRI versus ver values) no serious	imprecision s switch to an a	atypical AD) (follo	w-up mean 14 weeks; measured v	with: Quick	-	(0.26 lower to 0.09 higher) of Depressive Sy	LOW mptomate	ology
QIDS; c	trials  ion sympton hange score  randomised trials	natology ); Better serious <sup>1</sup>	inconsistency (switch to anotlindicated by low no serious inconsistency	ner SSRI versus ver values)  no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	w-up mean 14 weeks; measured v	with: Quick	-	(0.26 lower to 0.09 higher) of Depressive Sy SMD 0.12 lower (0.3 lower to 0.06 higher)	mptomate  ⊕⊕OO LOW	
NIDS; c	trials  on sympton hange score randomised trials  nuation for a g adverse ev	natology ); Better serious <sup>1</sup>	(switch to anothindicated by low no serious inconsistency no serious and serious no serious no serious no serious	ner SSRI versus ver values) no serious indirectness other SSRI vers	no serious imprecision	reporting bias <sup>3</sup>	238 ean 12 weeks; assessed with: Nut	239 mber of pa	rticipants o	(0.26 lower to 0.09 higher)  of Depressive Sy  SMD 0.12 lower (0.3 lower to 0.06 higher)  discontinuing for 37 fewer per	mptomate  mptoma	
NIDS; c	trials  on sympton hange score  randomised trials  nuation for a	serious¹ serious¹ nny reaso	(switch to anothindicated by low no serious inconsistency	ner SSRI versus ver values) no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	238 ean 12 weeks; assessed with: Nu	239 mber of pa	- rticipants (	(0.26 lower to 0.09 higher)  of Depressive Sy  SMD 0.12 lower (0.3 lower to 0.06 higher)	mptomato  Description of the control	
QIDS; c	trials  on sympton hange score randomised trials  nuation for a g adverse ev	serious¹ serious¹ nny reaso	(switch to anothindicated by low no serious inconsistency no serious and serious no serious no serious no serious	ner SSRI versus ver values) no serious indirectness other SSRI vers	no serious imprecision	reporting bias <sup>3</sup>	238 ean 12 weeks; assessed with: Nut	239 mber of pa	rticipants o	(0.26 lower to 0.09 higher)  of Depressive Sy  SMD 0.12 lower (0.3 lower to 0.06 higher)  discontinuing for 37 fewer per	mptomate  mptoma	
QIDS; c	trials  on sympton hange score randomised trials  nuation for a g adverse ev	serious¹ serious¹ nny reaso	(switch to anothindicated by low no serious inconsistency no serious and serious no serious no serious no serious	ner SSRI versus ver values) no serious indirectness other SSRI vers	no serious imprecision	reporting bias <sup>3</sup>	238 ean 12 weeks; assessed with: Nut	239 mber of pa	rticipants o	(0.26 lower to 0.09 higher)  of Depressive Sy  SMD 0.12 lower (0.3 lower to 0.06 higher)  discontinuing for  37 fewer per 1000 (from 100 fewer to 54 more)  37 fewer per	⊕⊕OO LOW  ⊕OOO VERY	
QIDS; c	trials  on sympton hange score randomised trials  nuation for a g adverse ev	serious¹ serious¹ nny reaso	(switch to anothindicated by low no serious inconsistency no serious and serious no serious no serious no serious	ner SSRI versus ver values) no serious indirectness other SSRI vers	no serious imprecision	reporting bias <sup>3</sup>	238 ean 12 weeks; assessed with: Nut	239 mber of pa	rticipants o	(0.26 lower to 0.09 higher)  of Depressive Sy  SMD 0.12 lower (0.3 lower to 0.06 higher)  discontinuing for  37 fewer per 1000 (from 100 fewer to 54 more)  37 fewer per 1000 (from 100 fewer to 54 more)	⊕⊕OO LOW  ⊕OOO VERY	
QIDS; c	trials  on sympton hange score randomised trials  nuation for a g adverse ev	serious¹ serious¹ nny reaso	(switch to anothindicated by low no serious inconsistency no serious and serious no serious no serious no serious	ner SSRI versus ver values) no serious indirectness other SSRI vers	no serious imprecision	reporting bias <sup>3</sup>	238 ean 12 weeks; assessed with: Nut	239 mber of pa	rticipants o	(0.26 lower to 0.09 higher)  of Depressive Sy  SMD 0.12 lower (0.3 lower to 0.06 higher)  discontinuing for  37 fewer per 1000 (from 100 fewer to 54 more)  37 fewer per	⊕⊕OO LOW  ⊕OOO VERY	

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3

4

7

9

Switching to another antidepressant or non-antidepressant agent (head-to-head comparisons)

			Quality ass	sessment			No of patients			Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Switch to another antidepressant/non- antidepressant agent (head-to- head)	Control	Relative (95% CI)	Absolute	Quality	Importance

<sup>&</sup>lt;sup>5</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>95%</sup> CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)

<sup>&</sup>lt;sup>8</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

	randomised	serious1	no serious	no serious	no serious	reporting bias <sup>2</sup>	102/587	217/810	RR 0.62	102 fewer per	⊕⊕00
	trials		inconsistency	indirectness	imprecision	reperming areas	(17.4%)	(26.8%)	(0.5 to	1000 (from 62	LOW
			,		·		,	,	0.77)	fewer to 134	
									,	fewer)	
										119 fewer per	
								31.4%		1000 (from 72	
										fewer to 157	
!!		CCDL		odin overbodio) (fo			ith. November of records according		4	fewer)	Dating C
ADRS		SSKI Ver	sus switch to ai	itipsychotic) (it	ollow-up 8-12 w	eeks; assessed w	ith: Number of people scorir	ng ≤8 on won	tgomery A	sperg Depression	Rating S
ADINO	"										
	randomised	serious <sup>1</sup>	no serious	no serious	very serious <sup>3</sup>	reporting bias <sup>2</sup>	29/198	27/203	RR 1.1	13 more per 1000	⊕000
	trials		inconsistency	indirectness	,	, ,	(14.6%)	(13.3%)	(0.68 to	(from 43 fewer to	
			_						1.8)	106 more)	LOW
										13 more per 1000	
								13.4%		(from 43 fewer to	
		SNRI ver	sus switch to a	ypical antidepr	essant) (follow-	up 8-14 weeks; as	ssessed with: Number of pec		≤7 on Hami	(from 43 fewer to 107 more)	for Depre
		SNRI ver	no serious	no serious	essant) (follow-	up 8-14 weeks; as	83/300 (27.7%)	ople scoring:		(from 43 fewer to 107 more)	⊕000
	randomised		no serious	no serious			83/300	ople scoring:	RR 1.16	(from 43 fewer to 107 more) ilton Rating Scale	⊕000
	randomised		no serious	no serious			83/300	71/294 (24.1%)	RR 1.16 (0.89 to	(from 43 fewer to 107 more) iton Rating Scale 39 more per 1000 (from 27 fewer to 126 more) 46 more per 1000	⊕000 VERY
	randomised		no serious	no serious			83/300	ople scoring:	RR 1.16 (0.89 to	(from 43 fewer to 107 more) iton Rating Scale 39 more per 1000 (from 27 fewer to 126 more) 46 more per 1000 (from 32 fewer to	⊕000 VERY
IAM-D)	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>2</sup>	83/300 (27.7%)	71/294 (24.1%) 28.9%	RR 1.16 (0.89 to 1.52)	(from 43 fewer to 107 more) iton Rating Scale 39 more per 1000 (from 27 fewer to 126 more) 46 more per 1000 (from 32 fewer to 150 more)	⊕000 VERY LOW
HAM-D)	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>2</sup>	83/300	71/294 (24.1%) 28.9%	RR 1.16 (0.89 to 1.52)	(from 43 fewer to 107 more) iton Rating Scale 39 more per 1000 (from 27 fewer to 126 more) 46 more per 1000 (from 32 fewer to 150 more)	⊕000 VERY LOW
HAM-D)	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>2</sup>	83/300 (27.7%)	71/294 (24.1%) 28.9%	RR 1.16 (0.89 to 1.52)	(from 43 fewer to 107 more) iton Rating Scale 39 more per 1000 (from 27 fewer to 126 more) 46 more per 1000 (from 32 fewer to 150 more) ≤8 on Montgomer	⊕OOO VERY LOW
HAM-D)	randomised trials on (switch to ion Rating S	serious <sup>4</sup> SSRI + a cale (MAD	no serious inconsistency  ntipsychotic verings))	no serious indirectness	serious <sup>5</sup> ntipsychotic-or	reporting bias <sup>2</sup>	83/300 (27.7%) 2 weeks; assessed with: Nui	71/294 (24.1%) 28.9% mber of peop	RR 1.16 (0.89 to 1.52)	(from 43 fewer to 107 more)  iton Rating Scale  39 more per 1000 (from 27 fewer to 126 more)  46 more per 1000 (from 32 fewer to 150 more)  ≤8 on Montgomer	⊕OOO VERY LOW y Asberg
HAM-D)	randomised trials on (switch to ion Rating Soundomised	serious <sup>4</sup> SSRI + a cale (MAD	no serious inconsistency ntipsychotic ver	no serious indirectness	serious <sup>5</sup> ntipsychotic-or	reporting bias <sup>2</sup>	83/300 (27.7%) 2 weeks; assessed with: Nu	71/294 (24.1%) 28.9%	RR 1.16 (0.89 to 1.52)	(from 43 fewer to 107 more) iton Rating Scale 39 more per 1000 (from 27 fewer to 126 more) 46 more per 1000 (from 32 fewer to 150 more) ≤8 on Montgomer	⊕OOO VERY LOW
HAM-D)	randomised trials on (switch to ion Rating Soundomised	serious <sup>4</sup> SSRI + a cale (MAD	no serious inconsistency  ntipsychotic verings))	no serious indirectness	serious <sup>5</sup> ntipsychotic-or	reporting bias <sup>2</sup>	83/300 (27.7%) 2 weeks; assessed with: Nui	71/294 (24.1%) 28.9% mber of peop	RR 1.16 (0.89 to 1.52) le scoring	(from 43 fewer to 107 more)  ilton Rating Scale  39 more per 1000 (from 27 fewer to 126 more)  46 more per 1000 (from 32 fewer to 150 more)  ≤8 on Montgomer  84 more per 1000 (from 4 fewer to 234 more)  84 more per 1000	⊕OOO VERY LOW y Asberg
HAM-D)	randomised trials on (switch to ion Rating Soundomised	serious <sup>4</sup> SSRI + a cale (MAD	no serious inconsistency  ntipsychotic verings))	no serious indirectness	serious <sup>5</sup> ntipsychotic-or	reporting bias <sup>2</sup>	83/300 (27.7%) 2 weeks; assessed with: Nui	71/294 (24.1%) 28.9% mber of peop	RR 1.16 (0.89 to 1.52) le scoring	(from 43 fewer to 107 more)  ilton Rating Scale  39 more per 1000 (from 27 fewer to 126 more)  46 more per 1000 (from 32 fewer to 150 more)  ≤8 on Montgomer  84 more per 1000 (from 4 fewer to 234 more)	⊕OOO VERY LOW y Asberg

	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>2</sup>	94/376	29/198	RR 1.45	66 more per 1000	⊕000
	trials		inconsistency	indirectness		, ,	(25%)	(14.6%)	(0.97 to	(from 4 fewer to	VERY
							,		2.17)	171 more)	LOW
										70 more per 1000	
								15.6%		(from 5 fewer to	
	- /!4-l- 4- (	0001		00DL AD) (5-1			la Namela a de la calacteria	>500/ !		183 more)	01- 6
							h: Number of people showing nt on HAM-D AND much/very				Scale for
	randamiaad	aariaua1	no serious	no corious	serious <sup>6</sup>	roporting bios <sup>2</sup>	127/385	196/616	RR 0.91	20 fower per	0000
	randomised trials	serious <sup>1</sup>	inconsistency	no serious indirectness	serious	reporting bias <sup>2</sup>	(33%)	(31.8%)	(0.74 to	29 fewer per 1000 (from 83	⊕OOO VERY
	แเสเร		inconsistency	indirectriess			(33%)	(31.0%)	•	fewer to 38 more)	LOW
									1.12)	lewer to 36 more)	LOVV
								450/		40 fewer per	
								45%		1000 (from 117 fewer to 54 more)	
	- /:4-b 4- (	CCDL		tinguals atial (fa	Ua 0 40	vanilari annananal viii	th: Number of people showing	- >500/ i		,	hann Dannasi
ing So	cale (MADRS	5))									
		serious <sup>1</sup>	no serious	no serious	serious <sup>7</sup>	reporting bias <sup>2</sup>	60/198	43/203		91 more per 1000	
	trials		inconsistency	indirectness			(30.3%)	(21.2%)	(1.02 to	(from 4 more to	VERY
									2.01)	214 more)	LOW
										96 more per 1000	
								22.4%		(from 4 more to	
										226 more)	
Depre	ession (HAM-	-D)/Quick	Inventory of De	pressive Symp	tomatology (Q	(IDS))	sessed with: Number of peop				_
		serious4	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>2</sup>	102/300	94/294		29 more per 1000	
	trials		inconsistency	indirectness			(34%)	(32%)	(0.88 to	(from 38 fewer to	VERY
									1.35)	112 more)	LOW
										38 more per 1000	
								42.1%		(from 51 fewer to	
										147 more)	
			tipsychotic vers le (MADRS))	sus switch to a	ntipsychotic-o	nly) (follow-up 8-12	weeks; assessed with: Numb	ber of peopl	e showing	≥50% improveme	nt on Montgom
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>7</sup>	reporting bias <sup>2</sup>	140/376	43/203	RR 1.54	114 more per	⊕000
		0011000		indirectness	Coriodo	roporting blus	(37.2%)	(21.2%)	(1.13 to	1000 (from 28	VERY
			Inconsisiency								
	trials		inconsistency	indirectiness			(=:=,=,	(= ::= /0/	•	,	
			inconsistency	indirectifess			(0.12.14)	(= 1.1= 70)	2.1)	more to 233 more)	LOW

								22.4%		121 more per 1000 (from 29 more to 246 more)	
	se (switch to sion Rating So			us switch to SS	RI-only) (follo	w-up 8-12 weeks;	assessed with: Number of pe	eople showir	ıg ≥50% im	provement on Mo	ntgomery
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>2</sup>	140/376 (37.2%)	60/198 (30.3%)		27 more per 1000 (from 55 fewer to 142 more)	⊕OOO VERY LOW
								31.4%		28 more per 1000 (from 57 fewer to 148 more)	
	se (switch to	SSRI vers	us switch to SN	RI) (follow-up n	nean 4 weeks;	assessed with: Nu	ımber of people rated as mud	ch or very m	uch improv	ved on Clinical Glo	bal Impre
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>2</sup>	36/55 (65.5%)	33/52 (63.5%)	RR 1.03 (0.78 to 1.37)	19 more per 1000 (from 140 fewer to 235 more)	⊕OOO VERY LOW
								63.5%		19 more per 1000 (from 140 fewer to 235 more)	
nrace						(follow-up 4-14 w ); Better indicated	eeks; measured with: Hamilt by lower values)	on Rating So	ale for De	pression (HAM-D;	change
	zuick invento										
		serious <sup>1</sup>	serious <sup>8</sup>	no serious indirectness	no serious imprecision	reporting bias <sup>2</sup>	378	608	-	SMD 0.08 higher (0.18 lower to 0.34 higher)	⊕OOO VERY LOW
ore)/C	randomised trials	serious <sup>1</sup>	switch to SSRI v	indirectness	imprecision		378 veeks; measured with: Montg		rg Depress	(0.18 lower to 0.34 higher)	VERY LOW

	randomised	serious <sup>1</sup>	very serious <sup>9</sup>	no serious	serious <sup>10</sup>	reporting bias <sup>2</sup>	389	206	-	SMD 0.44 lower	⊕OOO	
	trials			indirectness						(0.91 lower to	VERY	
										0.03 higher)	LOW	
										0.00 mgo.)	2011	
ressi	on symptom	atology (s	witch to SSRI +	antipsychotic v	versus switch	to SSRI-only) (folio	ow-up 8-12 weeks; measured v	vith: Monto	omery Asl	pera Depression F	Rating Sca	ale
			r indicated by lo			,, (			,	ос. д доргосо		
,	,g	,, =	, , , , , , , , , , , , , , , , , , , ,	,								
	randomised	serious1	no serious	no serious	no serious	reporting bias <sup>2</sup>	389	202	-	SMD 0.13 lower	⊕⊕00	
	trials	00000	inconsistency	indirectness	imprecision	oporting side	333			(0.35 lower to 0.1	LOW	
	triaio		inconsistency	mancomess	Impredictor					higher)	LOVV	
										riigrici)		
contir	nuation for a	ny reason	(switch to SSRI	versus switch	to non-SSRI A	D) (follow-up 4-12	weeks; assessed with: Number	er of partic	inants disc	ontinuing for any	reason (i	nclu
	events))	ily rouson	(SWITCH TO COIN	versus switter	to non cora A	D) (lollow up + 12	Wooks, assessed With Humb	or or partie	ipanto aloc	ontinuing for any	rouson (ii	
0.00	overito),											
	randomised	serious <sup>11</sup>	no serious	no serious	serious <sup>12</sup>	reporting bias <sup>2</sup>	70/373	75/345	RR 0.86	30 fewer per	⊕000	
	trials	3000	inconsistency	indirectness			(18.8%)	(21.7%)		1000 (from 76	VERY	
							(10.070)	(= 1.7 70)	1.16)	fewer to 35 more)		
									1.10)	iowor to oo more)	LOVV	
										28 fewer per		
								/				
								20.2%		1000 (from 71		
	nuation for a events))	ny reason	(switch to SSRI	versus switch	to antipsychol	tic) (follow-up 8-12	weeks; assessed with: Numb	20.2% er of partic	ipants dis	1000 (from 71 fewer to 32 more) continuing for any	reason (i	inclu
erse (	events))							er of partic		fewer to 32 more) continuing for any	· ·	inclu
erse e	randomised	ny reason	no serious	no serious	to antipsychol	reporting bias <sup>2</sup>	40/202	er of partic	RR 0.82	fewer to 32 more) continuing for any 44 fewer per	⊕000	inclu
erse (	events))							er of partic	RR 0.82 (0.56 to	fewer to 32 more) continuing for any 44 fewer per 1000 (from 107	⊕000 VERY	inclu
erse (	randomised		no serious	no serious			40/202	er of partic	RR 0.82	fewer to 32 more) continuing for any 44 fewer per	⊕000 VERY	inclu
erse e	randomised		no serious	no serious			40/202	er of partic	RR 0.82 (0.56 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)	⊕000 VERY	inclu
erse e	randomised		no serious	no serious			40/202	50/206 (24.3%)	RR 0.82 (0.56 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per	⊕000 VERY	inclu
erse (	randomised		no serious	no serious			40/202	er of partic	RR 0.82 (0.56 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113	⊕000 VERY	inclu
erse (	randomised trials	serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>12</sup>	reporting bias <sup>2</sup>	40/202 (19.8%)	50/206 (24.3%) 25.6%	RR 0.82 (0.56 to 1.18)	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more)	⊕000 VERY LOW	
erse (	randomised trials	serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>12</sup>	reporting bias <sup>2</sup>	40/202	50/206 (24.3%) 25.6%	RR 0.82 (0.56 to 1.18)	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more)	⊕000 VERY LOW	
rerse (	randomised trials	serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>12</sup>	reporting bias <sup>2</sup>	40/202 (19.8%)	50/206 (24.3%) 25.6%	RR 0.82 (0.56 to 1.18)	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more)	⊕000 VERY LOW	
continuon (i	randomised trials nuation for a ncluding adv	serious <sup>11</sup> ny reason	no serious inconsistency (switch to SNRI	no serious indirectness versus switch	serious <sup>12</sup> to atypical ant	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18)	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more) rticipants disconti	⊕OOO VERY LOW	
continuon (i	randomised trials  nuation for a ncluding adv	serious <sup>11</sup> ny reason verse ever	no serious inconsistency  (switch to SNRInts))	no serious indirectness  versus switch	serious <sup>12</sup>	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18)	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more) rticipants disconti	⊕OOO VERY LOW nuing for	
continuon (i	randomised trials nuation for a ncluding adv	serious <sup>11</sup> ny reason verse ever	no serious inconsistency (switch to SNRI	no serious indirectness versus switch	serious <sup>12</sup> to atypical ant	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18) nber of par RR 0.99 (0.44 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more)  rticipants disconti	⊕OOO VERY LOW nuing for	
continuon (i	randomised trials  nuation for a ncluding adv	serious <sup>11</sup> ny reason verse ever	no serious inconsistency  (switch to SNRInts))	no serious indirectness  versus switch	serious <sup>12</sup> to atypical ant	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18)	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more) rticipants disconti	⊕OOO VERY LOW nuing for	
econtinus (i	randomised trials  nuation for a ncluding adv	serious <sup>11</sup> ny reason verse ever	no serious inconsistency  (switch to SNRInts))	no serious indirectness  versus switch	serious <sup>12</sup> to atypical ant	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18) nber of par RR 0.99 (0.44 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more) rticipants disconti  2 fewer per 1000 (from 102 fewer to 225 more)	⊕OOO VERY LOW nuing for	
scontinus (i	randomised trials  nuation for a ncluding adv	serious <sup>11</sup> ny reason verse ever	no serious inconsistency  (switch to SNRInts))	no serious indirectness  versus switch	serious <sup>12</sup> to atypical ant	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18) nber of par RR 0.99 (0.44 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more)  rticipants disconti  2 fewer per 1000 (from 102 fewer to 225 more)  2 fewer per 1000	⊕OOO VERY LOW nuing for	
continuon (i	randomised trials  nuation for a ncluding adv	serious <sup>11</sup> ny reason verse ever	no serious inconsistency  (switch to SNRInts))	no serious indirectness  versus switch	serious <sup>12</sup> to atypical ant	reporting bias <sup>2</sup>	40/202 (19.8%) ow-up mean 8 weeks; assessed	50/206 (24.3%) 25.6% d with: Nur	RR 0.82 (0.56 to 1.18) nber of par RR 0.99 (0.44 to	fewer to 32 more) continuing for any  44 fewer per 1000 (from 107 fewer to 44 more)  46 fewer per 1000 (from 113 fewer to 46 more) rticipants disconti  2 fewer per 1000 (from 102 fewer to 225 more)	⊕OOO VERY LOW nuing for	

ra	andomised	serious <sup>11</sup>	no serious	no serious	serious <sup>12</sup>	reporting bias <sup>2</sup>	90/389	50/206	RR 0.89	27 fewer per	$\oplus$ OOO	ı
tr	rials		inconsistency	indirectness			(23.1%)	(24.3%)		1000 (from 85	VERY	
									1.21)	fewer to 51 more)	LOW	
								0= 00/		28 fewer per		
								25.6%		1000 (from 90		1
										fewer to 54 more)		
	adverse ev		(switch to SSRI	+ antipsychoti	c versus swit	ch to SSRI-only) (to	ollow-up 8-12 weeks; assesse	ed with: Num	iber of part	icipants discontir	nuing for	any
ra	andomised	serious <sup>11</sup>	no serious	no serious	serious15	reporting bias <sup>2</sup>	90/389	40/202	RR 1.12	24 more per 1000	⊕000	
tr	rials		inconsistency	indirectness			(23.1%)	(19.8%)		(from 44 fewer to	VERY	
			,				,	,	1.59)	117 more)	LOW	
									,	,		
										24 more per 1000		
								19.9%		(from 44 fewer to		1
										117 more)		
nts)					_					23 fewer per	9000	
ents)			no serious inconsistency	no serious indirectness	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%)	134/748 (17.9%)	RR 0.87	23 fewer per 1000 (from 61 fewer to 25 more)	⊕000 VERY LOW	
ents)	andomised		no serious	no serious	_		64/505	134/748	RR 0.87 (0.66 to	1000 (from 61 fewer to 25 more)	VERY	
ents)	andomised		no serious	no serious	_		64/505	134/748 (17.9%)	RR 0.87 (0.66 to	1000 (from 61 fewer to 25 more)	VERY	
nts)	andomised		no serious	no serious	_		64/505	134/748	RR 0.87 (0.66 to	1000 (from 61 fewer to 25 more) 11 fewer per 1000 (from 28	VERY	
ra tr	andomised rials	serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%)	134/748 (17.9%) 8.2%	RR 0.87 (0.66 to 1.14)	1000 (from 61 fewer to 25 more) 11 fewer per 1000 (from 28 fewer to 11 more)	VERY LOW	
ra tr continu	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2%	RR 0.87 (0.66 to 1.14)	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing	VERY LOW	idver
continuents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency events (switch	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2% th: Number of	RR 0.87 (0.66 to 1.14) of participa	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing	VERY LOW	ıdver
raccontinuents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2%	RR 0.87 (0.66 to 1.14) of participa RR 0.39 (0.16 to	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing  56 fewer per 1000 (from 8	VERY LOW	ıdver
continuents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency events (switch	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2% th: Number of	RR 0.87 (0.66 to 1.14) of participa	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing  56 fewer per 1000 (from 8 fewer to 77	VERY LOW	adver
rats) raccontinuents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency events (switch	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2% th: Number of	RR 0.87 (0.66 to 1.14) of participa RR 0.39 (0.16 to	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing  56 fewer per 1000 (from 8	VERY LOW	adver
raccontinuents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency events (switch	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2% th: Number of	RR 0.87 (0.66 to 1.14) of participa RR 0.39 (0.16 to	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing  56 fewer per 1000 (from 8 fewer to 77 fewer)	VERY LOW	adver
raccontinuents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency events (switch	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2% th: Number of	RR 0.87 (0.66 to 1.14) of participa RR 0.39 (0.16 to	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more)  156 fewer per 1000 (from 8 fewer to 77 fewer)  54 fewer per	VERY LOW	adver
scontinu ents)	andomised rials uation due t	serious <sup>11</sup>	no serious inconsistency events (switch	no serious indirectness to SSRI versus	serious <sup>14</sup>	reporting bias <sup>2</sup>	64/505 (12.7%) up 8-12 weeks; assessed wit	134/748 (17.9%) 8.2% th: Number of	RR 0.87 (0.66 to 1.14) of participa RR 0.39 (0.16 to	1000 (from 61 fewer to 25 more)  11 fewer per 1000 (from 28 fewer to 11 more) ints discontinuing  56 fewer per 1000 (from 8 fewer to 77 fewer)	VERY LOW	adver

- <sup>1</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment
- <sup>2</sup> Data cannot be extracted or is not reported for all outcomes and/or funding from pharmaceutical companies
- <sup>3</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)
- <sup>4</sup> Unclear (or high risk) randomisation method and unclear method of allocation concealment, and unclear blinding of intervention administrator(s)
- <sup>5</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)
- <sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)
- 7 Events<300

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- 8 I-squared>50%
- 9 l-squared>80%
- 10 10 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD -0.5)
- 11 Unclear randomisation method and method of allocation concealment and unclear blinding of intervention administrator(s)
- 12 12 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)
  - <sup>13</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline and unclear blinding of intervention administrator(s)
- 14 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)
  - <sup>15</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

## Chronic depression (chapter 9)

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#### Problem solving versus pill placebo for chronic depression

			Quality asse	essment			No of pa	itients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Problem solving	Pill placebo	Relative (95% CI)	Absolute		
Remission	(follow-up m	ean 11 we	eks; assessed with	: Number of peo	ple scoring <	 <7 on Hamilton Rat	ing Scale for	r Depressi	on (HAM-D))			
	randomised trials			no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	32/63 (50.8%)	25/62 (40.3%)	RR 1.26 (0.85 to 1.86)	105 more per 1000 (from 60 fewer to 347 more)		
							,	, ,	,	·		

<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and unclear blinding of intervention administrator(s)

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)

<sup>&</sup>lt;sup>3</sup> Efficacy data cannot be extracted and study funded by pharmaceutical company

						40.3%		105 more per 1000 (from 60 fewer to 347 more)	⊕OOO VERY LOW	
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#### Cognitive and cognitive behavioural therapies versus antidepressants for chronic depression

			Quality as	sessment			No of pa	atients		Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cognitive and cognitive behavioural therapies	Antidepressants	Relative (95% CI)	Absolute	Quality	Importanc
			gnitive behaviou ntgomery Asberg				s; assessed with: N	lumber of people s	coring <7/≤	8 on Hamilton Rat	ing Scale	for
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	105/308 (34.1%)	95/307 (30.9%)	RR 1.1 (0.83 to 1.46)	31 more per 1000 (from 53 fewer to 142 more)		
								29.1%		29 more per 1000 (from 49 fewer to 134 more)		
emissio	on (CBASP ve	ersus nefa	zodone) (follow-	up mean 12 wee	eks; assessed	with: Number of p	eople scoring ≤8 or	Hamilton Rating	Scale for De	epression (HAM-D)	)	
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	72/216 (33.3%)	64/220 (29.1%)	RR 1.15 (0.87 to 1.52)	44 more per 1000 (from 38 fewer to 151 more)	⊕000 VERY LOW	
								29.1%		44 more per 1000 (from 38 fewer to 151 more)		
emissio	on (CBASP ve	ersus esci	talopram) (follow	-up mean 8 wee	eks; assessed	with: Number of p	eople scoring ≤9 or	Montgomery Asb	erg Depres	sion Rating Scale	(MADRS)	))
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>6</sup>	1/29 (3.4%)	5/30 (16.7%)	RR 0.21 (0.03 to 1.67)	132 fewer per 1000 (from 162 fewer to 112 more)		

Intervention administrators and participants not blinded, although outcome assessment is blinded
 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)
 Medication and placebo supplied by pharmaceutical company and authors have some financial interests in pharmaceutical companies

										132 fewer per	⊕000
								16.7%		1000 (from 162	VERY
										fewer to 112 more)	LOW
	, , ,	<u> </u>		\ (f, II		1 24 1		.= 11 '''	5 " 0		
missio	n (problem s	solving ve	rsus paroxetine	) (follow-up mea	an 11 weeks; as	sessed with: Num	nber of people scorin	ng on Hamilton</td <td>n Rating Sca</td> <td>le for Depression (</td> <td>HAMI-D))</td>	n Rating Sca	le for Depression (	HAMI-D))
		serious <sup>7</sup>	no serious	no serious	very serious <sup>5</sup>	reporting bias <sup>6</sup>	32/63	26/57	RR 1.11	50 more per 1000	⊕000
	trials		inconsistency	indirectness			(50.8%)	(45.6%)	(0.77 to	(from 105 fewer to	
									1.62)	283 more)	LOW
									-	50 more per 1000	
								45.6%		(from 105 fewer to	
										283 more)	
							erg Depression Ratir			las c	
		serious <sup>1</sup>	serious <sup>8</sup>	no serious	very serious <sup>5</sup>	reporting bias <sup>3</sup>	33/245	49/250	RR 0.56	86 fewer per 1000	⊕000
	trials			indirectness			(13.5%)	(19.6%)	(0.21 to	(from 155 fewer to	
									1.49)	96 more)	LOW
									+	100 fewer per	
								22.7%	-	100 fewer per 1000 (from 179	
enone	o (CRASD va	oreus nofa	zodono) (follow	up moan 12 wo	oke: assocsad	with: Number of n	eonle showing >50°/		Hamilton P	1000 (from 179 fewer to 111 more)	ression (HAM.F
D HAN	ID score 8-1 randomised		no serious	no serious	eks; assessed serious <sup>9</sup>	with: Number of p	eople showing ≥50%	improvement or	RR 0.77	1000 (from 179 fewer to 111 more) ating Scale for Dep 43 fewer per 1000	⊕000
ID HAN	ID score 8-1	5)						improvement or		1000 (from 179 fewer to 111 more) ating Scale for Dep	
D HAN	ID score 8-1 randomised	5)	no serious	no serious			31/216	improvement or	RR 0.77 (0.5 to	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000	⊕OOO VERY
D HAN	ID score 8-1 randomised	5)	no serious	no serious			31/216	improvement or	RR 0.77 (0.5 to	1000 (from 179 fewer to 111 more) ating Scale for Dep 43 fewer per 1000 (from 93 fewer to 34 more)	⊕OOO VERY
D HAM	ID score 8-1 randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	reporting bias <sup>3</sup>	31/216 (14.4%)	41/220 (18.6%)	RR 0.77 (0.5 to 1.18)	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)	⊕000 VERY LOW
D HAN	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	reporting bias <sup>3</sup>	31/216	41/220 (18.6%)	RR 0.77 (0.5 to 1.18)	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)	⊕000 VERY LOW
sponse	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	reporting bias <sup>3</sup>	31/216 (14.4%)	41/220 (18.6%)	RR 0.77 (0.5 to 1.18)	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)  ry Asberg Depressi	⊕000 VERY LOW
sponse	randomised trials  e (CBASP ve	serious <sup>1</sup>	no serious inconsistency talopram) (follow	no serious indirectness v-up mean 8 we	serious <sup>9</sup>	reporting bias <sup>3</sup> with: Number of p	31/216 (14.4%) eople showing ≥50%	41/220 (18.6%) 18.6%	RR 0.77 (0.5 to 1.18) n Montgomen RR 0.26 (0.06 to	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)  ry Asberg Depression 197 fewer per 1000 (from 251	#000 VERY LOW  on Rating Scale
sponse	randomised trials  e (CBASP ve) randomised	serious <sup>1</sup>	no serious inconsistency talopram) (follow	no serious indirectness  v-up mean 8 we	serious <sup>9</sup>	reporting bias <sup>3</sup> with: Number of p	31/216 (14.4%) eople showing ≥50%	41/220 (18.6%) 18.6%	RR 0.77 (0.5 to 1.18)	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)  ry Asberg Depressi	⊕000 VERY LOW on Rating Scale
sponse	randomised trials  e (CBASP ve) randomised	serious <sup>1</sup>	no serious inconsistency talopram) (follow	no serious indirectness  v-up mean 8 we	serious <sup>9</sup>	reporting bias <sup>3</sup> with: Number of p	31/216 (14.4%) eople showing ≥50%	41/220 (18.6%) 18.6%	RR 0.77 (0.5 to 1.18) n Montgomen RR 0.26 (0.06 to	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)  ry Asberg Depression 197 fewer per 1000 (from 251	#000 VERY LOW  on Rating Scale
sponse	randomised trials  e (CBASP ve) randomised	serious <sup>1</sup>	no serious inconsistency talopram) (follow	no serious indirectness  v-up mean 8 we	serious <sup>9</sup>	reporting bias <sup>3</sup> with: Number of p	31/216 (14.4%) eople showing ≥50%	41/220 (18.6%) 18.6%	RR 0.77 (0.5 to 1.18) n Montgomen RR 0.26 (0.06 to	1000 (from 179 fewer to 111 more) ating Scale for Dep  43 fewer per 1000 (from 93 fewer to 34 more)  43 fewer per 1000 (from 93 fewer to 33 more)  ry Asberg Depression 197 fewer per 1000 (from 251 fewer to 32 more)	#000 VERY LOW  on Rating Scale

	randomised	serious1	very serious <sup>10</sup>	no serious	very serious <sup>11</sup>	reporting bias <sup>3</sup>	226	232	-	SMD 0.61 higher	⊕000
	trials			indirectness						(0.54 lower to 1.76	VERY
										higher)	LOW
	on symptom values)	atology (0	CBASP versus n	efazodone) (fol	low-up mean 12	weeks; measured	with: Hamilton Ra	ting Scale for Dep	pression (HA	M-D; change score	); Better in
	randomised	serious <sup>1</sup>	no serious	no serious	no serious	reporting bias <sup>3</sup>	216	220	_	SMD 0.11 higher	⊕⊕00
	trials	00000	inconsistency	indirectness	imprecision	roporting side				(0.08 lower to 0.3	
					in production					higher)	LOW
ressi er val		atology (	CBT versus fluo	ketine) (follow-	up mean 16 wee	ks; measured with	: Hamilton Rating S	Scale for Depress	ion (HAM-D;	change score); Be	tter indica
	randomised	serious <sup>12</sup>	no serious	no serious	serious <sup>13</sup>	none	10	12	_	SMD 1.3 higher	⊕⊕00
										Civib 1.0 mgmon	
		3011003								(0.36 to 2.24	10\\\
contin	trials	ny reason	inconsistency (any cognitive	indirectness		y versus any AD) (	follow-up 8-16 wee	eks; assessed wit	h: Number o	(0.36 to 2.24 higher)	LOW ontinuing f
contir	trials	ny reason	inconsistency (any cognitive	indirectness		y versus any AD) (	follow-up 8-16 wee 63/275 (22.9%)	67/270 (24.8%)	RR 0.92 (0.68 to	higher)  f participants disco	⊕000 VERY
scontir son in	trials  nuation for a cluding adversardomised	ny reason erse even	inconsistency  (any cognitive of ts)	indirectness or cognitive bel	navioural therap		63/275	67/270	RR 0.92	higher)  f participants disco	entinuing f
contir son in	trials  nuation for a cluding adversardomised	ny reason erse even	inconsistency  (any cognitive of ts)	indirectness or cognitive bel	navioural therap		63/275	67/270	RR 0.92 (0.68 to	higher)  f participants disco	⊕OOO VERY LOW
contir son in	trials  nuation for a cluding adversardomised	ny reason erse even	inconsistency  (any cognitive of ts)	indirectness or cognitive bel	navioural therap		63/275	67/270	RR 0.92 (0.68 to	higher)  f participants disconsisted from 79 fewer to 62 more)  18 fewer per 1000 (from 74 fewer to	⊕OOO VERY LOW
scontin	trials  nuation for a cluding adversed trials	ny reason erse even serious <sup>7</sup>	inconsistency  (any cognitive of ts)  no serious inconsistency	no serious indirectness	very serious <sup>14</sup>	reporting bias <sup>3</sup>	63/275 (22.9%)	67/270 (24.8%) 23.1%	RR 0.92 (0.68 to 1.25)	higher)  f participants disconnection  20 fewer per 1000 (from 79 fewer to 62 more)  18 fewer per 1000	⊕OOO VERY LOW
scontin	trials  nuation for a cluding adversardomised trials	ny reason erse even serious <sup>7</sup>	(any cognitive of ts)  no serious inconsistency  (CBASP versus	no serious indirectness	very serious <sup>14</sup>	reporting bias <sup>3</sup> 12 weeks; assesse	63/275 (22.9%) d with: Number of	67/270 (24.8%) 23.1% participants disc	RR 0.92 (0.68 to 1.25)	higher)  f participants disconding from 79 fewer to 62 more)  18 fewer per 1000 (from 74 fewer to 58 more)  r any reason include	⊕OOO VERY LOW
contir	trials  nuation for an cluding adversardomised trials	ny reason erse even serious <sup>7</sup>	inconsistency  (any cognitive of ts)  no serious inconsistency  (CBASP versus no serious	no serious indirectness  no serious indirectness  nefazodone) (f	very serious <sup>14</sup>	reporting bias <sup>3</sup>	63/275 (22.9%) d with: Number of	67/270 (24.8%) 23.1% participants disc	RR 0.92 (0.68 to 1.25) ontinuing for	higher)  f participants disconsisted from 79 fewer to 62 more)  18 fewer per 1000 (from 74 fewer to 58 more)  r any reason included fewer per 1000	⊕OOO VERY LOW
scontin	trials  nuation for a cluding adversardomised trials	ny reason erse even serious <sup>7</sup>	(any cognitive of ts)  no serious inconsistency  (CBASP versus	no serious indirectness	very serious <sup>14</sup>	reporting bias <sup>3</sup> 12 weeks; assesse	63/275 (22.9%) d with: Number of	67/270 (24.8%) 23.1% participants disc	RR 0.92 (0.68 to 1.25)	higher)  f participants discontinuous fewer per 1000 (from 79 fewer to 62 more)  18 fewer per 1000 (from 74 fewer to 58 more)  r any reason include	⊕OOO VERY LOW
scontin	trials  nuation for an cluding adversardomised trials	ny reason erse even serious <sup>7</sup>	inconsistency  (any cognitive of ts)  no serious inconsistency  (CBASP versus no serious	no serious indirectness  no serious indirectness  nefazodone) (f	very serious <sup>14</sup>	reporting bias <sup>3</sup> 12 weeks; assesse	63/275 (22.9%) d with: Number of	67/270 (24.8%) 23.1% participants disc	RR 0.92 (0.68 to 1.25) ontinuing for RR 0.92 (0.67 to	higher)  f participants disconsisted from 79 fewer to 62 more)  18 fewer per 1000 (from 74 fewer to 58 more)  r any reason included from 86 fewer to 1000 (from 86 fewer to 1000 (from 86 fewer to 1000 ferom 86 fewer to 1000 fewer t	⊕OOO VERY LOW
scontin	trials  nuation for an cluding adversardomised trials	ny reason erse even serious <sup>7</sup>	inconsistency  (any cognitive of ts)  no serious inconsistency  (CBASP versus no serious	no serious indirectness  no serious indirectness  nefazodone) (f	very serious <sup>14</sup>	reporting bias <sup>3</sup> 12 weeks; assesse	63/275 (22.9%) d with: Number of	67/270 (24.8%) 23.1% participants disc	RR 0.92 (0.68 to 1.25) ontinuing for RR 0.92 (0.67 to	higher)  f participants disconsisted from 79 fewer to 62 more)  18 fewer per 1000 (from 74 fewer to 58 more)  r any reason included from 86 fewer to 70 more)	⊕OOO VERY LOW

		serious4	no serious	no serious	very serious <sup>14</sup>	reporting bias <sup>6</sup>	2/29	5/31	RR 0.43	92 fewer per 1000		•
	trials		inconsistency	indirectness			(6.9%)	(16.1%)	(0.09 to	(from 147 fewer to		
									2.03)	166 more)	LOW	
										92 fewer per 1000		
								16.1%		(from 147 fewer to		
										166 more)		
Discontin	uation for ar	ny reason	(CBT versus fluc	exetine) (follow-	up mean 16 we	eks; assessed wi	th: Number of partic	ipants discontinu	ing for any	reason including a	dverse eve	ents)
		. 45	1 .		1					1		
			no serious	no serious	very serious <sup>14</sup>	none	6/18	3/13	RR 1.44	102 more per	⊕OOO	
	trials		inconsistency	indirectness			(33.3%)	(23.1%)	(0.44 to	1000 (from 129	VERY	
									4.74)	fewer to 863 more)	LOW	
										100		
								00.40/		102 more per		
								23.1%		1000 (from 129		
		_								fewer to 864 more)	lL_	
Discontin	uation due t	o adverse	events (CBASP	versus nefazod	one) (follow-up	mean 12 weeks;	assessed with: Num	ber of participant	s discontin	uing due to advers	e events)	
		. 7			. 16	3	0.1000	0.4.1000	DD 0.4	100 (		
			no serious		serious <sup>16</sup>	reporting bias <sup>3</sup>	3/228	31/226	RR 0.1	123 fewer per	⊕000	
	trials		inconsistency	indirectness			(1.3%)	(13.7%)	(0.03 to	1000 (from 95	VERY	
									0.31)	fewer to 133	LOW	
										fewer)		
										100 fower per		
										123 fewer per 1000 (from 95		
								13.7%		fewer to 133		
										fewer)		
										iewei)		

<sup>&</sup>lt;sup>1</sup> Non-blind intervention administrator(s) and participants, although the outcome assessor was blinded. Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

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<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Funding from pharmaceutical company

<sup>&</sup>lt;sup>4</sup> Unclear method of allocation concealment and non-blind intervention administrator(s) and participants, although the outcome assessor was blinded

<sup>&</sup>lt;sup>5</sup> 95% CI crosses line of no effect and both threshold for clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>6</sup> Data cannot be extracted or is not reported for all outcomes and funding from pharmaceutical company

<sup>&</sup>lt;sup>7</sup> Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>8</sup> I-squared=>50%

<sup>&</sup>lt;sup>9</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 0.75)

<sup>11 &</sup>lt;sup>10</sup> I-squared>80%

<sup>11 95%</sup> CI crosses line of no effect and threshold for both clinically important benefit (SMD -0.5) and clinically important harm (SMD 0.5)

<sup>&</sup>lt;sup>12</sup> Unclear randomisation method and method of allocation concealment, and non-blind intervention administrator(s) and participants (although outcome assessors are blinded). Unclear risk of attrition bias (drop-out>20% and completer analysis used but difference between groups<20%)

<sup>15 &</sup>lt;sup>13</sup> N<400

<sup>&</sup>lt;sup>14</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>15</sup> Unclear randomisation method and method of allocation concealment, and non-blind intervention administrator(s) and participants (although outcome assessors are blinded) <sup>16</sup> Events<300

# CBASP versus other psychological intervention for chronic depression

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			Quality ass	essment			No	of patients		Effect		
											Quality	Importa
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBASP	Other psych intervention	Relative (95% CI)	Absolute		
missio	n (CBASP vei	rsus other	psych interventio	n) (follow-up 16-2	20 weeks; ass	sessed with: Num	per of pe	ople scoring ≤8 o	on Hamilton Ra	ting Scale for Depression	n (HAM-E	D))
	randomised	very	no serious	no serious	serious <sup>2</sup>	none	35/138	17/126	RR 1.93 (1.14	125 more per 1000 (from	⊕OOO	
	trials	serious <sup>1</sup>	inconsistency	indirectness			(25.4%)	(13.5%)	to 3.26)	19 more to 305 more)	VERY	
			,				,	,	,	,	LOW	
								16.3%		152 more per 1000 (from		
								10.570		23 more to 368 more)		
missio	n (CBASP vei	rsus IPT) (1	follow-up mean 16	weeks; assesse	d with: Numb	er of people scor	ng ≤8 on	Hamilton Rating	Scale for Dep	ression (HAM-D))		
	·	1.	·	·						` '		
	randomised	serious <sup>3</sup>	no serious	no serious	serious4	none	8/14	3/15	RR 2.86 (0.94	372 more per 1000 (from	⊕⊕00	
	trials		inconsistency	indirectness			(57.1%)	(20%)	to 8.66)	12 fewer to 1000 more)	LOW	
								20%		372 more per 1000 (from		
								20%		12 fewer to 1000 more)		
missio	n (CBASP vei	rsus suppo	ortive psychothera	npv) (follow-up m	ean 20 weeks	s: assessed with:	Number	of people scoring	ı ≤8 on Hamilto	n Rating Scale for Depre	ssion (H	AM-D))
	(			, (Canada de 111		,			,	g	(	,,
	randomised	very	no serious	no serious	serious4	none	27/124	14/111	RR 1.73 (0.95	92 more per 1000 (from 6	⊕000	
	trials	serious1	inconsistency	indirectness			(21.8%)	(12.6%)	to 3.12)	fewer to 267 more)	VERY	
			,				,	,	,	,	LOW	
								10.00/		92 more per 1000 (from 6		
								12.6%		fewer to 267 more)		
enone	CRASP vor	sus other	neveh intervention	) (follow-up 16-2	U wooke: ace	assad with: Numb	or of noc	nle showing >50	% improvemen	nt on Hamilton Rating Sc	alo for De	onroccio
AM-D))		sus other	psych intervention	i) (10110W-up 10-2	o weeks, ass	essea with Halli	ei oi pec	pie snowing 250	76 IIIIpi Oveillei	it on Hamilton Rating 30	ale loi Di	chiessi
<i>D</i> ))												
	randomised	very	no serious	no serious	serious <sup>2</sup>	none	57/138	31/126	RR 1.7 (1.18	172 more per 1000 (from	⊕000	
	trials	serious <sup>1</sup>	inconsistency	indirectness	Scrious	none	(41.3%)	(24.6%)	to 2.44)	44 more to 354 more)	VERY	
	ululu	Jenous	inidentification	in directificas			(41.070)	(21.070)	10 2.44)	17 more to do minore)	LOW	
									1	179 more per 1000 (from	LOVV	
								25.5%		46 more to 367 more)		

	randomised	serious <sup>3</sup>	no serious	no serious	serious4	none	9/14	4/15	,	376 more per 1000 (from	
	trials		inconsistency	indirectness			(64.3%)	(26.7%)	to 6.08)	11 fewer to 1000 more)	LOW
							<del>                                     </del>		_	376 more per 1000 (from	
								26.7%		11 fewer to 1000 more)	
	(OD 4 OD						- '4l No l 6		> 500/ !	,	0 1 - 6
		sus suppo	ortive psychother	apy) (follow-up r	nean 20 wee	ks; assessed v	vith: Number of	people snowi	ng ≥50% improv	ement on Hamilton Ratin	g Scale for
ressic	n (HAM-D))										
	randomised	very	no serious	no serious	serious <sup>2</sup>	none	48/124	27/111	RR 1 59 (1 07	144 more per 1000 (from	⊕OOO
	trials	serious <sup>1</sup>	inconsistency	indirectness	CONCUC	110110	(38.7%)	(24.3%)	to 2.36)	17 more to 331 more)	VERY
		00000					(33.1.70)	(=, ,,)	10 2.00)	· · · · · · · · · · · · · · · · · · ·	LOW
								04.00/		143 more per 1000 (from	
								24.3%		17 more to 330 more)	
ressio	n symptoma	tology (CE	BASP versus other	r psych interver	ntion) (follow	-up 16-20 weel	ks: measured w	ith: Hamilton I	Rating Scale for	Depression (HAM-D; cha	nge score):
	by lower valu				, (		,				,,
	,										
	randomised	very	no serious	no serious	serious <sup>5</sup>	none	151	146	-	SMD 0.49 lower (0.98	<b>⊕</b> 000
	trials	serious1	inconsistency	indirectness						lower to 0 higher)	VERY
										<u> </u>	LOW
	n symptoma	tology (CE	BASP versus IPT)	(follow-up mear	n 16 weeks; r	neasured with	: Hamilton Ratir	ng Scale for De	epression (HAM	D; change score); Better	indicated by
	randomised	tology (CE	BASP versus IPT)	(follow-up mear	serious <sup>5</sup>	neasured with:	: Hamilton Ratin	ng Scale for De	epression (HAM		
			no serious						epression (HAM-	SMD 0.89 lower (1.66 to	⊕⊕ОО
	randomised			no serious					epression (HAM-		
lues)	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	14	15	-	SMD 0.89 lower (1.66 to	⊕⊕OO LOW
lues) pressio	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	14	15	-	SMD 0.89 lower (1.66 to 0.12 lower)	⊕⊕OO LOW
lues)	randomised trials on symptoma	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	14 weeks; measur	15 red with: Hami	-	SMD 0.89 lower (1.66 to 0.12 lower) e for Depression (HAM-D	⊕⊕OO LOW
lues)	randomised trials on symptomaticated by low randomised	serious <sup>3</sup> tology (CE er values	no serious inconsistency  BASP versus supplements of the serious	no serious indirectness portive psychoth	serious <sup>5</sup>	none	14	15	-	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D	⊕⊕OO LOW ; change sco
ues) pressic	randomised trials on symptomaticated by low	serious <sup>3</sup> tology (CE	no serious inconsistency BASP versus supp	no serious indirectness portive psychoth	serious <sup>5</sup>	none w-up mean 20	14 weeks; measur	15 red with: Hami	-	SMD 0.89 lower (1.66 to 0.12 lower) e for Depression (HAM-D	⊕⊕OO LOW ; change sco
lues) pressio	randomised trials on symptomaticated by low randomised	serious <sup>3</sup> tology (CE er values	no serious inconsistency  BASP versus supplements of the serious	no serious indirectness portive psychoth	serious <sup>5</sup>	none w-up mean 20	14 weeks; measur	15 red with: Hami	-	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D	⊕⊕OO LOW ; change sco
epressic	randomised trials on symptoma icated by low randomised trials	serious <sup>3</sup> tology (CE er values very serious <sup>1</sup>	no serious inconsistency  BASP versus suppose no serious inconsistency	no serious indirectness portive psychothem no serious indirectness	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none w-up mean 20 none	weeks; measur	15 red with: Hami 131	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)	⊕⊕OO LOW  ; change sco
pressic tter ind	randomised trials on symptoma icated by low randomised trials	serious <sup>3</sup> tology (CE er values very serious <sup>1</sup>	no serious inconsistency  BASP versus suppose no serious inconsistency	no serious indirectness portive psychothem no serious indirectness	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none w-up mean 20 none	weeks; measur	15 red with: Hami 131	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D	⊕⊕OO LOW  ; change sco
epressic	randomised trials on symptoma icated by low randomised trials	serious <sup>3</sup> tology (CE er values very serious <sup>1</sup>	no serious inconsistency  BASP versus suppose no serious inconsistency	no serious indirectness portive psychothem no serious indirectness	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none w-up mean 20 none	weeks; measur	15 red with: Hami 131	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)	⊕⊕OO LOW  ; change sco
epressic	randomised trials on symptoma icated by low randomised trials uation for any vents)	serious <sup>3</sup> tology (CE ver values) very serious <sup>1</sup> v reason (	no serious inconsistency  BASP versus supplements of the serious inconsistency  CBASP versus of	no serious indirectness portive psychothem no serious indirectness her psych interv	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none none none	14 weeks; measur	15 red with: Hami 131 with: Number	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)	⊕⊕OO LOW  ; change sco  ⊕OOO VERY LOW  son including
pressic tter ind	randomised trials on symptoma icated by low randomised trials uation for any vents)	serious³  tology (CE er values very serious¹  very y reason (	no serious inconsistency  BASP versus supplements of the serious inconsistency  CBASP versus of the serious of	no serious indirectness portive psychother no serious indirectness her psych intervals no serious	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none w-up mean 20 none	14 weeks; measur 137 eeks; assessed	15 red with: Hami 131 with: Number	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)  discontinuing for any reas	⊕⊕OO LOW  ; change sco  ⊕OOO VERY LOW  son including
epressic etter ind	randomised trials on symptoma icated by low randomised trials uation for any vents)	serious <sup>3</sup> tology (CE ver values) very serious <sup>1</sup> v reason (	no serious inconsistency  BASP versus supplements of the serious inconsistency  CBASP versus of	no serious indirectness portive psychothem no serious indirectness her psych interv	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none none none	14 weeks; measur	15 red with: Hami 131 with: Number	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)	⊕⊕OO LOW  ; change sco  ⊕OOO VERY LOW  son including
epressic etter ind	randomised trials on symptoma icated by low randomised trials uation for any vents)	serious³  tology (CE er values very serious¹  very y reason (	no serious inconsistency  BASP versus supplements of the serious inconsistency  CBASP versus of the serious of	no serious indirectness portive psychother no serious indirectness her psych intervals no serious	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none none none	14 weeks; measur 137 eeks; assessed	15 red with: Hami 131 with: Number	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)  discontinuing for any reas  59 fewer per 1000 (from 107 fewer to 26 more)	⊕⊕OO LOW  ; change sco  ⊕OOO VERY LOW  son including
epressic	randomised trials on symptoma icated by low randomised trials uation for any vents)	serious³  tology (CE er values very serious¹  very y reason (	no serious inconsistency  BASP versus supplements of the serious inconsistency  CBASP versus of the serious of	no serious indirectness portive psychother no serious indirectness her psych intervals no serious	serious <sup>5</sup> nerapy) (follo serious <sup>5</sup>	none none none	14 weeks; measur 137 eeks; assessed	15 red with: Hami 131 with: Number	- Iton Rating Scal	SMD 0.89 lower (1.66 to 0.12 lower)  e for Depression (HAM-D  SMD 0.33 lower (0.58 to 0.09 lower)  discontinuing for any reas	⊕⊕OO LOW  ; change sco  ⊕OOO VERY LOW  son including

2/15

2/15

RR 1 (0.16 to

0 fewer per 1000 (from

⊕000

none

very

randomised

serious<sup>3</sup>

no serious

1

2

3

4

6

7

8

9

no serious

## Cognitive and cognitive behavioural therapies + TAU/AD versus TAU/AD-only for chronic depression

			Quality ass	essment			No of patients			Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	()thor	Cognitive and cognitive behavioural therapies + TAU/AD	TAU/AD- only	Relative (95% CI)	Absolute	Quality	Importance
	•		TAU) (follow-up nor Depression (HA	· · · · · · · · · · · · · · · · · · ·	ssessed with:	Number of people	e scoring ≤13 on Beck De	pression li	nventory II (	BDI-II) AND ≥50% im	proveme	ent on BDI-
		- ,		no serious indirectness	serious <sup>2</sup>	none	12/52 (23.1%)	3/50 (6%)	RR 3.72 (1.1 to 12.54)	163 more per 1000 (from 6 more to 692 more)	⊕000 VERY LOW	
								6.2%		169 more per 1000 (from 6 more to 715 more)		

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>&</sup>lt;sup>4</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>5</sup> N<400

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)

<sup>&</sup>lt;sup>7</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias4	131/328	74/326	RR 1.71	161 more per 1000	⊕000
	trials	Conoac	inconsistency	indirectness	Jonous	roporting blue	(39.9%)	(22.7%)	(1.35 to	(from 79 more to	VERY
							(00.070)	(==:: /0)	2.15)	261 more)	LOW
									,	201111010)	LOW
										80 more per 1000	
								11.3%		(from 40 more to	
										` 130 more)	
spon	se (CBASP +	TAU/nefaz	odone versus T	AU/nefazodone	(follow-up 12-	52 weeks; assessed	vith: Number of peo	ple showing	≥50% improv	ement on Hamilton	Rating S
press	sion (HAM-D)/	Inventory	of Depressive S	ymptoms (IDS))							
	_			_	_						
	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias4	77/293	57/292	RR 1.35 (1	68 more per 1000	$\oplus$ OOO
	trials		inconsistency	indirectness			(26.3%)	(19.5%)	to 1.83)	(from 0 more to 162	
										more)	LOW
						<u> </u>				71 more per 1000	
								20.40/			
								20.4%		(from 0 more to 169	
			IBCT+TAU versi); Better indicate			; measured with: Han	nilton Rating Scale		n (HAM-D; cl	(from 0 more to 169 more)	Depressio
						; measured with: Han	nilton Rating Scale		n (HAM-D; cl	(from 0 more to 169 more)	Depression ⊕000
	ry (BDI-II; cha	nge score	); Better indicate	ed by lower valu	ies)			for Depressio	n (HAM-D; cl	(from 0 more to 169 more) nange score)/Beck D	
	ry (BDI-II; cha	nge score	); Better indicate	no serious	ies)			for Depressio	n (HAM-D; cl	(from 0 more to 169 more) nange score)/Beck D	⊕000
vento	randomised trials	very serious <sup>5</sup>	very serious <sup>6</sup>	no serious indirectness	serious <sup>7</sup>	none	56	for Depressio	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)	⊕000 VERY LOW
epress	ry (BDI-II; cha randomised trials sion symptom	very serious <sup>5</sup>	very serious <sup>6</sup> BASP + TAU/ne	no serious indirectness	serious <sup>7</sup>	none lone) (follow-up 8-52	56	for Depressio	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)	⊕000 VERY LOW
vento	ry (BDI-II; cha randomised trials sion symptom	very serious <sup>5</sup>	very serious <sup>6</sup> BASP + TAU/ne	no serious indirectness	serious <sup>7</sup>	none	56	for Depressio	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)	⊕000 VERY LOW
epress	ry (BDI-II; cha randomised trials sion symptom nventory of D	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> BASP + TAU/ne Symptoms (IDS	no serious indirectness fazodone versu ; change score)	serious <sup>7</sup> s TAU/nefazod; Better indicat	none lone) (follow-up 8-52 ed by lower values)	56 weeks; measured w	61 ith: Hamilton	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  of for Depression (HA	⊕OOO VERY LOW
vento	ry (BDI-II; cha randomised trials sion symptom nventory of D	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> BASP + TAU/ne	no serious indirectness  fazodone versu; change score)	serious <sup>7</sup> s TAU/nefazod; Better indicat	none lone) (follow-up 8-52	56	for Depressio	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  e for Depression (HA	⊕OOO VERY LOW M-D; cha
epress	ry (BDI-II; cha randomised trials sion symptom nventory of D	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> BASP + TAU/ne Symptoms (IDS	no serious indirectness fazodone versu ; change score)	serious <sup>7</sup> s TAU/nefazod; Better indicat	none lone) (follow-up 8-52 ed by lower values)	56 weeks; measured w	61 ith: Hamilton	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  of for Depression (HA	⊕OOO VERY LOW M-D; cha
epress	ry (BDI-II; cha randomised trials sion symptom nventory of D	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> BASP + TAU/ne Symptoms (IDS	no serious indirectness  fazodone versu; change score)	serious <sup>7</sup> s TAU/nefazod; Better indicat	none lone) (follow-up 8-52 ed by lower values)	56 weeks; measured w	61 ith: Hamilton	-	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  e for Depression (HA	⊕OOO VERY LOW M-D; cha
epress	ry (BDI-II; cha randomised trials sion symptom nventory of D randomised trials	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> Very serious <sup>6</sup> EBASP + TAU/ne Symptoms (IDS	no serious indirectness  fazodone versus change score)  no serious indirectness	serious <sup>7</sup> s TAU/nefazod; Better indicat  no serious imprecision	none lone) (follow-up 8-52 yed by lower values)	56 weeks; measured w	61 ith: Hamilton	- Rating Scale	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  for Depression (HA  SMD 0.8 lower (1.13 to 0.47 lower)	⊕OOO VERY LOW M-D; cha
epress core)/I	ry (BDI-II; cha randomised trials sion symptom nventory of D randomised trials sion symptom	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> Very serious <sup>6</sup> EBASP + TAU/ne Symptoms (IDS	no serious indirectness  fazodone versus change score)  no serious indirectness	serious <sup>7</sup> s TAU/nefazod; Better indicat  no serious imprecision	none lone) (follow-up 8-52 ed by lower values)	56 weeks; measured w	61 ith: Hamilton	- Rating Scale	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  for Depression (HA  SMD 0.8 lower (1.13 to 0.47 lower)	⊕OOO VERY LOW M-D; cha
epress	ry (BDI-II; cha randomised trials sion symptom nventory of D randomised trials	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> Very serious <sup>6</sup> EBASP + TAU/ne Symptoms (IDS	no serious indirectness  fazodone versus change score)  no serious indirectness	serious <sup>7</sup> s TAU/nefazod; Better indicat  no serious imprecision	none lone) (follow-up 8-52 yed by lower values)	56 weeks; measured w	61 ith: Hamilton	- Rating Scale	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  for Depression (HA  SMD 0.8 lower (1.13 to 0.47 lower)	⊕OOO VERY LOW M-D; cha
epress core)/I	ry (BDI-II; cha randomised trials  sion symptom nventory of Di randomised trials  sion symptom er values)	very serious <sup>5</sup> atology (Cepressive very serious <sup>8</sup>	very serious <sup>6</sup> BASP + TAU/ne Symptoms (IDS  serious <sup>9</sup> BT [group] + TA	no serious indirectness (change score) no serious indirectness (schange score)	serious <sup>7</sup> s TAU/nefazod; Better indicat no serious imprecision st + TAU) (follo	none lone) (follow-up 8-52 yed by lower values) none none	56 weeks; measured w 305 ; measured with: Bo	61 ith: Hamilton	- Rating Scale	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  for Depression (HA  SMD 0.8 lower (1.13 to 0.47 lower)  (BDI; change score)	⊕OOO VERY LOW M-D; cha ⊕OOO VERY LOW ; Better in
epress	ry (BDI-II; cha randomised trials sion symptom nventory of D randomised trials sion symptom	very serious <sup>5</sup> atology (Cepressive	very serious <sup>6</sup> Very serious <sup>6</sup> EBASP + TAU/ne Symptoms (IDS	no serious indirectness  fazodone versus change score)  no serious indirectness	serious <sup>7</sup> s TAU/nefazod; Better indicat  no serious imprecision	none lone) (follow-up 8-52 yed by lower values)	56 weeks; measured w	61 ith: Hamilton 305 eck Depression	- Rating Scale	(from 0 more to 169 more)  nange score)/Beck E  SMD 1.14 lower (2.1 to 0.19 lower)  for Depression (HA  SMD 0.8 lower (1.13 to 0.47 lower)	⊕OOO VERY LOW M-D; cha

serious<sup>12</sup>

none

15/66

4/64

RR 2.85

116 more per 1000

 $\oplus \oplus OO$ 

no serious

1

3 4

5

6

randomised

serious<sup>11</sup>

no serious

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline. Non-blind intervention administrator(s) and participants, although outcome assessors are blind. Unclear risk of attrition bias (>20% difference in drop-out between groups but ITT analysis used)

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Non-blind intervention administrator(s) or participants, although outcome assessors are blinded. Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>&</sup>lt;sup>4</sup> Funding from pharmaceutical company

<sup>&</sup>lt;sup>5</sup> Non-blind intervention administrator(s) and participants and outcome assessment either non-blind or blinding unclear

<sup>6</sup> I-squared=>80%

<sup>7</sup> N<400

1

2

3

5

9

10

12

14

<sup>8</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline in studies contributing >50% to analysis. Non-blind intervention administrator(s) and participants, although outcome assessors are blind. Unclear risk of attrition bias (drop-out>20% or difference between groups>20%)

9 I-squared>50%

<sup>10</sup> Unclear randomisation method and method of allocation concealment. Non-blind intervention administration and outcome assessment

11 Unclear (or high risk associated with) randomisation method, and non-blind intervention administrator(s) and participants

12 95% CI crosses both the line of no effect and the threshold for clinically important harm (RR 1.25)

<sup>13</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline in studies contributing >50% to analysis. Non-blind intervention administrator(s) and participants

11 <sup>14</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

<sup>15</sup> Unclear randomisation method and method of allocation concealment and non-blind intervention administrator(s) and participants

13 Non-blind intervention administrator(s) and participants

CBASP (maintenance treatment) versus assessment-only for relapse prevention in chronic depression

			Quality ass	essment			No of pat	ients		Effect		
											Quality	Importar
No of tudies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBASP (maintenance treatment)	Assessment- only	Relative (95% CI)	Absolute		
	follow-up me r a diagnosis			th: Number of po	eople scoring	g ≥16 on Hamilton	Rating Scale for De	pression (HAM	-D) on 2 con	secutive visits AND n	neeting D	SM-IV
		very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	1/42 (2.4%)	8/40 (20%)	RR 0.12 (0.02 to 0.91)	176 fewer per 1000 (from 18 fewer to 196 fewer)		
								20%		176 fewer per 1000 (from 18 fewer to 196 fewer)		
								, ,	core); Better	indicated by lower v	,	
		- ,	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	42	40	-	SMD 0.91 lower (1.37 to 0.45 lower)	⊕000 VERY LOW	

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#### IPT versus sertraline for chronic depression

			·									
			Quality as	sessment			No of	patients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IPT	Sertraline	Relative (95% CI)	Absolute		
Remission score>70)	•	ean 16 we	eks; assessed witl	n: Number of peo	ple scoring <7 or	n Hamilton Rating	Scale fo	r Depressi	on (HAM-D) Al	ND >50% improvement on	HAMD AN	ND GAF
1	randomised	serious <sup>1</sup>	no serious	no serious	very serious <sup>2</sup>	reporting bias <sup>3</sup>	5/23	10/24	RR 0.52 (0.21	200 fewer per 1000 (from	⊕000	
	trials		inconsistency	indirectness			(21.7%)	(41.7%)	to 1.29)	329 fewer to 121 more)	VERY	
											LOW	
								41.7%		200 fewer per 1000 (from		
								71.770		329 fewer to 121 more)		
	•		; assessed with: N sion (HAM-D))	umber of people	showing ≥40% in	nprovement on Mo	ontgome	ry Asberg	Depression Ra	ating Scale (MADRS)/≥50%	improve	ment on
2	randomised	very	no serious	no serious	serious <sup>5</sup>	reporting bias3	91/201	131/220	RR 0.76 (0.63	143 fewer per 1000 (from	⊕000	
	trials	serious4	inconsistency	indirectness			(45.3%)	(59.5%)	to 0.92)	48 fewer to 220 fewer)	VERY	
							,		,	•	LOW	
								59%		142 fewer per 1000 (from		
								J3 /0		47 fewer to 218 fewer)		<u> </u>

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and method of allocation concealment is unclear. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded. Unclear risk of attrition bias (drop-put>20% but difference between groups <20% and ITT analysis used)

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Funding from pharmaceutical company

<sup>4</sup> N<400

<sup>&</sup>lt;sup>5</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and method of allocation concealment is unclear. Non-blind intervention administrator(s) and participants

<sup>&</sup>lt;sup>6</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

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## IPT versus brief supportive psychotherapy (BSP) for chronic depression

			Quality asse	essment			No of patients			Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IPT versus brief supportive psychotherapy (BSP) for dysthymia	Control	Relative (95% CI)	Absolute	Quality	Importance
Remissio score>70	•	mean 16 v	weeks; assessed	with: Number o	f people sco	ring <7 on Hamilt	on Rating Scale for Depression	on (HAM	-D) AND >50	% improvement on I	HAMD AN	ID GAF
	randomised trials	serious <sup>1</sup>		no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	5/23 (21.7%)	3/26 (11.5%)	RR 1.88 (0.5 to 7.03)	102 more per 1000 (from 58 fewer to 696 more)	⊕000 VERY LOW	
								11.5%		101 more per 1000 (from 58 fewer to 693 more)		

<sup>&</sup>lt;sup>1</sup> Unclear randomisation and method of allocation concealment. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (Rr 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Study partially funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> High risk of bias associated with randomisation bias due to significant difference between groups at baseline. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>&</sup>lt;sup>5</sup> Events<300

<sup>&</sup>lt;sup>6</sup> N<400

<sup>&</sup>lt;sup>7</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

randomised	serious <sup>1</sup>	no serious	no serious	very	reporting bias3	8/23	8/26	RR 1.13	40 more per 1000	⊕000
trials		inconsistency	indirectness	serious <sup>2</sup>		(34.8%)	(30.8%)	(0.51 to	(from 151 fewer to	VERY
		j				,	, ,	2.52)	468 more)	LOW
									40 more per 1000	
							30.8%		(from 151 fewer to	
									` 468 more)	
	1			l	annouting thing3	22	00		CMD 0 00 laws	0000
randomised	serious <sup>1</sup>	no serious	no serious	very	reporting bias <sup>3</sup>	23	26	-	SMD 0.06 lower	⊕000
trials		inconsistency	indirectness	serious <sup>4</sup>					(0.63 lower to 0.5	VERY
									higher)	LOW
		/f - 11	40		Name la sur est un authorise					
ontinuation for	any reason	(tollow-up mea	n 16 weeks; ass	essea witn:	Number of particip	ants discontinuing for any	reason inci	uding adve	rse events)	
	serious <sup>5</sup>	no serious	no serious	serious <sup>6</sup>	reporting bias <sup>3</sup>	4/23	11/26	RR 0.41	250 fewer per 1000	⊕000
randomised	SCHOUS		indirectness			(17.4%)	(42.3%)	(0.15 to	(from 360 fewer to	VERY
randomiseo trials	Serious	inconsistency	ii iuli coli icoo			, ,	, ,	1.11)	47 more)	LOW
	Serious	inconsistency	indirectiness					1.11		
	Serious	inconsistency	indirectiness					1.11/	,	
	serious	inconsistency	illuli cetiess					1.11)	250 fewer per 1000	2011
	serious	inconsistency	indirectioss				42.3%	1.11)	,	2011

<sup>&</sup>lt;sup>1</sup> Randomisation method and method of allocation concealment unclear. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded. Unclear risk of attrition bias (drop-out>20% and difference between groups>20% but ITT analysis used)

#### IPT + TAU/AD versus TAU/AD-only for chronic depression

			Quality ass	sessment			No of p	patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IPT + TAU/AD	TAU/AD- only	Relative (95% CI)	Absolute		

Remission (IPT + TAU/AD versus TAU/AD-only) (follow-up 5-16 weeks; assessed with: Number of people scoring ≤7 on Hamilton Rating Scale for Depression (HAM-D)/<7 on HAMD-D >50% improvement on HAMD AND GAF score>70)

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Study partially funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (SMD -0.5) and clinically important harm (SMD 0.5)

<sup>&</sup>lt;sup>5</sup> Randomisation method and method of allocation concealment unclear. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded.

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)

	randomised	serious1	no serious	no serious	serious <sup>2</sup>	reporting bias3	23/45	16/45	RR 1.43 (0.88	153 more per 1000	$\oplus$ OOO	
	trials		inconsistency	indirectness		, ,	(51.1%)	(35.6%)	to 2.33)	(from 43 fewer to 473	VERY	
			-							more)	LOW	
										151 more per 1000		
								35.1%		(from 42 fewer to 467		
										more)		
missio	n (IPT + stanc	lard pharm	acotherapy vers	us standard phar	macotherapy + c	linical managemen	t) (follow-u	p mean 5 w	eeks; assesse	d with: Number of peop	le scoring:	≤7 on
			sion (HAM-D))	•		· ·	, ·		·	• •		
	_	_										
	randomised	serious4	no serious	no serious	serious <sup>2</sup>	none	12/24	6/21	RR 1.75 (0.8	214 more per 1000	⊕⊕00	
	trials		inconsistency	indirectness			(50%)	(28.6%)	to 3.84)	(from 57 fewer to 811	LOW	
							, ,	, ,	,	more)		
										,		
										215 more per 1000		
								28.6%		(from 57 fewer to 812		
										more)		
missi	n (IPT + sorte	aline vereu	s sertraline) (follo	ow-up mean 16 w	peks. assessed	with: Number of no	onle scorin	a <7 on Ha	milton Rating	Scale for Depression (H	AM-D) AND	>50%
JI O V C I	nent on HAME	AND CAI	30010-101									
	randomicad	aariaua1	no corious	no corious	von corious5	reporting bigs3	11/01	10/24	DD 4 36 (0.67	100 mars per 1000	2000	
	randomised	serious <sup>1</sup>	no serious	no serious	very serious <sup>5</sup>	reporting bias <sup>3</sup>	11/21	10/24	RR 1.26 (0.67	108 more per 1000 (from 138 fouver to 563)	⊕000 \/FD\/	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	reporting bias <sup>3</sup>	11/21 (52.4%)	10/24 (41.7%)	RR 1.26 (0.67 to 2.35)	(from 138 fewer to 562	VERY	
		serious <sup>1</sup>			very serious <sup>5</sup>	reporting bias <sup>3</sup>						
		serious <sup>1</sup>			very serious <sup>5</sup>	reporting bias <sup>3</sup>				(from 138 fewer to 562 more)	VERY	
		serious <sup>1</sup>			very serious <sup>5</sup>	reporting bias <sup>3</sup>		(41.7%)		(from 138 fewer to 562 more)  108 more per 1000	VERY	
		serious <sup>1</sup>			very serious <sup>5</sup>	reporting bias <sup>3</sup>				(from 138 fewer to 562 more) 108 more per 1000 (from 138 fewer to 563	VERY	
	<mark>trials</mark>		inconsistency	indirectness			(52.4%)	41.7%	to 2.35)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)	VERY LOW	
	trials e (IPT + TAU/ <i>I</i>	AD versus	inconsistency  TAU/AD-only) (fo	indirectness	ks; assessed wit		(52.4%)	41.7%	to 2.35)	(from 138 fewer to 562 more) 108 more per 1000 (from 138 fewer to 563	VERY LOW	ting Sc
	trials e (IPT + TAU/ <i>I</i>	AD versus	inconsistency  TAU/AD-only) (fo	indirectness	ks; assessed wit		(52.4%)	41.7%	to 2.35)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)	VERY LOW	ting Sc
	trials e (IPT + TAU// /250% improv	AD versus cement on h	inconsistency  TAU/AD-only) (foliamilton Rating S	indirectness  Illow-up 5-26 weel	ks; assessed wit	h: Number of peop	(52.4%)	(41.7%) 41.7% ≥40% impre	to 2.35)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depr	VERY LOW	ting So
	trials e (IPT + TAU/A /≥50% improv randomised	AD versus ement on h	inconsistency  TAU/AD-only) (fo	indirectness  Illow-up 5-26 weel Scale for Depress  no serious	ks; assessed wit		(52.4%) le showing	(41.7%) 41.7% ≥40% impro	to 2.35)  ovement on Mo	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the second s	VERY LOW	ting Sc
	trials e (IPT + TAU// /250% improv	AD versus cement on h	inconsistency  TAU/AD-only) (foliamilton Rating S	indirectness  Illow-up 5-26 weel	ks; assessed wit	h: Number of peop	(52.4%)	(41.7%) 41.7% ≥40% impre	to 2.35)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depr	very Low ression Rate	ting So
	trials e (IPT + TAU/A /≥50% improv randomised	AD versus ement on h	inconsistency  TAU/AD-only) (foliamilton Rating S	indirectness  Illow-up 5-26 weel Scale for Depress  no serious	ks; assessed wit	h: Number of peop	(52.4%) le showing	(41.7%) 41.7% ≥40% impro	to 2.35)  ovement on Mo	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the second fewer to 323 more)  63 more per 1000 (from 121 fewer to 323 more)	VERY LOW	ting So
	trials e (IPT + TAU/A /≥50% improv randomised	AD versus ement on h	inconsistency  TAU/AD-only) (foliamilton Rating S	indirectness  Illow-up 5-26 weel Scale for Depress  no serious	ks; assessed wit	h: Number of peop	(52.4%) le showing	(41.7%)  41.7%  ≥40% impression	to 2.35)  ovement on Mo	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depi	very Low ression Rate	ting So
	trials e (IPT + TAU/A /≥50% improv randomised	AD versus ement on h	inconsistency  TAU/AD-only) (foliamilton Rating S	indirectness  Illow-up 5-26 weel Scale for Depress  no serious	ks; assessed wit	h: Number of peop	(52.4%) le showing	(41.7%) 41.7% ≥40% impro	to 2.35)  ovement on Mo	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the second series of the s	very Low ression Rate	ting So
ADRS	e (IPT + TAU/A /≥50% improv randomised trials	AD versus cement on head very serious <sup>6</sup>	TAU/AD-only) (fo Hamilton Rating S	indirectness  Illow-up 5-26 week Scale for Depress  no serious indirectness	ks; assessed wition (HAM-D)) serious <sup>2</sup>	reporting bias <sup>3</sup>	(52.4%) le showing 151/257 (58.8%)	(41.7%)  41.7%  ≥40% impro  139/241 (57.7%)  58.3%	to 2.35)  Exercise to 1.11 (0.79 to 1.56)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depi	very Low	
ADRS	e (IPT + TAU/A/≥50% improv randomised trials e (IPT + stand	AD versus cement on he very serious cerious ard pharma	TAU/AD-only) (fo Hamilton Rating S	indirectness  Illow-up 5-26 week Scale for Depress  no serious indirectness  is standard pharr	ks; assessed wition (HAM-D)) serious <sup>2</sup>	reporting bias <sup>3</sup>	(52.4%) le showing 151/257 (58.8%)	(41.7%)  41.7%  ≥40% impro  139/241 (57.7%)  58.3%	to 2.35)  Exercise to 1.11 (0.79 to 1.56)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the fewer to 323 more)  63 more per 1000 (from 121 fewer to 323 more)  64 more per 1000 (from 122 fewer to 326 more)	very Low	
ADRS	e (IPT + TAU/A/≥50% improv randomised trials  e (IPT + standment on Hamil	very serious <sup>6</sup>	TAU/AD-only) (for lamilton Rating serious acotherapy versus Scale for Deprese	indirectness  Illow-up 5-26 week Scale for Depress  no serious indirectness  ins standard pharms sion (HAM-D))	ks; assessed wition (HAM-D)) serious <sup>2</sup> nacotherapy + cl	reporting bias <sup>3</sup>	(52.4%) le showing 151/257 (58.8%)	(41.7%)  41.7%  ≥40% impro  139/241 (57.7%)  58.3%  mean 5 wo	RR 1.11 (0.79 to 1.56)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the second of the s	Pession Rate  OOO VERY LOW  e showing	
ADRS	e (IPT + TAU/A/≥50% improv randomised trials  e (IPT + standment on Hamil	AD versus cement on he very serious cerious ard pharma	inconsistency  TAU/AD-only) (for lamilton Rating serious serious Scale for Depresence in o serious	indirectness  Illow-up 5-26 week Scale for Depress  no serious indirectness  is standard pharm ssion (HAM-D))  no serious	ks; assessed wition (HAM-D)) serious <sup>2</sup>	reporting bias <sup>3</sup>	(52.4%)  le showing  151/257 (58.8%)	(41.7%)  41.7%  ≥40% impro  139/241 (57.7%)  58.3%  mean 5 wo	RR 1.11 (0.79 to 1.56)  eeks; assessed	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the second of the s	Pession Rate  POOO VERY LOW  e showing	
ADRS	e (IPT + TAU/A/≥50% improv randomised trials  e (IPT + standment on Hamil	very serious <sup>6</sup>	TAU/AD-only) (for lamilton Rating serious acotherapy versus Scale for Deprese	indirectness  Illow-up 5-26 week Scale for Depress  no serious indirectness  ins standard pharms sion (HAM-D))	ks; assessed wition (HAM-D)) serious <sup>2</sup> nacotherapy + cl	reporting bias <sup>3</sup>	(52.4%) le showing 151/257 (58.8%)	(41.7%)  41.7%  ≥40% impro  139/241 (57.7%)  58.3%  mean 5 wo	RR 1.11 (0.79 to 1.56)	(from 138 fewer to 562 more)  108 more per 1000 (from 138 fewer to 563 more)  ontgomery Asberg Depression of the second of the s	Pession Rate  OOO VERY LOW  e showing	

										328 more per 1000	
								38.1%		(from 8 more to 914	
										more)	
			s sertraline) (follo Hamilton Rating S			: Number of peop	le showing ≥	:40% impro	vement on Mo	ntgomery Asberg Depre	ession Rating
	randomised	verv	no serious	no serious	serious <sup>8</sup>	reporting bias9	134/233	131/220	RR 0.97 (0.83	18 fewer per 1000 (from	⊕000
	trials	serious <sup>6</sup>	inconsistency	indirectness		. 0	(57.5%)	(59.5%)	to 1.13)	101 fewer to 77 more)	VERY
			,				,	,	,	,	LOW
								59%		18 fewer per 1000 (from	
								59%		100 fewer to 77 more)	
	Depression Ra	ting Scale	(MADRS; change	score); Better in	dicated by lower	values)			Table 101 Bopies	sion (HAM-D; change s	
	randomised	very	no serious	no serious	no serious	reporting bias9	268	254	-	SMD 0.16 lower (0.43	⊕OOO
	trials	serious <sup>6</sup>	inconsistency	indirectness	imprecision					lower to 0.11 higher)	VERY
											LOW
	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>10</sup>	none	24	21		SMD 0.71 lower (1.32 to	⊕⊕ОО
			moonsisterity	indirectriess						0.1 lower)	LOW
			,	versus moclober	mide + clinical ma	anagement) (follow	v-up mean 1	2 weeks; m	neasured with:	0.1 lower) Montgomery Asberg De	
	IADRS; change	e score); B	+ moclobemide etter indicated by	versus moclober lower values)					neasured with:	Montgomery Asberg De	epression Rat
	randomised	very	+ moclobemide etter indicated by	versus moclober lower values)	mide + clinical ma	anagement) (follow	v-up mean 1	2 weeks; m	neasured with:	Montgomery Asberg De SMD 0.03 lower (0.83	epression Rat
	IADRS; change	e score); B	+ moclobemide etter indicated by	versus moclober lower values)					neasured with:	Montgomery Asberg De	epression Rate
	randomised	very	+ moclobemide etter indicated by	versus moclober lower values)					neasured with:	Montgomery Asberg De SMD 0.03 lower (0.83	epression Rat
cale (M	randomised trials	very serious <sup>11</sup>	+ moclobemide etter indicated by no serious inconsistency	versus moclober lower values) no serious indirectness	very serious <sup>12</sup>	none eeks; measured w	11	13	-	Montgomery Asberg De SMD 0.03 lower (0.83	⊕OOO VERY LOW
cale (M	randomised trials	very serious <sup>11</sup>	r + moclobemide etter indicated by no serious inconsistency	versus moclober lower values) no serious indirectness	very serious <sup>12</sup>	none eeks; measured w	11	13	-	Montgomery Asberg Do SMD 0.03 lower (0.83 lower to 0.77 higher)	⊕OOO VERY LOW
epress	randomised trials sion symptoma Depression Ra	very serious <sup>11</sup> tology ( IP ting Scale	* + moclobemide etter indicated by no serious inconsistency  T + sertraline vers (MADRS; change	no serious indirectness sus sertraline) (for score); Better in	very serious <sup>12</sup> pollow-up 16-26 we dicated by lower	none eeks; measured w	11	13 Rating Sc	- ale for Depres	Montgomery Asberg Do SMD 0.03 lower (0.83 lower to 0.77 higher) sion (HAM-D; change so	⊕OOO VERY LOW
cale (M	randomised trials sion symptoma Depression Ra	very serious <sup>11</sup> tology ( IP' ting Scale	no serious inconsistency  T + sertraline vers (MADRS; change	no serious indirectness sus sertraline) (for score); Better in no serious	very serious <sup>12</sup> pollow-up 16-26 we dicated by lower no serious	none eeks; measured w	11	13 Rating Sc	- ale for Depres	SMD 0.03 lower (0.83 lower to 0.77 higher)  sion (HAM-D; change see SMD 0.06 lower (0.24	⊕OOO VERY LOW Core)/Montgoi
epress sberg l	randomised trials sion symptoma Depression Ra randomised trials	very serious <sup>11</sup> tology ( IP' ting Scale very serious <sup>6</sup>	no serious inconsistency  T + sertraline vers (MADRS; change inconsistency	no serious indirectness sus sertraline) (for score); Better in no serious indirectness	very serious <sup>12</sup> collow-up 16-26 wordicated by lower  no serious imprecision	none eeks; measured w values) reporting bias <sup>9</sup>	11 ith: Hamiltor	Rating Sc	ale for Depres	SMD 0.03 lower (0.83 lower to 0.77 higher)  sion (HAM-D; change see SMD 0.06 lower (0.24	#OOO VERY LOW
epress sberg l	randomised trials sion symptoma Depression Ra randomised trials	very serious <sup>11</sup> tology ( IP ting Scale very serious <sup>6</sup>	no serious inconsistency  T + sertraline vers (MADRS; change inconsistency	no serious indirectness sus sertraline) (for score); Better in no serious indirectness	very serious <sup>12</sup> collow-up 16-26 wordicated by lower  no serious imprecision  of (follow-up 5-16)	none eeks; measured w values) reporting bias <sup>9</sup>	11 ith: Hamiltor	Rating Sc 220	ale for Depres - pants disconti	SMD 0.03 lower (0.83 lower to 0.77 higher)  sion (HAM-D; change so SMD 0.06 lower (0.24 lower to 0.12 higher)  nuing for any reason in	#OOO VERY LOW
Depress	randomised trials sion symptoma Depression Ra randomised trials	very serious <sup>11</sup> tology ( IP' ting Scale very serious <sup>6</sup>	r + moclobemide etter indicated by no serious inconsistency  T + sertraline vers (MADRS; change no serious inconsistency  PT + TAU/AD vers	no serious indirectness sus sertraline) (for score); Better in no serious indirectness sus sertraline) (score); Better in serious indirectness sus TAU/AD-only	very serious <sup>12</sup> collow-up 16-26 wordicated by lower  no serious imprecision	none eeks; measured w values) reporting bias <sup>9</sup> weeks; assessed	11 233 with: Number	Rating Sc 220	ale for Depres - pants disconti	SMD 0.03 lower (0.83 lower to 0.77 higher)  sion (HAM-D; change so  SMD 0.06 lower (0.24 lower to 0.12 higher)	#OOO VERY LOW

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<sup>95%</sup> CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

Study partially funded by pharmaceutical company

Baseline group comparability is unclear and unclear method of allocation concealment. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>&</sup>lt;sup>5</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

High risk associated with randomisation method due to significant difference between groups at baseline. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded

<sup>&</sup>lt;sup>7</sup> I-squared>50%

<sup>&</sup>lt;sup>8</sup> Events<300

<sup>10</sup> <sup>9</sup> Data cannot be extracted or is not reported for all outcomes and study partially funded by pharmaceutical company

<sup>11</sup> 

<sup>11</sup> Unclear randomisation method and method of allocation concealment. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded. High risk of attrition bias

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<sup>14</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

## Brief supportive psychotherapy (BSP) versus sertraline for chronic depression

			Quality asse	essment			No of patients	s		Effect		
											Quality	Importan
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Brief supportive psychotherapy (BSP)	Sertraline	Relative (95% CI)	Absolute		
emissio core>70)	•	nean 16 w	veeks; assessed v	vith: Number of	people scori	ng <7 on Hamilton	n Rating Scale for Depr	ession (HA	.M-D) AND >	50% improvement on	HAMD A	ND GAF
		- ,		no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	3/26 (11.5%)	10/24 (41.7%)	RR 0.28 (0.09 to 0.89)	300 fewer per 1000 (from 46 fewer to 379 fewer)	⊕000 VERY LOW	
								41.7%		300 fewer per 1000 (from 46 fewer to 379 fewer)		
esponse	(follow-up n	nean 16 w	eeks; assessed w	rith: Number of p	people show	ing ≥50% improve	ment on Hamilton Ratio	ng Scale fo	r Depression	n (HAM-D))		
		very serious <sup>1</sup>		no serious indirectness	serious <sup>4</sup>	reporting bias <sup>3</sup>	8/26 (30.8%)	14/24 (58.3%)	RR 0.53 (0.27 to 1.03)	274 fewer per 1000 (from 426 fewer to 17 more)	⊕OOO VERY LOW	
	_			_			_	58.3%		274 fewer per 1000 (from 426 fewer to 17 more)		
pressio	on symptoma	tology (fo	llow-up mean 16	weeks; measure	ed with: Ham	ilton Rating Scale	for Depression (HAM-I	D; change s	score); Bette	r indicated by lower v	alues)	
		very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	reporting bias <sup>3</sup>	26	24	-	SMD 0.77 higher (0.19 to 1.34 higher)	⊕000 VERY LOW	
iscontin	uation for an	v reason (	follow-up mean 1	6 weeks: assess	sed with: Nu	mber of participar	nts discontinuing for an	v reason i	ncluding adv	erse events)	LOVV	

randomised	very	no serious	no serious	serious <sup>7</sup>	reporting bias3	11/26	5/24	RR 2.03	215 more per 1000	⊕OOO
trials	serious <sup>6</sup>	inconsistency	indirectness			(42.3%)	(20.8%)	(0.83 to	(from 35 fewer to 831	VERY
								4.99)	more)	LOW
									214 more per 1000	
							20.8%		(from 35 fewer to 830	
									more)	

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and method of allocation concealment is unclear. Non-blind intervention administrator(s) and participants, although outcome assessors are blinded. High risk of attrition bias (>20% drop-out and difference between groups >20%), although ITT analysis used

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#### SSRIs versus placebo for chronic depression

			Quality as	sessment			No of p	atients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SSRIs	Placebo	Relative (95% CI)	Absolute		
Remission	(any SSRI) (fo	ollow-up 1	1-13 weeks; assess	ed with: Number	of people scorin	ng <7/≤4/7/8 on Ham	ilton Rat	ing Scale	for Depression	n (HAM-D))		
5	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	137/301 (45.5%)	85/277 (30.7%)	RR 1.47 (1.15 to 1.87)	144 more per 1000 (from 46 more to 267 more)	⊕000 VERY LOW	
	( 1 !! ) (6		42				5 "	25.6%		120 more per 1000 (from 38 more to 223 more)		
Remission	i (sertraline) (f	ollow-up m	iean 12 weeks; ass	essed with: Num	ber of people sc	oring ≤4 on Hamilto	n Rating	Scale to	r Depression (	HAM-D))		
1		, ,		no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	63/134 (47%)	45/140 (32.1%) 32.1%	to 1.98)	148 more per 1000 (from 26 more to 315 more) 148 more per 1000 (from	⊕OOO VERY LOW	
Remission	(fluoxetine) (	follow-up r	nean 13 weeks; as	sessed with: Num	ber of people so	coring ≤7 on Hamilt	on Ratino		r Depression (	26 more to 315 more) HAM-D))		

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Study partially funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> No explanation was provided

<sup>6 &</sup>lt;sup>5</sup> N<400

<sup>&</sup>lt;sup>6</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and method of allocation concealment is unclear. Non-blind intervention administrator(s) and participants

<sup>&</sup>lt;sup>7</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

	randomised	serious⁵	no serious	no serious	serious <sup>6</sup>	reporting bias <sup>7</sup>	32/72	10/39		187 more per 1000 (from	⊕OOO
	trials		inconsistency	indirectness			(44.4%)	(25.6%)	to 3.14)	10 fewer to 549 more)	VERY
											LOW
								25.6%		187 more per 1000 (from	
								20.070		10 fewer to 548 more)	
iss	sion (escitalopra	m) (follow-	up mean 12 wee	ks; assessed with	: Number of peo	ple scoring ≤4 on H	amilton Ra	ting Scal	e for Depressi	on (HAM-D) AND HAMD	tem # 1 (depres
d) :	score=0)							_			
	randomised	serious <sup>5</sup>	no serious	no serious	serious <sup>6</sup>	reporting bias <sup>3</sup>	4/17	1/17	RR 4 (0.5 to	176 more per 1000 (from	⊕ООО
	trials		inconsistency	indirectness			(23.5%)	(5.9%)	32.2)	29 fewer to 1000 more)	VERY
											LOW
								5.9%		177 more per 1000 (from	
								3.970		30 fewer to 1000 more)	
iss	sion (paroxetine)	(follow-up	11-12 weeks; as	sessed with: Num	nber of people s	coring <7/≤8 on Han	nilton Ratin	g Scale f	or Depression	(HAM-D))	<u> </u>
	.,	•						_	·	·	
	randomised	serious8	serious <sup>9</sup>	no serious	very serious <sup>10</sup>	reporting bias <sup>11</sup>	38/78	29/81	RR 1.58 (0.68	208 more per 1000 (from	⊕OOO
	trials			indirectness			(48.7%)	(35.8%)	to 3.66)	115 fewer to 952 more)	VERY
							,	,	,	·	LOW
								30.7%		178 more per 1000 (from	
								30 /%			
						ving ≥50% improven much improved on C		nilton Ra	ting Scale for	98 fewer to 817 more)  Depression (HAM-D) AN	D HAMD
	10/AND much/ve	ery much ir	nproved on CGI-	I (score 1-2)/ AND/	OR much/very r	much improved on C	GI-I (score	nilton Ra 1-2))		Depression (HAM-D) AN	
	randomised		no serious	no serious			175/294	nilton Ra 1-2))	RR 1.62 (1.29	Depression (HAM-D) AN 235 more per 1000 (from	⊕000
	10/AND much/ve	ery much ir	nproved on CGI-	I (score 1-2)/ AND/	OR much/very r	much improved on C	GI-I (score	nilton Ra 1-2))		Depression (HAM-D) AN	⊕000 VERY
	randomised	ery much ir	no serious	no serious	OR much/very r	much improved on C	175/294	nilton Ra 1-2)) 100/264 (37.9%)	RR 1.62 (1.29	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)	⊕000
	randomised	ery much ir	no serious	no serious	OR much/very r	much improved on C	175/294	nilton Ra 1-2))	RR 1.62 (1.29	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from	⊕000 VERY
9≤′	randomised trials	serious <sup>1</sup>	nproved on CGI- no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	175/294 (59.5%)	1-2)) 100/264 (37.9%) 30.9%	RR 1.62 (1.29 to 2.03)	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)	⊕OOO VERY LOW
e≤′ oor	randomised trials	serious <sup>1</sup>	nproved on CGI- no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	175/294 (59.5%)	1-2)) 100/264 (37.9%) 30.9%	RR 1.62 (1.29 to 2.03)	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from	⊕OOO VERY LOW
e≤′ oor	randomised trials	serious <sup>1</sup>	nproved on CGI- no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias³ showing ≥50% impr	175/294 (59.5%)	1-2)) 100/264 (37.9%) 30.9%	RR 1.62 (1.29 to 2.03)	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)	⊕OOO VERY LOW
e≤′ oor	randomised trials	serious <sup>1</sup>	nproved on CGI- no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias³ showing ≥50% impr	175/294 (59.5%) ovement or (CGI-I))	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto	RR 1.62 (1.29 to 2.03) n Rating Scale	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)	⊕OOO VERY LOW
e≤′	randomised trials nse (sertraline) (10/Number of pe	serious <sup>1</sup> serious <sup>1</sup> follow-up repople rated	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of	serious <sup>2</sup> mber of people on Clinical Globa	reporting bias³ showing ≥50% impral Impressions scale	175/294 (59.5%) ovement or	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto	RR 1.62 (1.29 to 2.03) n Rating Scale	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  e for Depression (HAM-D	⊕OOO VERY LOW
e≤′	randomised trials  nse (sertraline) (10/Number of perandomised	serious <sup>1</sup> serious <sup>1</sup> follow-up repople rated	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious	serious <sup>2</sup> mber of people on Clinical Globa	reporting bias³ showing ≥50% impral Impressions scale	175/294 (59.5%) ovement or (CGI-I))	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto	RR 1.62 (1.29 to 2.03) n Rating Scale	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  6 for Depression (HAM-D)  254 more per 1000 (from	⊕OOO VERY LOW ) AND HAMD
e≤′ oor	randomised trials  nse (sertraline) (10/Number of perandomised	serious <sup>1</sup> serious <sup>1</sup> follow-up repople rated	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious	serious <sup>2</sup> mber of people on Clinical Globa	reporting bias³ showing ≥50% impral Impressions scale	175/294 (59.5%) ovement or (CGI-I))	100/264 (37.9%) 30.9% Hamilto 72/173 (41.6%)	RR 1.62 (1.29 to 2.03) n Rating Scale	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  6 for Depression (HAM-D)  254 more per 1000 (from	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY
e≤′ oor	randomised trials  nse (sertraline) (10/Number of perandomised	serious <sup>1</sup> serious <sup>1</sup> follow-up repople rated	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious	serious <sup>2</sup> mber of people on Clinical Globa	reporting bias³ showing ≥50% impral Impressions scale	175/294 (59.5%) ovement or (CGI-I))	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto	RR 1.62 (1.29 to 2.03) n Rating Scale	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  a for Depression (HAM-D)  254 more per 1000 (from 4 fewer to 683 more)	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY
e≤′	randomised trials  nse (sertraline) (10/Number of per randomised trials	serious¹  follow-up reople rated  serious¹	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious indirectness	serious <sup>2</sup> mber of people on Clinical Global serious <sup>6</sup>	reporting bias³  showing ≥50% impral Impressions scale reporting bias³	175/294 (59.5%) ovement or (CGI-I)) 102/168 (60.7%)	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto 72/173 (41.6%) 37.3%	RR 1.62 (1.29 to 2.03)  n Rating Scale  RR 1.61 (0.99 to 2.64)	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  254 more per 1000 (from 4 fewer to 683 more)  228 more per 1000 (from 4 fewer to 612 more)	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY LOW
oorre≤′	randomised trials  nse (sertraline) (10/Number of per randomised trials	serious¹  follow-up reople rated serious¹	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious indirectness	serious <sup>2</sup> mber of people on Clinical Global serious <sup>6</sup>	reporting bias³  showing ≥50% impral Impressions scale reporting bias³	175/294 (59.5%) ovement or (CGI-I)) 102/168 (60.7%)	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto 72/173 (41.6%) 37.3%	RR 1.62 (1.29 to 2.03)  n Rating Scale  RR 1.61 (0.99 to 2.64)	235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  254 more per 1000 (from 4 fewer to 683 more)  228 more per 1000 (from 4 fewer to 683 more)	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY LOW
oor e≤′	randomised trials  nse (sertraline) (10/Number of per randomised trials)  randomised trials	serious¹  follow-up reople rated serious¹	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious indirectness	serious <sup>2</sup> mber of people on Clinical Global serious <sup>6</sup>	reporting bias³  showing ≥50% impral Impressions scale reporting bias³	175/294 (59.5%) ovement or (CGI-I)) 102/168 (60.7%)	1-2)) 100/264 (37.9%) 30.9% 1 Hamilto 72/173 (41.6%) 37.3%	RR 1.62 (1.29 to 2.03)  n Rating Scale  RR 1.61 (0.99 to 2.64)	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  254 more per 1000 (from 4 fewer to 683 more)  228 more per 1000 (from 4 fewer to 612 more)	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY LOW
porre≤′	randomised trials  nse (sertraline) (10/Number of per randomised trials)  randomised trials	serious¹  follow-up reople rated serious¹	no serious inconsistency mean 12 weeks; as much or very	no serious indirectness  assessed with: Nu much improved of no serious indirectness	serious <sup>2</sup> mber of people on Clinical Global serious <sup>6</sup>	reporting bias³  showing ≥50% impral Impressions scale reporting bias³	175/294 (59.5%) ovement or (CGI-I)) 102/168 (60.7%)	72/173 (41.6%)	RR 1.62 (1.29 to 2.03)  n Rating Scale  RR 1.61 (0.99 to 2.64)  ating Scale for	Depression (HAM-D) AN  235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  254 more per 1000 (from 4 fewer to 683 more)  228 more per 1000 (from 4 fewer to 612 more)	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY LOW
porre≤′	randomised trials  nse (sertraline) (10/Number of per randomised trials  randomised trials  randomised trials	serious¹  follow-up reople rated serious¹  serious¹  follow-up reople rated	no serious inconsistency  mean 12 weeks; as much or very  serious9	no serious indirectness  assessed with: Nu much improved of indirectness  no serious indirectness  sessed with: Number	serious <sup>2</sup> mber of people on Clinical Globa  serious <sup>6</sup> er of people sho	reporting bias³  showing ≥50% imprestions scale reporting bias³  reporting bias³	175/294 (59.5%) ovement or (CGI-I)) 102/168 (60.7%) ment on Ha	72/173 (41.6%)	RR 1.62 (1.29 to 2.03)  n Rating Scale  RR 1.61 (0.99 to 2.64)  ating Scale for	235 more per 1000 (from 110 more to 390 more)  192 more per 1000 (from 90 more to 318 more)  254 more per 1000 (from 4 fewer to 683 more)  228 more per 1000 (from 4 fewer to 612 more)  Depression (HAM-D) AN	⊕OOO VERY LOW  ) AND HAMD  ⊕OOO VERY LOW

randomise trials  se (paroxetirery much important import	ne) (follow-uproved on Coed serious	no serious inconsistency  p mean 12 weeks; GGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  assessed with: N  no serious indirectness	very serious <sup>10</sup> lumber of people  serious <sup>2</sup>	reporting bias³  showing ≥50% imp  none	7/17 (41.2%) rovement (	5/17 (29.4%) 29.4% on Hamilt 6/19 (31.6%) 31.6%	RR 1.4 (0.55 to 3.55)  con Rating Sca  RR 2.11 (1.02 to 4.37)	262 more per 1000 (from 14 more to 721 more)  cale for Depression (HAI  118 more per 1000 (from 132 fewer to 750 more)  118 more per 1000 (from 132 fewer to 750 more)  le for Depression (HAM-  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	⊕OOO VERY LOW D) AND/OR ⊕⊕OO LOW
randomise trials  se (paroxetirery much important import	ne) (follow-uproved on Coed serious	no serious inconsistency  p mean 12 weeks; GGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  assessed with: N  no serious indirectness  p 8-13 weeks; mea	very serious <sup>10</sup> lumber of people  serious <sup>2</sup> asured with: Ham	reporting bias³  showing ≥50% imp  none  ilton Rating Scale f	7/17 (41.2%) rovement ( 14/21 (66.7%)	5/17 (29.4%) 29.4% on Hamilt 6/19 (31.6%) 31.6%	RR 1.4 (0.55 to 3.55)  con Rating Sca  RR 2.11 (1.02 to 4.37)	118 more per 1000 (from 132 fewer to 750 more) 118 more per 1000 (from 132 fewer to 750 more) 118 more per 1000 (from 132 fewer to 750 more) 119 for Depression (HAM-1351 more per 1000 (from 6 more to 1000 more) 1351 more per 1000 (from 6 more to 1000 more) 1351 more per 1000 (from 6 more to 1000 more) 1351 more per 1000 (from 6 more to 1000 more) 1351 more per 1000 (from 6 more to 1000 more) 1351 more per 1000 (from 6 more to 1000 more)	#OOO VERY LOW  D) AND/OR  ##OO LOW
randomise trials  se (paroxetirery much important import	ne) (follow-uproved on Coed serious	no serious inconsistency  p mean 12 weeks; GGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  assessed with: N  no serious indirectness  p 8-13 weeks; mea	very serious <sup>10</sup> lumber of people  serious <sup>2</sup> asured with: Ham	reporting bias³  showing ≥50% imp  none  ilton Rating Scale f	7/17 (41.2%) rovement ( 14/21 (66.7%)	5/17 (29.4%) 29.4% on Hamilt 6/19 (31.6%) 31.6%	RR 1.4 (0.55 to 3.55)  con Rating Sca  RR 2.11 (1.02 to 4.37)	118 more per 1000 (from 132 fewer to 750 more)  118 more per 1000 (from 132 fewer to 750 more)  Ile for Depression (HAM-  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	⊕OOO VERY LOW  D) AND/OR  ⊕⊕OO LOW
randomise trials  se (paroxetirery much important import	ne) (follow-uproved on Coed serious	no serious inconsistency  p mean 12 weeks; GGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  assessed with: N  no serious indirectness  p 8-13 weeks; mea	very serious <sup>10</sup> lumber of people  serious <sup>2</sup> asured with: Ham	reporting bias³  showing ≥50% imp  none  ilton Rating Scale f	7/17 (41.2%) rovement ( 14/21 (66.7%)	5/17 (29.4%) 29.4% on Hamilt 6/19 (31.6%) 31.6%	RR 1.4 (0.55 to 3.55)  con Rating Sca  RR 2.11 (1.02 to 4.37)	118 more per 1000 (from 132 fewer to 750 more)  118 more per 1000 (from 132 fewer to 750 more)  Ile for Depression (HAM-  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	⊕OOO VERY LOW  D) AND/OR  ⊕⊕OO LOW
randomise trials  se (paroxetirery much impery much imperior much impe	ne) (follow-uproved on Coed serious	no serious inconsistency  up mean 12 weeks; CGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  p 8-13 weeks; mea	serious <sup>2</sup> serious asured with: Ham	showing ≥50% imp none ilton Rating Scale f	(41.2%)  rovement ( 14/21 (66.7%)  or Depress	(29.4%) 29.4% on Hamilt 6/19 (31.6%) 31.6%	to 3.55)  con Rating Sca  RR 2.11 (1.02 to 4.37)	132 fewer to 750 more)  118 more per 1000 (from 132 fewer to 750 more)  Ile for Depression (HAM-  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	VERY LOW  D) AND/OR  D) ON AND/OR  ON O
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se (paroxetirery much impery much impery much impery much impersion sympton randomise trials	ne) (follow-uproved on Coed serious	inconsistency  up mean 12 weeks; CGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  p 8-13 weeks; mea	serious <sup>2</sup> serious asured with: Ham	showing ≥50% imp none ilton Rating Scale f	(41.2%)  rovement ( 14/21 (66.7%)  or Depress	(29.4%) 29.4% on Hamilt 6/19 (31.6%) 31.6%	to 3.55)  con Rating Sca  RR 2.11 (1.02 to 4.37)	132 fewer to 750 more)  118 more per 1000 (from 132 fewer to 750 more)  Ile for Depression (HAM-  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	VERY LOW  D) AND/OR  D) ON AND/OR  ON O
se (paroxeting randomise trials randomise trials randomise trials	proved on Code serious  matology (a	up mean 12 weeks; CGI-I (score 1-2))  no serious inconsistency  ny SSRI) (follow-up	no serious indirectness  p 8-13 weeks; mea	serious <sup>2</sup> asured with: Ham	none ilton Rating Scale f	14/21 (66.7%)	29.4% on Hamilt 6/19 (31.6%) 31.6%	RR 2.11 (1.02 to 4.37)	118 more per 1000 (from 132 fewer to 750 more)  Ile for Depression (HAM-  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	D) AND/OR  D) ON
randomise trials sion symptom randomise trials randomise trials randomise trials	proved on Code serious  matology (a	no serious inconsistency	no serious indirectness  p 8-13 weeks; mea	serious <sup>2</sup> serious <sup>2</sup> asured with: Ham	none ilton Rating Scale f	14/21 (66.7%)	6/19 (31.6%) 31.6% sion (HAN	RR 2.11 (1.02 to 4.37)	132 fewer to 750 more) lie for Depression (HAM- 351 more per 1000 (from 6 more to 1000 more) 351 more per 1000 (from 6 more to 1000 more) core); Better indicated by	⊕⊕OO LOW
randomise trials sion symptom randomise trials randomise trials randomise trials	proved on Code serious  matology (a	no serious inconsistency	no serious indirectness  p 8-13 weeks; mea	serious <sup>2</sup> serious <sup>2</sup> asured with: Ham	none ilton Rating Scale f	14/21 (66.7%)	6/19 (31.6%) 31.6% sion (HAN	RR 2.11 (1.02 to 4.37)	351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  351 more per 1000 (from 6 more to 1000 more)  core); Better indicated by	⊕⊕OO LOW
randomise trials sion symptom randomise trials randomise trials randomise trials	proved on Code serious  matology (a	no serious inconsistency	no serious indirectness  p 8-13 weeks; mea	serious <sup>2</sup> serious <sup>2</sup> asured with: Ham	none ilton Rating Scale f	14/21 (66.7%)	6/19 (31.6%) 31.6%	RR 2.11 (1.02 to 4.37)	351 more per 1000 (from 6 more to 1000 more) 351 more per 1000 (from 6 more to 1000 more) core); Better indicated by	⊕⊕OO LOW
randomise trials  sion symptom randomise trials  sion symptom randomise trials	serious matology (a	no serious inconsistency ny SSRI) (follow-up	p 8-13 weeks; mea	no serious	ilton Rating Scale f	(66.7%)	(31.6%) 31.6% sion (HAM	to 4.37)	6 more to 1000 more) 351 more per 1000 (from 6 more to 1000 more) core); Better indicated by	LOW lower value
randomise trials  sion symptom  randomise trials  randomise randomise	matology (a	inconsistency ny SSRI) (follow-up	p 8-13 weeks; mea	no serious	ilton Rating Scale f	(66.7%)	(31.6%) 31.6% sion (HAM	to 4.37)	6 more to 1000 more) 351 more per 1000 (from 6 more to 1000 more) core); Better indicated by	LOW lower value
randomise trials  sion symptom  randomise trials  randomise randomise	matology (a	inconsistency ny SSRI) (follow-up	p 8-13 weeks; mea	no serious	ilton Rating Scale f	(66.7%)	(31.6%) 31.6% sion (HAM	to 4.37)	6 more to 1000 more) 351 more per 1000 (from 6 more to 1000 more) core); Better indicated by	LOW lower value
randomise trials sion symptom		ny SSRI) (follow-up	p 8-13 weeks; mea	no serious		or Depress	31.6% Sion (HAM	,	351 more per 1000 (from 6 more to 1000 more) core); Better indicated by	lower value
randomise trials sion sympton randomise			no serious	no serious			sion (HAN	I-D; change so	6 more to 1000 more) core); Better indicated by	
randomise trials sion sympton randomise			no serious	no serious			sion (HAN	I-D; change so	6 more to 1000 more) core); Better indicated by	
randomise trials sion sympton randomise			no serious	no serious			sion (HAN	I-D; change so	core); Better indicated by	
randomise trials sion sympton randomise			no serious	no serious				I-D; change so	,	
randomise			indirectness	imprecision				-	SMD 0.69 lower (1.02 to	2000
randomise									0.35 lower)	VERY
randomise		1								LOW
randomise						1				
	matology (s	ertraline) (follow-u	p mean 12 weeks;	measured with:	Hamilton Rating Sc	ale for Dep	pression	(HAM-D; chang	ge score); Better indicate	d by lower v
	ed serious	1 very serious <sup>12</sup>	no serious	serious <sup>13</sup>	reporting bias <sup>3</sup>	167	172	_	SMD 0.61 lower (1.3	⊕000
ulais	Scrious	very serious	indirectness	3611003	reporting bias	107	112	_	lower to 0.07 higher)	VERY
			munectiess						lower to 0.07 migner)	LOW
										LOVV
sion sympton	matology (fl	uoxetine) (follow-u	ıp 8-13 weeks: me	asured with: Han	nilton Rating Scale	for Depres	sion (HAI	M-D: change s	core); Better indicated b	v lower valu
,			.,,			.с. дор.сс		,g. c	,,	,
randomise	ed serious	5 very serious <sup>12</sup>	no serious	serious <sup>13</sup>	reporting bias7	88	55	-	SMD 0.8 lower (1.81	⊕000
trials		,	indirectness		, ,				lower to 0.21 higher)	VERY
									3.10.7	LOW
				1	1			ĺ		
sion sympton										1
J.C.I Gyilipton	matology (e	scitalopram) (folloy	w-up mean 12 wee	eks: measured wi	th: Hamilton Rating	Scale for	Denressi	on (HAM-D: ch	nange score); Better indi	cated by low

	randomised	lserious⁵	no serious	no serious	serious14	reporting bias <sup>3</sup>	17	17		SMD 0.9 lower (1.61 to	⊕OOO
	trials	Serious	inconsistency	indirectness	Serious	reporting bias	17	17	-	0.19 lower)	VERY
	lilais		inconsistency	indirectriess						0.19 lower)	LOW
											LOVV
press	ion symptomat	ology (par	oxetine) (follow-u	p mean 12 weeks	; measured with	: Hamilton Rating S	cale for De	pression	(HAM-D; chan	ge score); Better indicat	ed by lower va
	randomised	serious <sup>5</sup>	no serious	no serious	serious <sup>14</sup>	none	21	19	-	SMD 0.77 lower (1.41 to	⊕⊕ОО
	trials		inconsistency	indirectness						0.12 lower)	LOW
iscont	inuation for any	reason (a	ny SSRI) (follow-i	up 8-13 weeks; as	sessed with: Nu	mber of participant	s discontin	uing for	any reason inc	luding adverse events)	
	1		1			1					
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	46/318	59/275	,	77 fewer per 1000 (from	⊕OOO
	trials		inconsistency	indirectness			(14.5%)	(21.5%)	to 0.96)	9 fewer to 124 fewer)	VERY
											LOW
								22.3%		80 fewer per 1000 (from	
										9 fewer to 129 fewer)	
iscont	inuation for any	reason (se	ertraline) (follow-	up mean 12 week	s; assessed with	: Number of partici	pants disc	ontinuing	for any reaso	n including adverse ever	nts)
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	reporting bias <sup>3</sup>	25/168	42/174	RR 0.62 (0.4	92 fewer per 1000 (from	⊕000
	trials	0011040	inconsistency	indirectness	0011000	roporting side		(24.1%)	to 0.97)	7 fewer to 145 fewer)	VERY
	criaio		moonloididing	ii iaii ooti looo			(11.070)	(= 1.170)	10 0.01)	7 101101 (0 1 10 101101)	
											1 OW/
										91 fewer per 1000 (from	LOW
								23.9%		91 fewer per 1000 (from 7 fewer to 143 fewer)	LOW
iscont	inuation for any	reason (fl	uoxetine) (follow	-up 8-13 weeks; as	ssessed with: No	umber of participan	ts disconti		any reason in	7 fewer to 143 fewer)	LOW
iscont	inuation for any	reason (fl	uoxetine) (follow-	-up 8-13 weeks; as		umber of participan	ts disconti		any reason in		LOW
iscont	inuation for any	reason (fl	uoxetine) (follow-	up 8-13 weeks; as	ssessed with: No	umber of participan	ts disconti			7 fewer to 143 fewer)	±000
iscont								nuing for		7 fewer to 143 fewer) cluding adverse events)	
iscont	randomised			no serious			15/110	nuing for	RR 1.17 (0.11	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)	⊕000
scont	randomised			no serious			15/110	13/65 (20%)	RR 1.17 (0.11	7 fewer to 143 fewer) cluding adverse events) 34 more per 1000 (from	⊕OOO VERY
scont	randomised			no serious			15/110	nuing for	RR 1.17 (0.11	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)	⊕OOO VERY
	randomised trials	serious <sup>5</sup>	serious <sup>9</sup>	no serious indirectness	very serious <sup>15</sup>	reporting bias <sup>7</sup>	15/110 (13.6%)	13/65 (20%)	RR 1.17 (0.11 to 12.85)	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from	⊕OOO VERY LOW
	randomised trials inuation for any	serious <sup>5</sup>	serious <sup>9</sup> scitalopram) (follo	no serious indirectness ow-up mean 12 w	very serious <sup>15</sup>	reporting bias <sup>7</sup>	15/110 (13.6%)	13/65 (20%) 13.3%	RR 1.17 (0.11 to 12.85)	7 fewer to 143 fewer) cluding adverse events) 34 more per 1000 (from 178 fewer to 1000 more) 23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of	⊕OOO VERY LOW
	randomised trials inuation for any randomised	serious <sup>5</sup>	serious <sup>9</sup> scitalopram) (follono serious	no serious indirectness  ow-up mean 12 woon no serious	very serious <sup>15</sup>	reporting bias <sup>7</sup>	15/110 (13.6%)	13/65 (20%) 13.3% liscontinu	RR 1.17 (0.11 to 12.85) uing for any rea	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from 118 fewer to 1000 more)	⊕OOO VERY LOW
	randomised trials inuation for any	serious <sup>5</sup>	serious <sup>9</sup> scitalopram) (follo	no serious indirectness ow-up mean 12 w	very serious <sup>15</sup>	reporting bias <sup>7</sup>	15/110 (13.6%)	13/65 (20%) 13.3% liscontinu	RR 1.17 (0.11 to 12.85)	7 fewer to 143 fewer) cluding adverse events) 34 more per 1000 (from 178 fewer to 1000 more) 23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of	⊕OOO VERY LOW   ⊕OOO VERY
	randomised trials inuation for any randomised	serious <sup>5</sup>	serious <sup>9</sup> scitalopram) (follono serious	no serious indirectness  ow-up mean 12 woon no serious	very serious <sup>15</sup>	reporting bias <sup>7</sup>	15/110 (13.6%)	13/65 (20%) 13.3% liscontinu	RR 1.17 (0.11 to 12.85) uing for any rea	7 fewer to 143 fewer) cluding adverse events) 34 more per 1000 (from 178 fewer to 1000 more) 23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of	⊕OOO VERY LOW
scont	randomised trials inuation for any randomised trials	serious <sup>5</sup> reason (es	serious <sup>9</sup> scitalopram) (follono serious inconsistency	no serious indirectness  ow-up mean 12 woon no serious indirectness	very serious <sup>15</sup> eeks; assessed very serious <sup>15</sup>	reporting bias <sup>7</sup> with: Number of par  reporting bias <sup>3</sup>	15/110 (13.6%) ticipants d	13/65 (20%) 13.3% liscontinu 0/17 (0%) 0%	RR 1.17 (0.11 to 12.85) uing for any rea RR 6.3 (0.35 to 113.81)	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of the second including a	⊕OOO VERY LOW events)  ⊕OOO VERY LOW
iscont	randomised trials inuation for any randomised trials	serious <sup>5</sup> reason (es	serious <sup>9</sup> scitalopram) (follono serious inconsistency	no serious indirectness  ow-up mean 12 woon no serious indirectness	very serious <sup>15</sup> eeks; assessed very serious <sup>15</sup>	reporting bias <sup>7</sup> with: Number of par  reporting bias <sup>3</sup>	15/110 (13.6%) ticipants d	13/65 (20%) 13.3% liscontinu 0/17 (0%) 0%	RR 1.17 (0.11 to 12.85) uing for any rea RR 6.3 (0.35 to 113.81)	7 fewer to 143 fewer) cluding adverse events) 34 more per 1000 (from 178 fewer to 1000 more) 23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of	⊕OOO VERY LOW  ⊕OOO VERY LOW
scont	randomised trials inuation for any randomised trials inuation for any	serious <sup>5</sup> reason (es	serious <sup>9</sup> scitalopram) (followaroxetine) (followaroxetine)	no serious indirectness  ow-up mean 12 we indirectness  r-up mean 12 week	very serious <sup>15</sup> eeks; assessed very serious <sup>15</sup> ks; assessed wif	reporting bias <sup>7</sup> with: Number of par  reporting bias <sup>3</sup>	15/110 (13.6%) ticipants d	13/65 (20%) 13.3% liscontinu 0/17 (0%) 0%	RR 1.17 (0.11 to 12.85)  sing for any real RR 6.3 (0.35 to 113.81)	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of the control of the	events)  #OOO VERY LOW  #OOO VERY LOW  pents)
scont	randomised trials inuation for any randomised trials	serious <sup>5</sup> reason (es	serious <sup>9</sup> scitalopram) (following inconsistency aroxetine) (following inconsistency	no serious indirectness  ow-up mean 12 woon no serious indirectness	very serious <sup>15</sup> eeks; assessed very serious <sup>15</sup>	reporting bias <sup>7</sup> with: Number of partice th: Number of partice	15/110 (13.6%) ticipants d 3/19 (15.8%)	13/65 (20%) 13.3% liscontinu 0/17 (0%) 0% continuin	RR 1.17 (0.11 to 12.85)  sing for any real RR 6.3 (0.35 to 113.81)  g for any reason	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of the fewer to 1000 more)	events)  #OOO VERY LOW  #OOO VERY LOW  Ponts)
scont	randomised trials  inuation for any randomised trials  inuation for any randomised	serious <sup>5</sup> reason (es	serious <sup>9</sup> scitalopram) (followaroxetine) (followaroxetine)	no serious indirectness  ow-up mean 12 we no serious indirectness  r-up mean 12 week	very serious <sup>15</sup> eeks; assessed very serious <sup>15</sup> ks; assessed wif	reporting bias <sup>7</sup> with: Number of partice th: Number of partice	15/110 (13.6%) ticipants d 3/19 (15.8%)	13/65 (20%) 13.3% liscontinu 0/17 (0%) 0%	RR 1.17 (0.11 to 12.85)  sing for any real RR 6.3 (0.35 to 113.81)	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of the control of the	#000 VERY LOW POOD VERY LOW POOD VERY LOW VERY LOW POOD VERY LOW VERY LOW VERY LOW VERY POOD VER
iscont	randomised trials  inuation for any randomised trials  inuation for any randomised	serious <sup>5</sup> reason (es	serious <sup>9</sup> scitalopram) (following inconsistency aroxetine) (following inconsistency	no serious indirectness  ow-up mean 12 we no serious indirectness  r-up mean 12 week	very serious <sup>15</sup> eeks; assessed very serious <sup>15</sup> ks; assessed wif	reporting bias <sup>7</sup> with: Number of partice th: Number of partice	15/110 (13.6%) ticipants d 3/19 (15.8%)	13/65 (20%) 13.3% liscontinu 0/17 (0%) 0% continuin	RR 1.17 (0.11 to 12.85)  sing for any real RR 6.3 (0.35 to 113.81)  g for any reason	7 fewer to 143 fewer) cluding adverse events)  34 more per 1000 (from 178 fewer to 1000 more)  23 more per 1000 (from 118 fewer to 1000 more) ason including adverse of the fewer to 1000 more)	events)  #OOO VERY LOW  #OOO VERY LOW  Ponts)

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Unclear (or high risk of bias associated with) randomisation method and unclear method of allocation concealment. Unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>3</sup> Funding from pharmaceutical company

<sup>&</sup>lt;sup>4</sup> High risk of bias associated with randomisation method due to significant differences between groups at baseline and unclear method of allocation concealment. Unclear blinding of intervention administration and outcome assessment. Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>&</sup>lt;sup>5</sup> Unclear randomisation method and method of allocation concealment. Unclear blinding of intervention administration and outcome assessment

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

Data is not reported for all outcomes

<sup>8</sup> Unclear blinding of intervention administrator(s)

<sup>&</sup>lt;sup>10</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>11</sup> Data is not reported for all outcomes and funding from pharmaceutical company

<sup>&</sup>lt;sup>12</sup> I-squared>80%

<sup>13</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (SMD -0.5)

<sup>14</sup> N<400

<sup>15</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

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# Sertraline versus imipramine for chronic depression

			Quality a	ssessment			No of	patients		Effect		
											Quality	Importan
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sertraline	Imipramine	Relative (95% CI)	Absolute		
emissio	n (follow-up n	nean 12 we	eeks: assessed w	ith: Number of p	eople scoring ≤4	on Hamilton Rating	Scale for D	epression (F	IAM-D)/≤7 on	HAM-D AND much/ve	rv much	improved (
	ore 1-2))		· · · <b>,</b> · · · · · · · · · · · · · · · · · · ·				,		, -			
	lancation to a d	L	I		: 2		400/555	00/000	DD 4.44	00 1000		<u> </u>
	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	133/555 (24%)	88/338 (26%)	RR 1.11	29 more per 1000 (from 29 fewer to 102	⊕OOO VERY	
	uiais	Serious	inconsistency	lituliectriess			(24 /0)	(2076)	(0.09 to 1.39)	more)	LOW	
										111010)	LOVV	
										31 more per 1000		
								20.20/		(from 31 fewer to 110		
								28.2%		`		
										more)		
								Rating Scale		more) n (HAM-D) AND HAM		D much/ve
								Rating Scale		more)		D much/ve
	proved on CG			(mildly ill)/Numb	er of people rated	d as much or very r		Rating Scale		more) n (HAM-D) AND HAM ressions scale (CGI-I)	)	D much/ve
		I-I (score 1	-2) AND CGI-S≤3				nuch improv	Rating Scale red on Clinic	al Global Imp	more) on (HAM-D) AND HAM ressions scale (CGI-I) 17 fewer per 1000		D much/ve
	randomised	I-I (score 1	-2) AND CGI-S≤3	no serious	no serious	d as much or very r	299/555	Rating Scale red on Clinic	al Global Imp RR 0.97	more) on (HAM-D) AND HAM ressions scale (CGI-I) 17 fewer per 1000	⊕⊕OO	D much/ve
	randomised	I-I (score 1	-2) AND CGI-S≤3	no serious	no serious	d as much or very r	299/555	Rating Scale red on Clinic	al Global Imp RR 0.97	more) In (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)	⊕⊕OO	D much/ve
	randomised	I-I (score 1	-2) AND CGI-S≤3	no serious	no serious	d as much or very r	299/555	Rating Scale yed on Clinic 191/338 (56.5%)	al Global Imp RR 0.97	more) in (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000	⊕⊕OO	D much/ve
	randomised	I-I (score 1	-2) AND CGI-S≤3	no serious	no serious	d as much or very r	299/555	Rating Scale red on Clinic	al Global Imp RR 0.97	more) In (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000 (from 81 fewer to 58	⊕⊕OO	D much/ve
uch imp	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	299/555 (53.9%)	Rating Scale yed on Clinic 191/338 (56.5%) 57.7%	RR 0.97 (0.86 to 1.1)	more) In (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000 (from 81 fewer to 58 more)	⊕⊕OO LOW	D much/ve
uch imp	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	299/555 (53.9%)	Rating Scale yed on Clinic 191/338 (56.5%) 57.7%	RR 0.97 (0.86 to 1.1)	more) In (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000 (from 81 fewer to 58	⊕⊕OO LOW	D much/ve
uch imp	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision  with: Hamilton R	reporting bias <sup>3</sup>	299/555 (53.9%)	Rating Scale yed on Clinic 191/338 (56.5%) 57.7%	RR 0.97 (0.86 to 1.1)	more) In (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000 (from 81 fewer to 58 more)	⊕⊕OO LOW	D much/ve
uch imp	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>3</sup>	299/555 (53.9%)	Rating Scale yed on Clinic 191/338 (56.5%) 57.7%	RR 0.97 (0.86 to 1.1)	more) in (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000 (from 81 fewer to 58 more) er indicated by lower	⊕⊕OO LOW	D much/ve
uch imp	randomised trials  on symptomate randomised	serious <sup>4</sup> serious <sup>4</sup> tology (followry	no serious inconsistency  low-up mean 12 v	no serious indirectness  veeks; measured	no serious imprecision  with: Hamilton R	reporting bias <sup>3</sup>	299/555 (53.9%)	Rating Scale yed on Clinic 191/338 (56.5%) 57.7%	RR 0.97 (0.86 to 1.1)	more) In (HAM-D) AND HAM ressions scale (CGI-I)  17 fewer per 1000 (from 79 fewer to 57 more)  17 fewer per 1000 (from 81 fewer to 58 more)  er indicated by lower  SMD 0.05 higher	⊕⊕OO LOW	D much/ve

Discontinu	uation due to a	adverse ev	rents (follow-up me	ean 12 weeks; as

2	randomised	serious4	serious <sup>6</sup>	no serious	serious <sup>7</sup>	reporting bias <sup>3</sup>	97/560	95/345	RR 0.61	107 fewer per 1000	⊕000	
	trials			indirectness			(17.3%)	(27.5%)	(0.39 to 0.95)	(from 14 fewer to 168	VERY	
										fewer)	LOW	
										111 fewer per 1000		
								28.5%		(from 14 fewer to 174		
										fewer)		
Discontin	uation due to	adverse ev	vents (follow-up m	ean 12 weeks: as	ssessed with: No	umber of participan	ts discontir	nuina due to	adverse even	ts)		
				, , , , , , , , , , , , , , , , , , , ,				9		,		
	randomised	serious4	no serious	no serious	serious <sup>7</sup>	reporting bias <sup>3</sup>	35/560	50/345	RR 0.45	80 fewer per 1000	⊕000	
	trials		inconsistency	indirectness			(6.3%)	(14.5%)	(0.29 to 0.71)	(from 42 fewer to 103	VERY	
			·							fewer)	LOW	
										84 fewer per 1000		
	1	1				1		15.2%		(from 44 fewer to 108		
								13.2 /0		(IIOIII 44 IEWEI 10 100		

<sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline and method of allocation concealment unclear. Unclear blinding of intervention administration and outcome assessment. Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

#### Sertraline + IPT versus IPT-only for chronic depression

No of										Quality	Importance
studies	n Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sertraline + IPT	IPT- only	Relative (95% CI)	Absolute		
Remission (follow- core>70)	up mean 16 w	eeks; assessed wit	h: Number of peo	ple scoring <7 o	on Hamilton Rating	Scale for De	pressio	n (HAM-D) ANI	D >50% improvement on	HAMD AN	ID GAF
randomis trials	ed very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	,	5/23 (21.7%) 21.7%	5.79)	307 more per 1000 (from 0 more to 1000 more) 306 more per 1000 (from 0 more to 1000 more)	VERY LOW	

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Funding from pharmaceutical company

<sup>&</sup>lt;sup>4</sup> Unclear randomisation method and method of allocation concealment. Blinding of intervention administration and outcome assessment is unclear

<sup>&</sup>lt;sup>5</sup> N<400

<sup>&</sup>lt;sup>6</sup> I-squared>50%

<sup>&</sup>lt;sup>7</sup> Events<300

	randomised	very	no serious	no serious	serious <sup>2</sup>	reporting bias⁵	134/233	91/201	RR 1.26 (1.05	118 more per 1000 (from	$\oplus$ OOO	
	trials	serious4	inconsistency	indirectness			(57.5%)	(45.3%)	to 1.52)	23 more to 235 more)	VERY	
											LOW	
								40.7%		106 more per 1000 (from		
								40.770		20 more to 212 more)		
	randomised	very	no serious	no serious	no serious	reporting bias <sup>5</sup>	233	201	-	SMD 0.5 lower (0.7 to	⊕000	
	randomicod	vorv	no corious	no corious	no corious	roporting bige <sup>5</sup>	233	201		SMD 0.5 lower (0.7 to	0000	
	randomised trials	very serious <sup>4</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias <sup>5</sup>	233	201	-	SMD 0.5 lower (0.7 to 0.31 lower)	⊕000 VERY	
						reporting bias⁵	233	201	-	,		
	trials	serious <sup>4</sup>	inconsistency	indirectness	imprecision				-	0.31 lower)	VERY	
iscontii	trials	serious <sup>4</sup>	inconsistency	indirectness	imprecision	reporting bias <sup>5</sup> of participants disc			- son including	0.31 lower)	VERY	
isconti	trials	serious <sup>4</sup>	inconsistency	indirectness	imprecision				son including	0.31 lower)	VERY	
isconti	trials uation for any	serious <sup>4</sup> / reason (f	inconsistency ollow-up mean 16	indirectness weeks; assesse	imprecision ed with: Number	of participants disc	continuing fo	r any reas	RR 1.1 (0.31	0.31 lower) adverse events)	VERY LOW	
Disconti	trials  nuation for any	serious <sup>4</sup> / reason (f	inconsistency ollow-up mean 16 no serious	indirectness weeks; assesse	imprecision ed with: Number	of participants disc	continuing fo	r any reas	RR 1.1 (0.31	0.31 lower) adverse events)  17 more per 1000 (from	VERY LOW	
Disconti	trials  nuation for any	serious <sup>4</sup> / reason (f	inconsistency ollow-up mean 16 no serious	indirectness weeks; assesse	imprecision ed with: Number	of participants disc	continuing fo	r any reas	RR 1.1 (0.31	0.31 lower) adverse events)  17 more per 1000 (from	VERY LOW ⊕OOO VERY	

<sup>&</sup>lt;sup>1</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline, and method of allocation concealment is unclear. Non-blind intervention administrator(s) and participants, although outcome assessors are blind

#### TCAs versus placebo

			Quality as	sessment			No of	patients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TCAs	Placebo	Relative (95% CI)	Absolute		
Remission	n (imipramine)	(follow-up	o 6-26 weeks; asse	ssed with: Numb	er of people sco	oring ≤4/6 on Hamil	ton Rati	ng Scale	for Depression	n (HAM-D)/<8 on Montgo	mery Asber	g

Depression Rating Scale (MADRS))

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> Study partially funded by pharmaceutical company

<sup>&</sup>lt;sup>4</sup> High risk of bias associated with randomisation method due to significant difference between groups at baseline. Non-blind intervention administrator(s) and participants, although outcome assessors are blind

<sup>&</sup>lt;sup>5</sup> Data is not reported for all outcomes and funding from pharmaceutical company

<sup>&</sup>lt;sup>6</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	109/332	80/335	RR 1.38 (1.02	91 more per 1000 (from	⊕⊕00	
	trials		inconsistency	indirectness			(32.8%)		to 1.86)	5 more to 205 more)	LOW	
							,	,	,	,		
								19.2%		73 more per 1000 (from		
								19.2%		4 more to 165 more)		
pons	e (anv TCA) (fo	ollow-up 6	-26 weeks: asses	sed with: Number	r of people rated	d as much or very	much impre	oved on	Clinical Global	Impressions scale (CGI	-I)/Number of	f people
				cale for Depressi			,				,	. роср
			Ū	•	, ,,							
	randomised	serious1	no serious	no serious	no serious	none	267/410	152/421	RR 1.85 (1.51	307 more per 1000 (from	⊕⊕⊕О	
	trials		inconsistency	indirectness	imprecision		(65.1%)	(36.1%)	to 2.26)	184 more to 455 more)	MODERATE	
								33.3%		283 more per 1000 (from		
								33.3%		170 more to 420 more)		
ons	e (imipramine)	(follow-u	p 6-26 weeks: ass	sessed with: Num	ber of people ra	ted as much or v	erv much im	proved	on Clinical Glo	bal Impressions scale (C	GI-I)/Numbe	r of pe
				cale for Depressi			o. <b>,</b>	<b>P. O . O .</b> .			.,	. с. рс.
					, ,,							
	randomised	serious1	serious <sup>3</sup>	no serious	no serious	none	212/321	125/337	RR 1.86 (1.43	319 more per 1000 (from	⊕⊕ОО	
	trials			indirectness	imprecision			(37.1%)	to 2.4)	159 more to 519 more)	LOW	
							, ,	,	,	,		
								00.00/		291 more per 1000 (from		
								33.8%		145 more to 473 more)		
sponse	e (amineptine)	(follow-u	n mean 13 weeks	: assessed with: N	Number of peop	le rated as much	or very muc	h improv	ed on Clinical	Global Impressions sca	le (CGI-I))	
	- (	,		,							- ( - //	
	randomised	serious4	no serious	no serious	serious <sup>2</sup>	none	55/89	27/84	RR 1.92 (1.35	296 more per 1000 (from	$\oplus \oplus OO$	
	trials		inconsistency	indirectness			(61.8%)	(32.1%)	to 2.73)	113 more to 556 more)	LOW	
			,				,	,	,	,		
								00.40/		295 more per 1000 (from		
								32.1%		112 more to 555 more)		
ressi	on symptomat	ology (an	v TCA) (follow-up	8-13 weeks: mea	sured with: Han	nilton Rating Sca	le for Denres	sion (H	M-D: change	score)/Montgomery Asb	era Denressi	on Rat
			etter indicated by		04.04	ton rtating oou	ю ю. Боргос		un D, onlango		o.g 20p.000.	on ruc
(	Dito, change	000.0,, 2	ono. maioatoa b	, 101101 141400,								
	randomised	serious1	serious <sup>3</sup>	no serious	no serious	none	337	342	-	SMD 0.63 lower (0.95 to	⊕⊕00	
	trials			indirectness	imprecision	10110				0.3 lower)	LOW	
				man oou loo						0.0 .0	2011	
ressi	on symptomat	ology (im	inramine) (follow.	un 8-12 weeks: m	easured with: H	lamilton Rating S	cale for Den	ression	(HAM-D: chance	ge score); Better indicate	ed by lower v	alues)
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	on Symptomat	ology (IIII	ipiaiiiiio) (ioiiow	up o 12 weeks, iii	icasarca with. I	idillitoii itatilig o	odic for Dep	10001011	(TIAM D, OTIGITS	go soorej, Better maioat	ca by lower v	ulucoj
	randomised	serious <sup>1</sup>	very serious <sup>5</sup>	no serious	no serious	none	230	237	_	SMD 0.64 lower (1.21 to	⊕000	
	trials	Johnous	very serious	indirectness	imprecision	IIIIC	200	201	_	,	VERY LOW	
	uidio			indirectiress	imprecision					0.00 lower)	VERT LOW	
		-1				41 14	1 - L D	!	-4:	ADD0: -h		
	on symptomat	ology (am	ineptine) (tollow-	up mean 13 week	s; measured wi	tn: wontgomery A	asperg Depr	ession F	ating Scale (M	ADRS; change score); E	setter indicate	ed by lo
res)												

	randomised	serious <sup>4</sup>	no serious	no serious	serious <sup>6</sup>	none	107	105	_	SMD 0.61 lower (0.88 to	⊕⊕ОО
	trials	3011003	inconsistency	indirectness	3011003	TIOTIC	107	100		0.33 lower)	LOW
	titais		inconsistency	indirectiness						0.00 lower)	LOVV
conti	nuation for any	roseon (s	any TCA) (follow-i	in 6-26 wooks: a	seesed with: Nu	mbor of particing	ante discont	inuina fa	r any roason i	ncluding adverse events	1
COIILI	iluation for any	y reason (a	ally ICA) (IOIIOW-C	ip 0-20 weeks, a	ssesseu witti. Nu	iliber of participa	ants discont	illullig it	ally reason ii	icidality adverse events	)
	randomised	serious <sup>7</sup>	no serious	no serious	serious <sup>8</sup>	none	147/468	135/467	RR 1.06 (0.85	17 more per 1000 (from	⊕⊕ОО
	trials		inconsistency	indirectness	00110010		(31.4%)		to 1.31)	43 fewer to 90 more)	LOW
	i. i.a.i.o			aooaoo			(011170)	(=0.070)	(0 1101)	10 101101 to 00 111010)	LOW
										19 more per 1000 (from	
								31.6%		47 fewer to 98 more)	
isconti	nuation for any	ı roason (i	minramine) (follo	wun 6-26 waaks	· accessed with	Number of partic	inante diece	ntinuin	for any reason	n including adverse eve	nte)
i 300ii tii	iluation for any	y reason (i	imprainine) (iono	W-up 0-20 Weeks	, assessed with.	Number of partic	ipants disc	, inclinating	ior any reason	in including adverse eve	1113)
	randomised	serious <sup>7</sup>	no serious	no serious	serious <sup>8</sup>	none	107/357	93/359	RR 1.11 (0.83	28 more per 1000 (from	⊕⊕ОО
	trials		inconsistency	indirectness				(25.9%)	to 1.49)	44 fewer to 127 more)	LOW
							(3070)	(=0.070)			
										27 more per 1000 (from	
								24.3%		41 fewer to 119 more)	
ieconti	nuation for any	roseon (	aminentine) (feller	v-un moan 12 w	oke: seeseed w	ith: Number of n	articinante d	liscontin	uing for any ro	ason including adverse	evente)
i3conti	iluation for all	y reason (a	annieptine) (iolio	w-up illealt 13 We	ens, assessed W	idi. Number of p	articipants (	ai3COIIIII	uning for ally re	ason including adverse	events)
	randomised	serious <sup>9</sup>	no serious	no serious	very serious <sup>10</sup>	none	40/111	42/108	RR 0.93 (0.66	27 fewer per 1000 (from	⊕000
	trials	ociiodo	inconsistency	indirectness	very serious	Horic		(38.9%)	to 1.31)	132 fewer to 121 more)	
	titalo		inconsistency	mancomess			(0070)	(00.070)	10 1.01)	102 lewer to 121 more)	VLICI LOVV
										27 fewer per 1000 (from	
								38.9%		132 fewer to 121 more)	
icconti	nuation due to	advorce	events (any TCA) (	follow up 6 26 w	ooke: assessed v	with: Number of r	participants	disconti	nuing due to a	,	
isconti	iluation due to	auverse	vents (any TCA) (	ioliow-up 6-20 w	eeks, assesseu v	vitii. Nullibel Oi p	Jarticipants	uisconti	numy due to at	averse events)	
	randomised	serious <sup>7</sup>	no serious	no serious	serious <sup>2</sup>	none	63/468	10/467	RR 5 77 (3 09	102 more per 1000 (from	⊕⊕ОО
	trials	0011000	inconsistency	indirectness	Conodo	Horio	(13.5%)		to 10.79)	45 more to 210 more)	LOW
	titalo		inconsistency	mancomess			(10.070)	(2.170)	10 10.70)	40 more to 2 to more)	LOVV
										67 more per 1000 (from l	
								1.4%		67 more per 1000 (from	
41				) (f-II 0 00	<u></u>	deside Nessels	- f			29 more to 137 more)	
isconti	nuation due to	adverse e	events (imipramine	e) (follow-up 6-20	6 weeks; assesse	d with: Number	of participar			29 more to 137 more)	
isconti		1						its disco	ntinuing due to	29 more to 137 more) adverse events)	0000
isconti	randomised	adverse e	no serious	no serious	serious <sup>2</sup>	d with: Number o	58/357	ots disco	ntinuing due to	29 more to 137 more) adverse events)  122 more per 1000 (from	⊕⊕00 LOW
isconti		1						ots disco	ntinuing due to	29 more to 137 more) adverse events)	⊕⊕OO LOW
isconti	randomised	1	no serious	no serious			58/357	ots disco	RR 5.87 (3.05 to 11.29)	29 more to 137 more) adverse events)  122 more per 1000 (from 51 more to 258 more)	
isconti	randomised	1	no serious	no serious			58/357	ots disco	RR 5.87 (3.05 to 11.29)	29 more to 137 more)  adverse events)  122 more per 1000 (from 51 more to 258 more)  93 more per 1000 (from	
	randomised trials	serious <sup>7</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	58/357 (16.2%)	9/359 (2.5%)	RR 5.87 (3.05 to 11.29)	29 more to 137 more) 2 adverse events)  122 more per 1000 (from 51 more to 258 more)  93 more per 1000 (from 39 more to 196 more)	
	randomised trials	serious <sup>7</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	58/357 (16.2%)	9/359 (2.5%)	RR 5.87 (3.05 to 11.29)	29 more to 137 more)  adverse events)  122 more per 1000 (from 51 more to 258 more)  93 more per 1000 (from	
	randomised trials nuation due to	serious <sup>7</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup> an 13 weeks; asse	none essed with: Num	58/357 (16.2%) ber of partic	9/359 (2.5%) 1.9%	RR 5.87 (3.05 to 11.29)	29 more to 137 more) 2 adverse events)  122 more per 1000 (from 51 more to 258 more)  93 more per 1000 (from 39 more to 196 more)  ue to adverse events)	
	randomised trials	serious <sup>7</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	58/357 (16.2%)	9/359 (2.5%)	RR 5.87 (3.05 to 11.29)	29 more to 137 more) 2 adverse events)  122 more per 1000 (from 51 more to 258 more)  93 more per 1000 (from 39 more to 196 more)	

								0.9%		35 more per 1000 (from 4 fewer to 360 more)	⊕000 VERY LOW	
--	--	--	--	--	--	--	--	------	--	--	------------------	--

<sup>&</sup>lt;sup>1</sup> Unclear (or high risk of bias associated with) randomisation method and unclear method of allocation concealment. Unclear blinding of intervention administration and outcome assessment. Unclear risk of attrition bias (drop-out>20% and/or difference between groups>20% but ITT analysis used)

2

3

#### TCA versus antipsychotic for chronic depression

	. ,											
			Quality asse	essment			No	of patients		Effect		
											Quality	Importance
No of	Design	Risk of	Inconsistency	Indirectness	Imprecision	Other	TCA	Antipsychotic	Relative	Absolute		
studies	Design	bias	inconsistency	munechiess	Imprecision	considerations	ICA	Antipayenotic	(95% CI)	Absolute		
Remissio	n (imipramine	versus an	nisulpride) (follow-	up mean 26 week	s; assessed	with: Number of p	eople so	oring <8 on M	ontgomery Asb	erg Depression Rating So	cale (MAD	RS))
1	randomised	serious1	no serious	no serious	very serious <sup>2</sup>	reporting bias3	24/73	26/73	RR 0.92 (0.59	28 fewer per 1000 (from	$\oplus$ OOO	
	trials		inconsistency	indirectness			(32.9%)	(35.6%)	to 1.45)	146 fewer to 160 more)	VERY	
											LOW	
								35.6%		28 fewer per 1000 (from		
								33.0%		146 fewer to 160 more)		
Response	(any TCA ver	sus amisu	Ipride) (follow-up	13-26 weeks; ass	essed with: N	lumber of people	rated as	much or very	much improved	on Clinical Global Impre	ssions so	ale (CGI-I))
•	` ,		. ,	·				Í	•	· ·		, ,,
2	randomised	serious4	no serious	no serious	serious <sup>5</sup>	none	101/162	101/150	RR 0.92 (0.78	54 fewer per 1000 (from	⊕⊕00	
	trials		inconsistency	indirectness			(62.3%)	(67.3%)	to 1.09)	148 fewer to 61 more)	LOW	
			,				,	,	,	,	==	1
								07.00/		54 fewer per 1000 (from		1
								67.3%		148 fewer to 61 more)		1
Resnonse	l (aminentine)	versus am	isulnride) (follow-i	n mean 13 weeks	s. seebeeby	vith: Number of ne	onle rat	ed as much or	very much imr	proved on Clinical Global	Impressio	ne scale
(CGI-I))	(allillisptille	torous arri	iodipilao) (lollow-c	ip ilicali 10 week	, a5555564 v	Titli. Italiibei oi pe	opis rat	ou us much of	vory maon min	noved on onlinear Global	р. 63310	nio ocale
(55. 1))												

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> I-squared>50%

<sup>&</sup>lt;sup>4</sup> Unclear randomisation method and method of allocation concealment. Blinding of intervention administration and outcome assessment is unclear. Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>&</sup>lt;sup>5</sup> I-squared>80%

<sup>8 &</sup>lt;sup>6</sup> N<400 9 <sup>7</sup> Unclea

<sup>&</sup>lt;sup>7</sup> Unclear (or high risk of bias associated with) randomisation method and unclear method of allocation concealment. Unclear blinding of intervention administration

<sup>&</sup>lt;sup>8</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

<sup>11 &</sup>lt;sup>9</sup> Unclear randomisation method and method of allocation concealment. Blinding of intervention administration unclear

<sup>12 10 95%</sup> CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

1	randomised	serious4	no serious	no serious	serious <sup>6</sup>	none	55/89	54/77	RR 0.88 (0.71	84 fewer per 1000 (from	0000	
	trials	Serious	inconsistency	indirectness	serious	none	(61.8%)	(70.1%)	to 1.1)	203 fewer to 70 more)	⊕⊕OO LOW	
	triais		inconsistency	indirectiness			(01.070)	(70.170)	10 1.1)	200 lewer to 70 more)	LOVV	
										84 fewer per 1000 (from		
								70.1%		203 fewer to 70 more)		
Doenone	o (iminramino	Voreue an	ricularida) (fallow	un maan 26 waa	ke: accoccod	Lwith: Number of	poople rate	nd as much o	r vorv much imr	proved on Clinical Global	Impression	ne ecalo
CGI-I))	e (iiiiipraiiiiile	versus an	iisuipride) (ioliow	v-up illeali 20 wee	:K5, a5565560	i with. Number of	people rate	su as much o	i very much mi	noved on Chilical Global	iiipiessioi	is scale
	_											
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	46/73	47/73	RR 0.98 (0.77	13 fewer per 1000 (from	⊕OOO	
	trials		inconsistency	indirectness			(63%)	(64.4%)	to 1.25)	148 fewer to 161 more)	VERY	
									4		LOW	
								64.4%		13 fewer per 1000 (from		
										148 fewer to 161 more)		
				amisulpride) (follo	ow-up mean 1	3 weeks; measure	ed with: Mo	ontgomery As	berg Depressio	n Rating Scale (MADRS;	change sco	ore);
etter in	dicated by low	er values)										
		_										
	randomised	serious4	no serious	no serious	serious <sup>7</sup>	none	107	101	-	SMD 0.06 higher (0.21	⊕⊕⊙⊙	
	trials		inconsistency	indirectness						lower to 0.33 higher)	LOW	
									4 11 41 1			avente)
iscontir	nuation for any	/ reason (a	any TCA versus a	misulpride) (follo	w-up 13-26 w	eeks; assessed w	rith: Numbe	er of participa	ints discontinui	ng for any reason includi	ng adverse	events
iscontir	nuation for any	reason (a	any TCA versus a	misulpride) (follo	w-up 13-26 w	eeks; assessed w	ith: Numbe	er of participa	ints discontinui	ng for any reason includi	ng adverse	events
iscontii	randomised	serious <sup>8</sup>	no serious	no serious	serious <sup>9</sup>	none	75/184	67/177	RR 1.09 (0.84	34 more per 1000 (from	⊕⊕OO	events)
iscontii										•		events)
iscontii	randomised		no serious	no serious			75/184	67/177	RR 1.09 (0.84	34 more per 1000 (from	⊕⊕OO	events)
iscontii	randomised		no serious	no serious			75/184	67/177 (37.9%)	RR 1.09 (0.84	34 more per 1000 (from	⊕⊕OO	events)
iscontii	randomised		no serious	no serious			75/184	67/177	RR 1.09 (0.84	34 more per 1000 (from 61 fewer to 151 more)	⊕⊕OO	events
	randomised trials	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	none	75/184 (40.8%)	67/177 (37.9%) 38.3%	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more) 34 more per 1000 (from 61 fewer to 153 more)	⊕⊕OO LOW	
iscontii	randomised trials	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	none	75/184 (40.8%)	67/177 (37.9%) 38.3%	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more) 34 more per 1000 (from	⊕⊕OO LOW	
iscontii	randomised trials	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	none	75/184 (40.8%)	67/177 (37.9%) 38.3%	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more) 34 more per 1000 (from 61 fewer to 153 more)	⊕⊕OO LOW	
scontin	randomised trials	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	none	75/184 (40.8%)	67/177 (37.9%) 38.3%	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more) 34 more per 1000 (from 61 fewer to 153 more)	⊕⊕OO LOW	
iscontii	randomised trials nuation for any	serious <sup>8</sup>	no serious inconsistency	no serious indirectness s amisulpride) (fo	serious <sup>9</sup>	none 13 weeks; asses	75/184 (40.8%) ssed with: N	67/177 (37.9%) 38.3% Number of parts	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  atinuing for any reason in 4 more per 1000 (from	⊕⊕OO LOW	
iscontii	randomised trials nuation for any	serious <sup>8</sup>	no serious inconsistency	no serious indirectness	serious <sup>9</sup>	none 13 weeks; asses	75/184 (40.8%)	67/177 (37.9%) 38.3% Number of par	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more) 34 more per 1000 (from 61 fewer to 153 more) ntinuing for any reason in	⊕⊕OO LOW	
iscontii	randomised trials nuation for any	serious <sup>8</sup>	no serious inconsistency	no serious indirectness s amisulpride) (fo	serious <sup>9</sup>	none 13 weeks; asses	75/184 (40.8%) ssed with: N	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%)	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  ntinuing for any reason in 4 more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW	
iscontii	randomised trials nuation for any	serious <sup>8</sup>	no serious inconsistency	no serious indirectness s amisulpride) (fo	serious <sup>9</sup>	none 13 weeks; asses	75/184 (40.8%) ssed with: N	67/177 (37.9%) 38.3% Number of parts	RR 1.09 (0.84 to 1.4)	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  ntinuing for any reason in 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW	
iscontii vents)	randomised trials  nuation for any  randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency	no serious indirectness s amisulpride) (fo	serious <sup>9</sup> bllow-up mear  very serious <sup>10</sup>	none  13 weeks; asses	75/184 (40.8%) seed with: N	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%)	RR 1.09 (0.84 to 1.4)  ticipants discording to 1.45)	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  atinuing for any reason in 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW	verse
iscontii vents)	randomised trials  nuation for any  randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency	no serious indirectness s amisulpride) (fo	serious <sup>9</sup> bllow-up mear  very serious <sup>10</sup>	none  13 weeks; asses	75/184 (40.8%) seed with: N	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%)	RR 1.09 (0.84 to 1.4)  ticipants discording to 1.45)	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  ntinuing for any reason in 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW	verse
iscontii vents)	randomised trials  nuation for any  randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency	no serious indirectness s amisulpride) (fo	serious <sup>9</sup> bllow-up mear  very serious <sup>10</sup>	none  13 weeks; asses	75/184 (40.8%) seed with: N	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%)	RR 1.09 (0.84 to 1.4)  ticipants discording to 1.45)	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  atinuing for any reason in 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW	verse
iscontii vents)	randomised trials  nuation for any randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency  amineptine versus  no serious inconsistency  mipramine versus	no serious indirectness s amisulpride) (fo	serious <sup>9</sup> llow-up mear  very serious <sup>10</sup>	none  13 weeks; asses  none  26 weeks; asses	75/184 (40.8%) seed with: N 40/111 (36%)	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%) 35.6%	RR 1.09 (0.84 to 1.4)  ticipants discontained in the second secon	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  at more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  ntinuing for any reason in	⊕⊕OO LOW  cluding ad  ⊕OOO VERY LOW	verse
iscontii vents)	randomised trials  randomised trials  randomised trials  randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency  no serious no serious inconsistency  mipramine versus	no serious indirectness s amisulpride) (for no serious indirectness s amisulpride) (for no serious indirectness	serious <sup>9</sup> bllow-up mear  very serious <sup>10</sup>	none  13 weeks; asses	75/184 (40.8%) seed with: N 40/111 (36%)	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%) 35.6% Number of part	RR 1.09 (0.84 to 1.4)  ticipants discontained to 1.45  RR 1.01 (0.71 to 1.45)  rticipants discontained to 1.45	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  at more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  at more per 1000 (from 103 fewer to 160 more)  at more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW  cluding ad  ⊕OOO VERY LOW  cluding ad	verse
iscontii vents)	randomised trials  nuation for any randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency  amineptine versus  no serious inconsistency  mipramine versus	no serious indirectness s amisulpride) (fo	serious <sup>9</sup> llow-up mear  very serious <sup>10</sup>	none  13 weeks; asses  none  26 weeks; asses	75/184 (40.8%) seed with: N 40/111 (36%)	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%) 35.6%	RR 1.09 (0.84 to 1.4)  ticipants discontained in the second secon	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  at more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  ntinuing for any reason in	⊕⊕OO LOW  cluding ad  ⊕OOO VERY LOW  cluding ad  ⊕OOO VERY	verse
iscontii vents)	randomised trials  randomised trials  randomised trials  randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency  no serious no serious inconsistency  mipramine versus	no serious indirectness s amisulpride) (for no serious indirectness s amisulpride) (for no serious indirectness	serious <sup>9</sup> llow-up mear  very serious <sup>10</sup>	none  13 weeks; asses  none  26 weeks; asses	75/184 (40.8%) seed with: N 40/111 (36%)	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%) 35.6% Number of part	RR 1.09 (0.84 to 1.4)  ticipants discontained to 1.45  RR 1.01 (0.71 to 1.45)  rticipants discontained to 1.45	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  ntinuing for any reason in 4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  ntinuing for any reason in 70 more per 1000 (from 78 fewer to 279 more)	⊕⊕OO LOW  cluding ad  ⊕OOO VERY LOW  cluding ad	verse
iscontii vents)	randomised trials  randomised trials  randomised trials  randomised trials	serious <sup>8</sup> reason (a	no serious inconsistency  no serious no serious inconsistency  mipramine versus	no serious indirectness s amisulpride) (for no serious indirectness s amisulpride) (for no serious indirectness	serious <sup>9</sup> llow-up mear  very serious <sup>10</sup>	none  13 weeks; asses  none  26 weeks; asses	75/184 (40.8%) seed with: N 40/111 (36%)	67/177 (37.9%) 38.3% Number of part 37/104 (35.6%) 35.6% Number of part	RR 1.09 (0.84 to 1.4)  ticipants discontained to 1.45  RR 1.01 (0.71 to 1.45)  rticipants discontained to 1.45	34 more per 1000 (from 61 fewer to 151 more)  34 more per 1000 (from 61 fewer to 153 more)  at more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  4 more per 1000 (from 103 fewer to 160 more)  at more per 1000 (from 103 fewer to 160 more)  at more per 1000 (from 103 fewer to 160 more)	⊕⊕OO LOW  cluding ad  ⊕OOO VERY LOW  cluding ad  ⊕OOO VERY	verse

	randomised	serious8	no serious	no serious	serious <sup>5</sup>	reporting bias <sup>3</sup>	22/184	10/177	RR 2.16 (1.08	66 more per 1000 (from 5	⊕000
	trials		inconsistency	indirectness			(12%)	(5.6%)	to 4.35)	more to 189 more)	VERY
			·				, ,	, í	,	·	LOW
								6.4%		74 more per 1000 (from 5	
								0.470		more to 214 more)	
sconti	nuation due to	adverse e	vents (amineptin	e versus amisulp	ride) (follow-u	p mean 13 weeks	assessed	d with: Numbe	er of participant	s discontinuing due to ad	verse even
	randomised	serious8	no serious	no serious	very	none	5/111	2/104	RR 2.34 (0.46	26 more per 1000 (from	$\oplus$ OOO
	trials		inconsistency	indirectness	serious <sup>10</sup>		(4.5%)	(1.9%)	to 11.81)	10 fewer to 208 more)	VERY
											LOW
								1.9%		25 more per 1000 (from	
								1.970		10 fewer to 205 more)	
coonti	nuation due to	adverse e	vents (imipramin	e versus amisulp	ride) (follow-u	p mean 26 weeks	assessed	d with: Numbe	er of participant	s discontinuing due to ad	verse ever
Sconti											
SCOIILI				no serious	serious9	reporting bias <sup>3</sup>	17/73	8/73	RR 2.12 (0.98	123 more per 1000 (from	⊕OOO
SCOTILI	randomised	serious8	no serious	no senous						0.5 ( 000 )	
Sconti	randomised trials	serious <sup>8</sup>	no serious inconsistency	indirectness			(23.3%)	(11%)	to 4.61)	2 fewer to 396 more)	VERY
Sconti		serious <sup>8</sup>					(23.3%)	(11%)	to 4.61)	2 fewer to 396 more)	VERY LOW
Sconu		serious <sup>8</sup>					(23.3%)	(11%)	to 4.61)	2 fewer to 396 more)  123 more per 1000 (from 2 fewer to 397 more)	

<sup>&</sup>lt;sup>1</sup> Randomisation method and method of allocation concealment is unclear. Blinding of intervention administrator is also unclear and there is an unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

3

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8

10

11

12

#### Duloxetine versus placebo for chronic depression

			Quality asse	ssment			No of pa	tients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Duloxetine	Placebo	Relative (95% CI)	Absolute		

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data is not reported or cannot be extracted for all outcomes

<sup>&</sup>lt;sup>4</sup> Randomisation method and method of allocation concealment is unclear. Blinding of intervention administration and outcome assessment is also unclear and there is an unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

<sup>&</sup>lt;sup>5</sup> Events<300

<sup>&</sup>lt;sup>6</sup> 95% CI crosses both the line of no effect and the threshold for clinically important harm (RR 0.75)

<sup>9 &</sup>lt;sup>7</sup> N<40

<sup>&</sup>lt;sup>8</sup> Randomisation method and method of allocation concealment is unclear. Blinding of intervention administration is also unclear

<sup>&</sup>lt;sup>9</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

<sup>&</sup>lt;sup>10</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

serious<sup>2</sup>

no serious

indirectness

Remission (follow-up mean 10 weeks; assessed with: Number of people scoring ≤4 on Hamilton Rating Scale for Depression (HAM-D) AND HAMD item # 1 (depressed mood) score=0)

16/29

(55.2%)

(14.3%)

to 10.13)

RR 3.86 (1.47 409 more per 1000 (from 67

more to 1000 more)

 $\oplus$ OOO

VERY LOW

reporting bias3

#### Phenelzine versus placebo for chronic depression

no serious

inconsistency

randomised

trials

1 2

3 4

5

6

very

serious1

			Quality asse	ssment			No of pa	tients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phenelzine	Placebo	Relative (95% CI)	Absolute		
Response	(follow-up me	an 6 week	s; assessed with:	Number of people	rated as mu	ch or very much in	nproved on	Clinical	Global Impress	ions scale (CGI-I))		
	randomised trials			no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	7/12 (58.3%)	9/27 (33.3%) 33.3%	RR 1.75 (0.85 to 3.58)	250 more per 1000 (from 50 fewer to 860 more) 250 more per 1000 (from 50 fewer to 859 more)	⊕OOO VERY LOW	

<sup>3</sup> Data is not reported or cannot be extracted for all outcomes

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# Phenelzine versus imipramine for chronic depression

			Quality asse	essment			No of p	atients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phenelzine	Imipramine	Relative (95% CI)	Absolute		
Response	(follow-up me	ean 6 weel	ks; assessed with:	Number of peop	le rated as m	uch or very much	improved o	n Clinical G	lobal Impressi	ons scale (CGI-I))		
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	reporting bias <sup>3</sup>	7/12 (58.3%)	14/18 (77.8%)	RR 0.75 (0.44 to 1.28)	194 fewer per 1000 (from 436 fewer to 218 more)	⊕000 VERY LOW	
								77.8%		195 fewer per 1000 (from 436 fewer to 218 more)		
Depressio	n symptomat	ology (foll	ow-up mean 6 wee	eks; measured wi	th: Hamilton	Rating Scale for D	epression (	HAM-D at er	ndpoint); Bette	r indicated by lower value	es)	
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	16	16	-	SMD 0.73 lower (1.45 to 0.01 lower)	⊕⊕OO LOW	
Discontinu	uation for any	reason (fo	ollow-up mean 6 w	eeks; assessed v	vith: Number	of participants di	scontinuing	for any reas	son including	adverse events)		
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>6</sup>	none	3/19 (15.8%)	4/20 (20%)	RR 0.79 (0.2 to 3.07)	42 fewer per 1000 (from 160 fewer to 414 more) 42 fewer per 1000 (from	⊕000 VERY LOW	
Discontinu	uation due to	adverse ev	vents (follow-up m	ean 6 weeks; ass	sessed with:	Number of particip	pants discor	20%	to adverse ev	160 fewer to 414 more)		
										· ·	0000	
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>6</sup>	none	3/19 (15.8%)	4/20 (20%)	RR 0.79 (0.2 to 3.07)	42 fewer per 1000 (from 160 fewer to 414 more)	⊕000 VERY LOW	
								20%		42 fewer per 1000 (from 160 fewer to 414 more)		

<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administrator(s)

<sup>&</sup>lt;sup>2</sup> 95% CI crosses line of no effect and threshold for both clinically important harm (RR 0.75) and clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data is not reported or cannot be extracted for all outcomes

<sup>&</sup>lt;sup>4</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment

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# Moclobemide versus placebo for chronic depression

			Quality asse	essment			No of pati	ients		Effect		
											Quality	Important
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Moclobemide	Placebo	Relative (95% CI)	Absolute		
Remissio	n (follow-up m	ean 8 wee	ks; assessed with	: Number of peop	ole scoring ≤₄	4 on Hamilton Rati	ng Scale for D	epressio	on (HAM-D))			
1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	33/104	16/97	RR 1.92 (1.13	152 more per 1000 (from	⊕⊕OO	
	trials		inconsistency	indirectness			(31.7%)	(16.5%)		21 more to 374 more)	LOW	
								16.5%		152 more per 1000 (from 21 more to 375 more)		
Response	(follow-up m	ean 8 weel	ks; assessed with:	Number of peop	le showing ≥	50% improvement	on Hamilton F	Rating So	cale for Depres	sion (HAM-D))		
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	74/104 (71.2%)	29/97 (29.9%)	RR 2.38 (1.71 to 3.31)	413 more per 1000 (from 212 more to 691 more)	⊕⊕OO LOW	
								29.9%		413 more per 1000 (from 212 more to 691 more)		
Depressio	on symptomat	ology (foll	ow-up mean 8 wee	eks; measured wi	th: Hamilton	Rating Scale for D	epression (HA	M-D; ch	ange score); Be	etter indicated by lower va	lues)	
I	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	104	97	-	SMD 1.03 lower (1.33 to 0.74 lower)	⊕⊕OO LOW	
Discontin	l uation for any	reason (fo	l ollow-up mean 8 w	eeks; assessed v	with: Number	of participants dis	continuing fo	r any rea	son including	adverse events)		
	randomised	serious <sup>1</sup>	no serious	no serious	very	none	13/108	15/104	RR 0.83 (0.42	25 fewer per 1000 (from	⊕OOO	
	trials		inconsistency	indirectness	serious <sup>4</sup>		(12%)	(14.4%)	to 1.67)	84 fewer to 97 more)	VERY LOW	
								14.4%		24 fewer per 1000 (from 84 fewer to 96 more)		
Discontin	uation due to	adverse ev	vents (follow-up m	ean 8 weeks; ass	sessed with:	Number of particip	ants discontir	nuing du	e to adverse ev	ents)		
	randomised	serious <sup>1</sup>	no serious	no serious	very	none	7/108	2/104	DD 3 37 (0 72	46 more per 1000 (from 5		

								1.9%		45 more per 1000 (from 5 fewer to 282 more)	⊕000 VERY LOW	
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<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment

#### Moclobemide versus imipramine for chronic depression

			Quality asse	essment			No of pa	atients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Moclobemide	Imipramine	Relative (95% CI)	Absolute		
Remission	ı (follow-up m	ean 8 wee	eks; assessed with	: Number of peo	ple scoring ≤	4 on Hamilton Rat	ing Scale for I	Depression	(HAM-D))			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	33/104 (31.7%)	19/94 (20.2%)	RR 1.57 (0.96 to 2.56)	115 more per 1000 (from 8 fewer to 315 more) 115 more per 1000 (from	LOW	
Response	(follow-up m	ean 8 wee	ks; assessed with	Number of peop	ole showing 2	≥50% improvemen	t on Hamilton	20.2% Rating Scal	e for Depression	8 fewer to 315 more)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	74/104 (71.2%)	65/94 (69.1%)	RR 1.03 (0.86 to 1.23)	21 more per 1000 (from 97 fewer to 159 more)	⊕⊕OO LOW	
_			_					69.2%		21 more per 1000 (from 97 fewer to 159 more)		
Depressio	n symptomat	ology (foll	ow-up mean 8 wee	eks; measured w	ith: Hamilton	Rating Scale for I	Depression (H	AM-D; chan	ge score); Beti	ter indicated by lower va	lues)	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	104	94	-	SMD 0.16 lower (0.44 lower to 0.12 higher)	⊕⊕OO LOW	
Discontinu	uation for any	reason (f	ollow-up mean 8 w	eeks; assessed	with: Numbe	r of participants di	scontinuing fo	or any reaso	on including ac	Iverse events)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	13/108 (12%)	15/103 (14.6%)	RR 0.83 (0.41 to 1.65)	25 fewer per 1000 (from 86 fewer to 95 more)	⊕000 VERY LOW	
								14.6%		25 fewer per 1000 (from 86 fewer to 95 more)		

<sup>&</sup>lt;sup>2</sup> Events<300

<sup>&</sup>lt;sup>3</sup> N<400

<sup>&</sup>lt;sup>4</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

Discontin	uation due to	adverse e	vents (follow-up n	nean 8 weeks; ass	sessed with:	Number of particip	oants disconti	nuing due t	o adverse eve	nts)		
					1	1						
1	randomised	serious <sup>1</sup>	no serious	no serious	very	none	7/108	11/103	RR 0.61 (0.24	42 fewer per 1000 (from	⊕OOO	
	trials		inconsistency	indirectness	serious <sup>5</sup>		(6.5%)	(10.7%)	to 1.51)	81 fewer to 54 more)	VERY	
											LOW	
								10.7%		42 fewer per 1000 (from		
								10.7%		81 fewer to 55 more)		

<sup>&</sup>lt;sup>1</sup> Unclear randomisation method and method of allocation concealment, and unclear blinding of intervention administration and outcome assessment

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## Amisulpride versus placebo for chronic depression

			Quality asse	ssment			No of pat	ients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Amisulpride	Placebo	Relative (95% CI)	Absolute		
	(5.11									4550		
Remission (follow-up mean 26 weeks; assessed with: Number of people scoring <8 on Montgomery Asberg Depression Rating Scale (MADRS))												
	randomised trials			no serious indirectness	serious <sup>2</sup>	reporting bias <sup>3</sup>	26/73 (35.6%)	16/73 (21.9%)	RR 1.62 (0.95 to 2.77)	136 more per 1000 (from 11 fewer to 388 more)	⊕000 VERY LOW	
								21.9%		136 more per 1000 (from 11 fewer to 388 more)	LOW	
Response	(follow-up 13	-26 weeks	; assessed with: N	umber of people	rated as muc	h or very much im	proved on Cl	inical Gl	obal Impressio	ns scale (CGI-I))		
	randomised trials			no serious indirectness	serious <sup>4</sup>	none	101/150 (67.3%)	52/157 (33.1%)	RR 2.03 (1.59 to 2.61)	341 more per 1000 (from 195 more to 533 more)	⊕⊕OO LOW	
								33.2%		342 more per 1000 (from 196 more to 535 more)		
Depressio	n symptomato	ology (follo	ow-up mean 13 we	eks; measured w	ith: Montgom	nery Asberg Depre	ssion Rating	Scale (M	ADRS; change	score); Better indicated b	y lower v	alues)
	randomised trials			no serious indirectness	serious <sup>5</sup>	none	101	105	-	SMD 0.68 lower (0.97 to 0.4 lower)	⊕⊕OO LOW	
Discontinu	uation for any	reason (fo	llow-up 13-26 wee	ks; assessed wit	 h: Number of	participants disco	ntinuina for	anv reas	on including a	dverse events)	<u> </u>	

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Events<300

<sup>2</sup> 3 4 <sup>4</sup> N<400

<sup>&</sup>lt;sup>5</sup> 95% CI crosses line of no effect and threshold for both clinically important benefit (RR 0.75) and clinically important harm (RR 1.25)

2	randomised	serious <sup>6</sup>	no serious	no serious	serious <sup>7</sup>	none	67/177	78/181	RR 0.87 (0.68	56 fewer per 1000 (from	⊕⊕00	
	trials		inconsistency	indirectness			(37.9%)	(43.1%)	to 1.12)	138 fewer to 52 more)	LOW	
								44.1%		57 fewer per 1000 (from		
										141 fewer to 53 more)		
Discontinuation due to adverse events (follow-up 13-26 weeks; assessed with: Number of participants discontinuing due to adverse events)												
_												
2		serious <sup>6</sup>	no serious		serious <sup>8</sup>	reporting bias <sup>3</sup>	10/177		,	38 more per 1000 (from 1	⊕OOO	
	trials		inconsistency	indirectness			(5.6%)	(1.7%)	to 11.9)	fewer to 181 more)	VERY	
											LOW	
								1.8%		42 more per 1000 (from 1		
								1.070		fewer to 196 more)		

Unclear randomisation method and method of allocation concealment and unclear blinding of intervention administrator(s). Unclear risk of attrition bias (drop-out>20% but difference between groups<20% and ITT analysis used)

#### Complex depression (chapter 10) 10

# CBT/behavioural therapies versus psychodynamic therapies

	Quality assessment							atients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT/behavioural therapies	Psychodynamic therapies	Relative (95% CI)	Absolute		
Depressio	on symptoma	atology at	endpoint (meas	ured with: BDI;	Better indica	ted by lower valu	es)					
				no serious indirectness	serious <sup>2</sup>	none	26	25	-	MD 6.35 lower (13.18 lower to 0.47 higher)	⊕000 VERY LOW	CRITICAL

<sup>&</sup>lt;sup>2</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 1.25)

<sup>&</sup>lt;sup>3</sup> Data is not reported or cannot be extracted for all outcomes

<sup>&</sup>lt;sup>4</sup> Events<300

<sup>4</sup> 5 6 <sup>5</sup> N<400

<sup>&</sup>lt;sup>6</sup> Unclear randomisation method and method of allocation concealment and unclear blinding of intervention administrator(s).

<sup>&</sup>lt;sup>7</sup> 95% CI crosses both line of no effect and threshold for clinically important benefit (RR 0.75)

<sup>&</sup>lt;sup>8</sup> 95% CI crosses both line of no effect and threshold for clinically important harm (RR 1.25)

)	randomised	very	no serious	no serious	serious <sup>2</sup>	none	26	25	-	MD 0.3 lower (0.86	⊕000	CRITICAL
	trials	serious <sup>1</sup>	inconsistency	indirectness						lower to 0.25	VERY	
			,							higher)	LOW	
										,		
epression	on symptom	atology (f	ollow-up 24 wee	ks; measured v	vith: BDI; Be	tter indicated by lo	wer values)					
	randomised	very	no serious	no serious	serious <sup>3</sup>	none	12	12	-	MD 9.00 lower	⊕000	CRITICAL
	trials	serious <sup>1</sup>	inconsistency	indirectness						(16.09 to 1.91	VERY	
										lower)	LOW	
epression	on symptom	atology (f	ollow-up 36 wee	ks; measured v	vith: BDI; Be	etter indicated by lo	wer values)					
	randomised	very	no serious	no serious	very	none	12	12	-	MD 3.00 lower	⊕OOO	CRITICAL
	trials	serious1	inconsistency	indirectness	serious4					(11.84 lower to 5.84	VERY	
										higher)	LOW	
epressio	on symptom	atology (f	ollow-up 1 vears	: measured wit	h: BDI: Bette	er indicated by low	er values)					
Бриссон				,	221, 2011	,	·					
	randomised	- ,	no serious	no serious	very	none	14	13	-	MD 0.25 higher	$\oplus$ OOO	CRITICA
	trials	serious <sup>1</sup>	inconsistency	indirectness	serious4					(6.87 lower to 7.37	VERY	
										higher)	LOW	
uicide a	ttempts (follo	ow-up 24	weeks)									
	randomised	very	no serious	no serious	very	none	3/12	4/12	RR 0.75	83 fewer per 1000	⊕000	CRITICAL
	trials	,	inconsistency	indirectness	serious <sup>4</sup>	110110	(25%)	(33.3%)	(0.21 to	(from 263 fewer to	VERY	01411074
	indio	CONOGO	inconcionation	in an oour ooc	Concac		(2070)	(00.070)	2.66)	553 more)	LOW	
									,	,		
										83 fewer per 1000		
								33.3%		(from 263 fewer to		
										553 more)		
uicide a	ttempts (2 ye	ear follow	-up) (follow-up 2	years)	•							
	randomised	very	no serious	no serious	very	none	5/12	6/12	RR 0.83	85 fewer per 1000	⊕000	CRITICAL
	trials	serious1	inconsistency	indirectness	serious4		(41.7%)	(50%)	(0.35 to	(from 325 fewer to	VERY	
									2.00)	500 more)	LOW	
										85 fewer per 1000		
								50%		(from 325 fewer to		
								30 /0		500 more)		
iscontin	uations for a	any reaso	n .							,		
		,										

randomised very

<sup>1</sup> High ROB across multiple domains

<sup>3</sup> OIS not met (<400 participants)

<sup>2</sup> 95% CI crosses one clinical decision threshold

4 95% CI crosses two clinical decision thresholds

trials

no serious

serious<sup>1</sup> inconsistency

# Pharmacotherapy versus combination therapy (pharmacotherapy + SPSP)

no serious

indirectness

very serious<sup>4</sup>

none

			Quality ass	essment			No of patients			Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pharmacotherapy versus combi therapy (pharm + SPSP)	Control	Relative (95% CI)	Absolute	Quality	<u>Importance</u>
Depressi	on symptoma	atology (m	neasured with: H	AM-D 17; Better	indicated by	lower values)						
2		very serious <sup>1</sup>	very serious <sup>2</sup>		very serious <sup>3</sup>	none	46	58	-	MD 8 higher (1.35 lower to 17.34 higher)	⊕OOO VERY LOW	CRITICAL
Depressi	on symptoma	atology at	endpoint (pharm	protocol versu	ıs pharm + S	PSP) (follow-up m	ean 24 weeks; measured with	h: HAM-C	17; Better	indicated by lower v	alues)	
1	randomised trials		no serious inconsistency		very serious <sup>5</sup>	none	36	49	-	MD 3.79 higher (0.36 to 7.22 higher)	⊕000 VERY LOW	CRITICAL
Depressi	on symptoma	atology (lo	ofepramine alone	versus lofepra	mine + RET)	(Better indicated	by lower values)					
1		- ,	no serious inconsistency	no serious indirectness	serious <sup>7</sup>	none	10	9	-	MD 13.4 higher (5.92 to 20.88 higher)	⊕000 VERY LOW	CRITICAL

7/36

(19.4%)

RR 0.73

(0.33 to 1.60)

73 fewer per 1000

(from 181 fewer to

162 more)

73 fewer per 1000

(from 181 fewer to 162 more)

10/37

(27%)

27%

CRITICAL

⊕000 VERY

LOW

Remissio	emission at endpoint (follow-up mean 24 weeks; assessed with: HAM-D 17)											
1	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	7/36 (19.4%)	23/49 (46.9%)	RR 0.41 (0.2 to 0.86)	277 fewer per 1000 (from 66 fewer to 376 fewer)	⊕000 VERY LOW	CRITICAL
Disconti	nuations for a	anv reaso	n					0%		-		
1	1		no serious	no serious	Von	none	0/10	1/10	RR 0.33	67 fewer per 1000	⊕000	CRITICAL
1			inconsistency	indirectness	very serious <sup>3</sup>	none	(0%)	(10%)	(0.02 to 7.32)	(from 98 fewer to 632 more)	⊎000 VERY LOW	CRITICAL
									1.52)	67 fewer per 1000	LOW	
								10%		(from 98 fewer to 632 more)		

<sup>&</sup>lt;sup>1</sup> High or unclear ROB across multiple domains

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# Psychotic depression (chapter 10)

# Antidepressants versus other pharmacological interventions

### 11 Antidepressants versus placebo

Quality assessment		No of patients	S		Effect				
					Quality	Importance			
No of studies Design Risk of bias Inconsistency Indirectness Imprecisi	Other considerations	Antidepressant versus placebo	Control	Relative (95% CI)	Absolute				
Depressive symptoms at endpoint (HAMD 17) - TCA versus placebo (Better indicated by lower values)									

<sup>&</sup>lt;sup>2</sup> I2 >80%

<sup>&</sup>lt;sup>3</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>4</sup> High risk of bias for selective outcome reporting and allocation concealment unlikely to affect results, however unclear effect of bias from missing outcome data

<sup>&</sup>lt;sup>5</sup> Confidence intervals cross 1 minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 events for dichotomous outcomes).

<sup>&</sup>lt;sup>6</sup> High ROB across multiple domains

<sup>&</sup>lt;sup>7</sup> OIS not met (<400 participants)

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							1	1				
1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	69	67	-	MD 3 lower (4.71 to	$\oplus \oplus OO$	CRITICAL
	trials		inconsistency	indirectness						1.29 lower)	LOW	
										,		
Remissio	n - TCA versu	s placebo	)				<u> </u>					
1	randomised	serious <sup>3</sup>	no serious	no serious	very	none	4/10	0/10	RR 9 (0.55 to	-	⊕OOO	CRITICAL
	trials		inconsistency	indirectness	serious4		(40%)	(0%)	147.95)		VERY	
			oonolotonoj		00.100.0		(1070)	(0,0)			LOW	
								0%		_	LOVV	
								0 /0		-		L
Response - TCA versus placebo												
1	randomised	serious1	no serious	no serious	serious <sup>5</sup>	none	53/69	15/67	not pooled	not pooled	$\oplus \oplus OO$	CRITICAL
	trials		inconsistency	indirectness			(76.8%)	(22.4%)			LOW	
			,				,	,				
								22.4%		not pooled		
		<u> </u>	L .					22.470		not pooled		<u> </u>
Disconti	nuation - TCA	versus pl	acebo									
2	randomised	serious <sup>3</sup>	no serious	no serious	very	none	7/86	3/87	RR 1.88 (0.4	30 more per 1000 (from	$\oplus$ OOO	CRITICAL
	trials		inconsistency	indirectness	serious4		(8.1%)	(3.4%)	to 8.82)	21 fewer to 270 more)	VERY	
			,				,	, ,	,	,	LOW	
									1	101 more per 1000		
								11.5%		(from 69 fewer to 899		
								11.5%		,		
										more)		

<sup>&</sup>lt;sup>1</sup> Unclear ROB across multiple domians

## Antidepressants versus antidepressants

	Quality assessment									Effect	Quality	<b>Importance</b>
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressant versus antidepressant	Control	Relative (95% CI)	Absolute		
Depressi	Depressive symptoms at endpoint - TCA versus SNRI (Better indicated by lower values)											
1		no serious risk of bias		no serious indirectness	very serious <sup>1</sup>	none	17	12	-	MD 1.1 higher (1.47 lower to 3.67 higher)	⊕⊕OO LOW	CRITICAL

OIS not met (<400 participants)</li>
 High ROB in one domain and unclear in several others

<sup>&</sup>lt;sup>4</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>5</sup> OIS not met (<300 events)

	randomised	no serious	no serious	no serious	very	none	12	10	-	MD 0.3 higher (8.72	$\oplus \oplus OO$	CRITICA
	trials	risk of bias	inconsistency	indirectness	serious <sup>1</sup>					lower to 9.32 higher)	LOW	
nissio	n - SSRI vers	sus SNRI		_								
	randomised	serious <sup>2</sup>	no serious	no serious	serious <sup>3</sup>	none	9/11	6/11	RR 1.5 (0.82	273 more per 1000	⊕⊕ОО	CRITICA
	trials		inconsistency	indirectness			(81.8%)	(54.5%)	to 2.75)	(from 98 fewer to	LOW	
										955 more)		
										273 more per 1000		
								54.6%		(from 98 fewer to		
										956 more)		L
nissio	n - SSRI (ser	traline) vers	us SSRI (paroxe	etine)								
	randomised	serious <sup>2</sup>	no serious	no serious	serious <sup>3</sup>	none	13/18	3/14	RR 3.37	508 more per 1000	⊕⊕ОО	CRITIC
	trials		inconsistency	indirectness			(72.2%)	(21.4%)	(1.19 to	(from 41 more to	LOW	
									9.57)	1000 more)		
										507 more per 1000		
								21.4%		(from 41 more to		
										1000 more)		
nissio	n - TCA vers	us SNRI										
	randomised	no serious	no serious	no serious	serious <sup>3</sup>	none	15/20	11/12	RR 0.82 (0.6	165 fewer per 1000	⊕⊕⊕О	CRITIC
	trials	risk of bias	inconsistency	indirectness			(75%)	(91.7%)		(from 367 fewer to	MODERATE	
										101 more)		
										165 fewer per 1000		
								91.7%		(from 367 fewer to		
										101 more)		
pons	e - TCA versu	ıs atypical A	DM			•						
	randomised	serious <sup>4</sup>	no serious	no serious	very	none	9/15	7/15	RR 1.29	135 more per 1000	⊕000	CRITIC
	trials		inconsistency	indirectness	serious1		(60%)	(46.7%)	(0.65 to		VERY LOW	
									2.54)	719 more)		
										135 more per 1000		
								46.7%		(from 163 fewer to		
	l	I	1		1	1			1	` 719 more)		1

1	randomised	no serious	no serious	no serious	serious <sup>3</sup>	none	16/20	12/13	RR 0.87	120 fewer per 1000	⊕⊕⊕О	CRITICAL
		risk of bias	inconsistency	indirectness	0011000	110110	(80%)	(92.3%)			MODERATE	0.4
							(00,0)	(======================================	1.13)	120 more)	MODEROTIL	
									- /	,		
										120 fewer per 1000		
								92.3%		(from 314 fewer to		
										120 more)		
Response	e - TCA versu	is SSRI										
l,	randomised	serious <sup>4</sup>	no serious	no serious	serious <sup>3</sup>	none	16/25	7/25	RR 2.29	361 more per 1000	⊕⊕OO	CRITICAL
	trials	0011000	inconsistency	indirectness	CONTOGO	110110	(64%)	(28%)	(1.14 to	(from 39 more to	LOW	OT IT TO TE
							(0.70)	(==,,,	4.58)	1000 more)	2011	
									/	,		
									]	361 more per 1000		
								28%		(from 39 more to		
										1000 more)		
Discontin	uation - TCA	versus aty	pical antidepress	ant		•	·					
	randomised	serious <sup>4</sup>	no serious	no serious	very	none	4/15	8/15	RR 0.5 (0.19	267 fewer per 1000	⊕OOO	CRITICAL
	trials	3011003	inconsistency	indirectness	serious <sup>1</sup>	Horic	(26.7%)	(53.3%)		(from 432 fewer to	VERY LOW	ORTHOAL
	uidio		inconsistency	indirectiness	Scrious		(20.170)	(00.070)	10 1.01)	165 more)	VEIXI LOW	
										100 111010)		
										266 fewer per 1000		
								53.3%		(from 432 fewer to		
										165 more)		
Discontin	uation - TCA	versus SSI	રા	•			•					
ı l.	randomised	serious <sup>4</sup>	no serious	no serious	very	none	4/25	2/25	RR 2 (0.4 to	80 more per 1000	⊕000	CRITICAL
	trials	Serious	inconsistency	indirectness	serious <sup>1</sup>	Hone	(16%)	(8%)	9.95)	(from 48 fewer to	VERY LOW	CITITIOAL
	uiais		inconsistency	indirectiness	SCHOUS		(1070)	(070)	0.00)	716 more)	VEIXT LOW	
										r to more)		
									1	80 more per 1000		
								8%		(from 48 fewer to		
										716 more)		
Discontin	uation - TCA	versus SNI	રા							,	1	
		laa aasia	la a a sui a co	luna naminus	l.am.		3/20	4/40	RR 1.95	70 1000	0000	CRITICAL
		no serious	no serious	no serious	very	none		1/13		73 more per 1000	⊕⊕00	CRITICAL
	trials	risk of bias	inconsistency	indirectness	serious <sup>5</sup>		(15%)	(7.7%)	(0.23 to	(from 59 fewer to	LOW	
									16.79)	1000 more)		
										73 more per 1000		
								7.7%		(from 59 fewer to		
										1000 more)		

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randomised	serious <sup>2</sup>	no serious	no serious	very	none	0/12	2/12	RR 0.2 (0.01	133 fewer per 1000	⊕000	CRITICA
trials		inconsistency	indirectness	serious <sup>1</sup>		(0%)	(16.7%)	to 3.77)	(from 165 fewer to	VERY LOW	
									462 more)		
								1	134 fewer per 1000		
							16.7%		(from 165 fewer to		
									463 more)		
ontinuation - SS	RI (sertralir	ne) versus SSRI (p	aroxetine)								
randomised	serious <sup>2</sup>	no serious	no serious	serious <sup>3</sup>	none	0/18	5/14	RR 0.07 (0	332 fewer per 1000	⊕⊕OO	CRITIC
trials		inconsistency	indirectness			(0%)	(35.7%)		(from 357 fewer to	LOW	
									71 more)		
								1	332 fewer per 1000		
							35.7%		(from 357 fewer to		
									71 more)		
continuation - SS	RI versus S	INRI							71 more)		
randomised		no serious	no serious	very	none	0/11		RR 0.2 (0.01	145 fewer per 1000	⊕000	CRITIC
			no serious indirectness	very serious <sup>1</sup>	none	0/11 (0%)	2/11 (18.2%)		145 fewer per 1000 (from 180 fewer to	⊕000 VERY LOW	CRITIC
randomised		no serious			none				145 fewer per 1000		CRITIC
randomised		no serious			none				145 fewer per 1000 (from 180 fewer to		CRITIC
randomised		no serious			none				145 fewer per 1000 (from 180 fewer to 498 more)		CRITIC
randomised		no serious			none		(18.2%)		145 fewer per 1000 (from 180 fewer to 498 more) 146 fewer per 1000		CRITIC
randomised trials	serious <sup>2</sup>	no serious	indirectness	serious <sup>1</sup>			(18.2%)		145 fewer per 1000 (from 180 fewer to 498 more) 146 fewer per 1000 (from 180 fewer to		CRITIC
randomised trials	serious <sup>2</sup>	no serious inconsistency	indirectness	serious¹  TCA (imipra			18.2%		145 fewer per 1000 (from 180 fewer to 498 more) 146 fewer per 1000 (from 180 fewer to		CRITIO
randomised trials	serious <sup>2</sup>	no serious inconsistency	indirectness ramine) versus	serious¹  TCA (imipra	mine)	(0%)	18.2%	to 3.74)	145 fewer per 1000 (from 180 fewer to 498 more) 146 fewer per 1000 (from 180 fewer to 499 more) 133 fewer per 1000 (from 165 fewer to	VERY LOW	
randomised trials	serious <sup>2</sup>	no serious inconsistency  cts - TCA (clomip	ramine) versus no serious	serious¹  TCA (imipra	mine)	0/12	18.2%	to 3.74)	145 fewer per 1000 (from 180 fewer to 498 more) 146 fewer per 1000 (from 180 fewer to 499 more)	VERY LOW	
randomised trials	serious <sup>2</sup>	no serious inconsistency  cts - TCA (clomip	ramine) versus no serious	serious¹  TCA (imipra	mine)	0/12	18.2%	to 3.74)	145 fewer per 1000 (from 180 fewer to 498 more)  146 fewer per 1000 (from 180 fewer to 499 more)  133 fewer per 1000 (from 165 fewer to 462 more)	VERY LOW	
randomised trials	serious <sup>2</sup>	no serious inconsistency  cts - TCA (clomip	ramine) versus no serious	serious¹  TCA (imipra	mine)	0/12	18.2%	to 3.74)	145 fewer per 1000 (from 180 fewer to 498 more) 146 fewer per 1000 (from 180 fewer to 499 more) 133 fewer per 1000 (from 165 fewer to	VERY LOW	

<sup>&</sup>lt;sup>1</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>2</sup> Unclear ROB across multiple domains

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>4</sup> High ROB in at least one domain and unclear in several others

<sup>&</sup>lt;sup>5</sup> No explanation was provided

1 Antidepressants versus antipsychotics

			Quality assess	ment			No of patients				•	Importanc
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressant versus antipsychotic	Control	Relative (95% CI)	Absolute		
emission	- TCA versus	antipsychotic										
		no serious risk of bias		no serious indirectness	very serious <sup>1</sup>	none	7/19 (36.8%)	3/17 (17.6%)	not pooled	not pooled	⊕⊕OO LOW	CRITICA
								17.7%		not pooled		
iscontinu	ation - TCA ve	rsus antipsych	otic									
		no serious risk of bias		no serious indirectness	very serious <sup>1</sup>	none	2/19 (10.5%)	1/17 (5.9%)	not pooled	not pooled	⊕⊕OO LOW	CRITICA
								5.9%		not pooled		

<sup>1</sup> 95% CI crosses two clinical decision thresholds

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3

Antidepressants versus combined antipsychotic and antidepressants

			Quality asse	ssment			No of patients Effect			Effect	Quality	Importance
No of studies	Design   Inconsistent			Indirectness	Imprecision	Other considerations	antingvenotic +  Control    Angoliite		Absolute			
)epressio	on symptom	atology at e	ndpoint (HAMD-	17) - SNRI versu	s antipsycho	otic + SNRI (Bette	r indicated by lower value	s)				
										⊕⊕OO LOW	CRITICAL	

ra	andomised	very	no serious	no serious	very	none	17	18	-	MD 0.9 higher (5	⊕000	CRITICA
		serious <sup>2</sup>	inconsistency	indirectness	serious <sup>1</sup>		•••	10		lower to 6.8 higher)		0141107
			,							, ,	12.11.2011	
pressio	n symptom	atology at e	endpoint (HAMD	-17) - TCA vers	us antipsych	otic + SNRI (Bette	r indicated by lower val	ues)				
ra	andomised	no serious	no serious	no serious	very	none	17	24	-	MD 1.4 lower (4.12	⊕⊕00	CRITICA
			inconsistency	indirectness	serious <sup>1</sup>					lower to 1.32	LOW	
			,							higher)		
emission	- TCA vers	us TCA + a	ntipsychotic									
lrs	andomised	no serious	no serious	no serious	serious <sup>3</sup>	none	7/17	14/18	RR 0.53	366 fewer per 1000	⊕⊕⊕О	CRITICA
			inconsistency	indirectness	SCHOUS	none	(41.2%)	(77.8%)	(0.28 to		MODERATE	ORTHO
u	laio	nok or blub	moondistency	indirectiness			(41.270)	(11.070)	0.98)	560 fewer)	MODEIVATE	
										366 fewer per 1000		
								77.8%		(from 16 fewer to		
										560 fewer)		
			chotic + SNRI	lan antique	i3	la ana	44/42	20/04	DD 4.4	02 1000	0000	CDITIC
		no serious		no serious indirectness	serious <sup>3</sup>	none	11/12 (91.7%)	20/24 (83.3%)	RR 1.1 (0.86 to	83 more per 1000 (from 117 fewer to	⊕⊕⊕O	CRITICA
u	iais	lisk of blas	inconsistency	indirectiess			(91.7%)	(03.3%)	1.41)	342 more)	MODERATE	
									1.11)	0 12 more)		
										83 more per 1000		
								83.3%		(from 117 fewer to		
										342 more)		
emission	- TCA vers	us antipsyo	chotic + SNRI									
ra	andomised	no serious	no serious	no serious	serious <sup>3</sup>	none	15/17	20/24	RR 1.06	50 more per 1000	⊕⊕⊕О	CRITICA
tr	rials	risk of bias	inconsistency	indirectness			(88.2%)	(83.3%)	(0.83 to	(from 142 fewer to	MODERATE	
									1.36)	300 more)		
										50 more per 1000		
								83.3%		(from 142 fewer to		
										300 more)		
esponse	- SNRI vers	us antipsy	chotic + SNRI									
ra	andomised	no serious		no serious	serious <sup>4</sup>	none	12/12	23/24	RR 1.02	19 more per 1000	⊕⊕⊕О	CRITICA
tr	rials	risk of bias	inconsistency	indirectness			(100%)	(95.8%)	(0.88 to	(from 115 fewer to	MODERATE	
					1				1.18)	172 more)		

								95.8%		19 more per 1000 (from 115 fewer to		
								00.070		172 more)		
pons	e - Tetracycli	ic versus ar	itipsychotic + T	CA								
	lana de astro e d	t		I	serious <sup>3</sup>	1	40/47	47/40	DD 0.75	000 f 1000		ODITIO
	randomised trials	very serious²	no serious inconsistency	no serious indirectness	serious	none	12/17 (70.6%)	17/18 (94.4%)	RR 0.75 (0.54 to	236 fewer per 1000 (from 434 fewer to	⊕000 VERY LOW	CRITIC
	lilais	Serious	inconsistency	indirectiness			(70.078)	(34.470)	1.04)	38 more)	VERT LOW	
									1.04)	30 more)		
										236 fewer per 1000		
								94.4%		(from 434 fewer to		
										38 more)		
pons	e - TCA vers	us antipsyc	hotic + SNRI									
	randomised	no serious	no serious	no serious	serious <sup>4</sup>	none	16/17	23/24	RR 0.98	19 fewer per 1000	⊕⊕⊕О	CRITIC
	trials	risk of bias	inconsistency	indirectness			(94.1%)	(95.8%)	(0.85 to	(from 144 fewer to	MODERATE	
									1.14)	134 more)		
										19 fewer per 1000		
								95.8%		(from 144 fewer to		
										134 more)		
conti	nuation - SNF	RI versus ar	tipsychotic + S	NRI								
	randomised	no serious	no serious	no serious	very	none	1/13	2/26	RR 1 (0.1 to	0 fewer per 1000	$\oplus \oplus OO$	CRITIC
	trials		inconsistency	indirectness	serious <sup>1</sup>		(7.7%)	(7.7%)	10.04)	(from 69 fewer to	LOW	
			,				,	, ,	,	695 more)		
								7 70/		0 fewer per 1000		
								7.7%		(from 69 fewer to		
										696 more)		
conti	nuation Tota	racyclic vor	sus antinevehot	ic + TCA								
conti	nuation - Teti	racyclic vers	sus antipsychot	ic + TCA								
conti	randomised	very	no serious	no serious	very	none	9/21	7/25	RR 1.53	148 more per 1000		CRITIC
conti		very			very serious <sup>1</sup>	none	9/21 (42.9%)		RR 1.53 (0.69 to 3.4)	(from 87 fewer to	⊕000 VERY LOW	CRITIC
conti	randomised	very	no serious	no serious		none						CRITIC
conti	randomised	very	no serious	no serious		none				(from 87 fewer to 672 more)		CRITIC
conti	randomised	very	no serious	no serious		none				(from 87 fewer to		CRITIC

3/20

2/26

RR 1.95

73 more per 1000

1

2

4

5

6

8

randomised

no serious no serious

Combined antidepressants and antipsychotics versus other pharmacological interventions 7

no serious

very

none

Antidepressants plus antipsychotics versus antidepressants plus placebo

Quality assessment	No of patients	Effect	Quality	Importance	

CRITICAL

⊕⊕00

2

3

## Antidepressants plus antipsychotics versus antipsychotics plus placebo

				Quality asse	ssment			No of patients			Effect		
												Quality	Importance
	o of udies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressant + antipsychotic versus antipsychotic + placebo	Control	Relative (95% CI)	Absolute		
Rer	nissio	n - SSRI + ar	ntipsychoti	c versus antipsy	chotic + placeb	0						•	•

<sup>95%</sup> CI crosses two clinical decision thresholds

1	randomised	no serious	no serious	no serious	serious <sup>1</sup>	none	54/81	31/61	RR 1.31	158 more per 1000	$\oplus \oplus \oplus O$	CRITICAL
	trials	risk of bias	inconsistency	indirectness			(66.7%)	(50.8%)	(0.98 to	(from 10 fewer to	MODERATE	
									1.75)	381 more)		
										157 more per 1000		
								50.8%		(from 10 fewer to		
										381 more)		
Treatmer	nt discontinu	ation - SSR	RI + antipsychotic	versus antipsy	chotic + pla	cebo						
1	randomised	no serious	no serious	no serious	serious <sup>1</sup>	none	48/129	69/130	RR 0.7	159 fewer per	⊕⊕⊕О	CRITICAL
	trials	risk of bias	inconsistency	indirectness			(37.2%)	(53.1%)	(0.53 to	1000 (from 42	MODERATE	
									0.92)	fewer to 249 fewer)		
										159 fewer per		
								53.1%		1000 (from 42		
										fewer to 250 fewer)		ļ

<sup>1</sup> 95% CI crosses one clinical decision threshold

2

1

3

4 Antipsychotics versus other pharmacological interventions

5 Antipsychotics versus placebo

			Quality asse	essment			No of patient	S		Effect	Quality	Importance
No of studies	Inconsistency Indirectness Impre					Other considerations	Antipsychotic versus placebo	Control	Relative (95% CI)	Absolute		
Response	- Olanzapine	versus p	lacebo									
	randomised trials			no serious indirectness	very serious <sup>2</sup>	none	32/63 (50.8%)	28/53 (52.8%)		32 fewer per 1000 (from 174 fewer to 164 more)		CRITICAL
			,					55.2%	,	33 fewer per 1000 (from 182 fewer to 171 more)		

	Treatment	discontinua	tion - Olar	izapine versus pla	cebo								
	2	randomised	serious1	no serious	no serious	serious <sup>3</sup>	none	38/101	47/100	RR 0.8 (0.58	94 fewer per 1000 (from	⊕⊕OO	CRITICAL
		trials		inconsistency	indirectness			(37.6%)	(47%)	to 1.09)	197 fewer to 42 more)	LOW	
									47.2%		94 fewer per 1000 (from 198 fewer to 42 more)		
Į			L								190 lewel to 42 more)		
1	¹ Unclear F	OB in most do	omains an	d high ROB in one									

<sup>&</sup>lt;sup>2</sup> 95% CI crosses two clinical decision thresholds

## Antipsychotics versus antipsychotics plus antidepressants

			Quality asse	essment			No of patients			Effect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antipsychotic versus antipsychotic + antidepressant	Control	Relative (95% CI)	Absolute	<b>Quality</b>	Importance
Response	e - antipsycho	otic versu	s SSRI + antipsyc	chotic								
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	15/35 (42.9%)	14/14 (100%)	RR 0.45 (0.3 to 0.66)	550 fewer per 1000 (from 340 fewer to 700 fewer)	⊕⊕OO LOW	CRITICAL
								100%		550 fewer per 1000 (from 340 fewer to 700 fewer)		
Treatmen	t discontinua	tion - ant	ipsychotic versus	antipsychotic -	+SSRI			-				
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	13/48 (27.1%)	11/25 (44%)	RR 0.62 (0.32 to 1.17)	167 fewer per 1000 (from 299 fewer to 75 more)	⊕⊕OO LOW	CRITICAL
								44%		167 fewer per 1000 (from 299 fewer to 75 more)		

<sup>&</sup>lt;sup>1</sup> Unclear ROB in most domains, and high ROB in one <sup>2</sup> OIS not met (<300 participants) <sup>3</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

# 1 Benzodiazepines versus other pharmacological interventions

# 2 Benzodiazepines versus placebo

			Quality ass	essment			No of patients	3		Effect		
											Quality	Important
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Benzodiazepines versus placebo	Control	Relative (95% CI)	Absolute		
pressi	on symptoma	tology at	endpoint (HAMD-	17) - Lorazepam	versus place	ebo (Better indicat	ted by lower values)	<u> </u>				
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	59	67	-	MD 3.7 lower (5.6 to	⊕⊕00	CRITICA
	trials		inconsistency	indirectness						1.8 lower)	LOW	
epressi	on symptoma	tology at	endpoint (HAMD-	 17) - Alprazolam	versus place	 ebo (Better indica	ted by lower values)					
•	, ,			, ,		,						
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	none	62	67	-	MD 3.2 lower (5.03 to 1.37 lower)	⊕⊕OO LOW	CRITICAL
espons	e - Lorazepan	ı versus p	lacebo									
	randomised	serious <sup>1</sup>		no serious	serious <sup>3</sup>	none	40/59		RR 3.03 (1.88		⊕⊕00	CRITICA
	trials		inconsistency	indirectness			(67.8%)	(22.4%)	to 4.89)	(from 197 more to 871	LOW	
										more)		
										455 more per 1000		
								22.4%		(from 197 more to 871		
										more)		
espons	e - Alprazolan	n versus p	olacebo									
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	41/62	15/67	RR 2.95 (1.83	437 more per 1000	⊕⊕00	CRITICAL
	trials		inconsistency	indirectness			(66.1%)	(22.4%)	to 4.77)	(from 186 more to 844	LOW	
										more)		
										437 more per 1000		
								22.4%		(from 186 more to 844		
										(		

1	randomised	serious <sup>1</sup>	no serious	no serious	very	none	7/66	7/74	RR 1.12 (0.42	11 more per 1000	⊕000	CRITICAL
	trials		inconsistency	indirectness	serious4		(10.6%)	(9.5%)	to 3.03)	(from 55 fewer to 192	VERY	
										more)	LOW	
									-	44 4000		
								0.50/		11 more per 1000		
								9.5%		(from 55 fewer to 193 more)		
T 4	4 -11 41	4! Al								more)		
reatmen	t discontinua	tion - Aip	razolam versus p	lacebo								
1	randomised	serious <sup>1</sup>	no serious	no serious	very	none	8/70	7/74	RR 1.21 (0.46	20 more per 1000	⊕000	CRITICAL
•	trials	0011000	inconsistency	indirectness	serious <sup>4</sup>		(11.4%)	(9.5%)	to 3.16)	(from 51 fewer to 204	VERY	0.10
			,				,	,	,	more)	LOW	
										,		
										20 more per 1000		
								9.5%		(from 51 fewer to 205		
										more)		
Discontin	uation due to	side effe	cts - Lorazepam v	ersus placebo								
					I	1			1			
1		serious <sup>1</sup>	no serious	no serious	very	none	1/66	0/74	RR 3.36 (0.14	-	⊕000	CRITICAL
	trials		inconsistency	indirectness	serious <sup>4</sup>		(1.5%)	(0%)	to 81.05)		VERY	
								00/			LOW	
								0%		-		
Discontin	uation due to	side effe	cts - Alprazolam	versus placebo								
1	randomised	serious <sup>1</sup>	no serious	no serious	very	none	3/70	0/74	RR 7.39 (0.39	_	⊕000	CRITICAL
	trials	0011003	inconsistency	indirectness	serious <sup>4</sup>	none	(4.3%)	(0%)	to 140.62)		VERY	CATTOAL
	li idio		inocholotoricy	indirectricss	ocrious		(4.570)	(070)	10 140.02)		LOW	
								0%	-	_	LOVV	
	200: 1.1							J 70				

<sup>&</sup>lt;sup>1</sup> Unclear ROB in most domains

## Benzodiazepines versus antidepressants

			Quality asse	essment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Benzodiazepines versus antidepressants	Control	Relative (95% CI)	Absolute		
Depression	on symptoma	tology at	endpoint (HAMD-	17) - Lorazepam	versus TCA	(Better indicated	by lower values)					

<sup>&</sup>lt;sup>2</sup> OIS not met (<400 participants)
<sup>3</sup> OIS not met (<300 events)
<sup>4</sup> 95% CI crosses two clinical decision thresholds

tria			no serious	no serious	very	none				MD 0.7 lower (2.59		CRITICA
	ais		inconsistency	indirectness	serious <sup>2</sup>					lower to 1.19 higher)	⊕OOO VERY	0.1
	G.10				00.1000					101101 to 1110 111g.101)	LOW	
											2011	
pression	symptoma	tology at	endpoint (HAME	)-17) - Alprazola	m versus TO	A (Better indicate	ed by lower values)					
	- <b>,</b> ,		(	,		(=	<b>,</b> ,					
rar	ndomised	serious1	no serious	no serious	very	none	62	69	-	MD 0.2 lower (2.02	⊕000	CRITICA
tria	als		inconsistency	indirectness	serious <sup>2</sup>					lower to 1.62 higher)	VERY	
			•							,	LOW	
sponse - l	Lorazepam	versus 1	CA									
	_											
rar	ndomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	40/59	53/69	RR 0.88	92 fewer per 1000	$\oplus \oplus OO$	CRITICA
tria	als		inconsistency	indirectness			(67.8%)	(76.8%)	(0.71 to 1.1)	(from 223 fewer to 77	LOW	
										more)		
										92 fewer per 1000		
								76.8%		(from 223 fewer to 77		
										more)		
sponse - /	Alprazolan	versus 1	ГСА									
			no serious	no serious	serious <sup>3</sup>	none	41/62	53/69	RR 0.86	108 fewer per 1000	$\oplus \oplus OO$	CRITICA
tria	als		inconsistency	indirectness			(66.1%)	(76.8%)	(0.69 to 1.07)	(from 238 fewer to 54	LOW	
										more)		
										108 fewer per 1000		
								76.8%		(from 238 fewer to 54		
										more)		
eatment di	liscontinua	tion - Lor	azepam versus	TCA								
						1						
			no serious	no serious	very	none	7/66	3/72	RR 2.55	65 more per 1000	$\oplus$ OOO	CRITICA
tria	als		inconsistency	indirectness	serious <sup>2</sup>		(10.6%)	(4.2%)	(0.69 to 9.44)	(from 13 fewer to 352		
										more)	LOW	
										0.5		
								4.057		65 more per 1000		
								4.2%		(from 13 fewer to 354		
										more)		
eatment di	liscontinua	tion - Alp	razolam versus	TCA								
					1							
			no serious	no serious	serious <sup>3</sup>	none	8/70	3/72	RR 2.74	73 more per 1000	$\oplus \oplus OO$	CRITICA
tria	als		inconsistency	indirectness			(11.4%)	(4.2%)	(0.76 to 9.92)	(from 10 fewer to 372	LOW	
								1		more)		1

								4.2%		73 more per 1000 (from 10 fewer to 375 more)		
Discontin	uation due to	side effe	cts - Lorazepam v	ersus TCA								
1	randomised trials			no serious indirectness	very serious <sup>2</sup>	none	1/66 (1.5%)	0/72 (0%)	RR 3.27 (0.14 to 78.87)	-	⊕000 VERY LOW	CRITICAL
Discontin	uation due to	side effe	cts - Alprazolam	versus TCA								
1	randomised trials			no serious indirectness	very serious <sup>2</sup>	none	3/70 (4.3%)	(0%)	RR 7.2 (0.38 to 136.84)	-	⊕000 VERY LOW	CRITICAL
								0%		-		

<sup>&</sup>lt;sup>1</sup> Unclear ROB in most domains

## Benzodiazepines versus benzodiazepines

			Quality asso	essment			No of patients			Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Benzodiazepines versus benzodiazepines	Control	Relative (95% CI)	Absolute		
Depression	on symptoma	tology at	endpoint (HAMD-	17) - Lorazepam	versus alpra	azolam (Better inc	licated by lower values)		,			
1	randomised trials	serious <sup>1</sup>		no serious indirectness	very serious <sup>2</sup>	none	59	62	-	MD 0.5 lower (2.5 lower to 1.5 higher)	⊕OOO VERY LOW	CRITICAL
Response	e - Lorazepan	versus a	Iprazolam									
1	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>3</sup>	none	40/59 (67.8%)	(66.1%)	RR 1.03 (0.8 to 1.32)	20 more per 1000 (from 132 fewer to 212 more)	⊕⊕OO LOW	CRITICAL
								66.1%		(from 132 fewer to 212 more)		

<sup>&</sup>lt;sup>2</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

randomise	serious1	no serious	no serious	very	none	7/66	8/70	RR 0.93	8 fewer per 1000	⊕000	CRITIC
trials	Serious	inconsistency	indirectness	serious <sup>2</sup>	none	(10.6%)	(11.4%)	(0.36 to	(from 73 fewer to 162		CKITIC
uiais		inconsistency	indirectiess	Serious		(10.0%)	(11.470)	2.42)	more)	LOW	
								2.42)	more)	LOW	
									8 fewer per 1000		
							11.4%				
							11.4%		(from 73 fewer to 162		
									more)		
		1							111010)		
ontinuation due	to side effe	ects - Lorazepam	versus alprazola	am					more)		
ntinuation due	to side effe	ects - Lorazepam	versus alprazola	am					inicio)		
randomise	_	no serious	versus alprazola	very	none	1/66	3/70	RR 0.35	28 fewer per 1000	⊕000	CRITIC
	_				none	1/66 (1.5%)	3/70 (4.3%)	RR 0.35 (0.04 to	,	⊕OOO VERY	CRITIC
randomise		no serious	no serious	very	none				28 fewer per 1000		CRITIC
randomise		no serious	no serious	very	none			(0.04 to	28 fewer per 1000 (from 41 fewer to 99	VERY	CRITIC
randomise		no serious	no serious	very	none			(0.04 to	28 fewer per 1000 (from 41 fewer to 99 more)	VERY	CRITI
randomise		no serious	no serious	very	none			(0.04 to	28 fewer per 1000 (from 41 fewer to 99	VERY	CRITI

<sup>&</sup>lt;sup>1</sup> Unclear ROB across most domains

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Relapse prevention (chapter 11)

5 6

- 7 Psychological interventions
- 8 Psychological interventions versus control
- CBT/CT versus control for relapse prevention

			Quality asses	ssment			No of p	oatients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	СВТ/СТ	Control	Relative (95% CI)	Absolute		
Relapse (fo	llow-up 12 mo	onths)										

<sup>&</sup>lt;sup>2</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

4	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	95/246	124/225	RR 0.71 (0.53	160 fewer per 1000 (from 28	$\oplus \oplus OO$	CRITICAL
	trials		inconsistency	indirectness			(38.6%)	(55.1%)	to 0.95)	fewer to 259 fewer)	LOW	
								55.5%		161 fewer per 1000 (from 28		
										fewer to 261 fewer)		
Relapse	follow-up 24 m	onths)										
3	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	131/224	144/202	RR 0.82 (0.69	128 fewer per 1000 (from 14	⊕⊕00	CRITICAL
	trials		inconsistency	indirectness			(58.5%)	(71.3%)	to 0.98)	fewer to 221 fewer)	LOW	
								73.9%		133 fewer per 1000 (from 15		
	1		1					13.970		fewer to 229 fewer)		
										101101 10 ==0 101101)		

<sup>&</sup>lt;sup>1</sup> ROB unclear or high in 1-2 domains for each study <sup>2</sup> 95% CI crosses one clinical decision threshold

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#### MBCT versus control for relapse prevention 4

			Quality as	sessment			No of pat	ients		Effect	Quality	<b>Importance</b>
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MBCT versus control	Control	Relative (95% CI)	Absolute		
Relapse (	follow-up 12	months)										
9	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	247/525 (47%)	281/475 (59.2%) 59.4%	RR 0.79 (0.7 to 0.89)	124 fewer per 1000 (from 65 fewer to 177 fewer) 125 fewer per 1000 (from 65 fewer to 178 fewer)	⊕⊕OO LOW	CRITICAL
Relapse (	follow-up 24	months)										
2	randomised trials		no serious inconsistency	no serious indirectness	no serious imprecision	none	148/313 (47.3%)	161/314 (51.3%) 53.5%	RR 0.92 (0.79 to 1.08)	41 fewer per 1000 (from 108 fewer to 41 more) 43 fewer per 1000 (from 112 fewer to 43 more)	⊕⊕⊕O MODERATE	CRITICAL

## IPT versus control for relapse prevention

			Overlite and	<b>-</b>			Nf.	-4!4-		P# 4		
			Quality asse	ssment			NO OT P	atients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IPT	Control	Relative (95% CI)	Absolute		
Studies		Dias				Considerations			(93/8 01)			
Relapse (f	ollow-up 12 m	onths)			<u> </u>		Į.					
3	randomised	very	no serious	no serious	serious <sup>2</sup>	none	69/118	57/75	RR 0.77 (0.63	175 fewer per 1000 (from 38	⊕ООО	CRITICAL
	trials		inconsistency	indirectness			(58.5%)	(76%)	to 0.95)	fewer to 281 fewer)	VERY	
									·		LOW	
								78.3%		180 fewer per 1000 (from 39		
								70.070		fewer to 290 fewer)		
Relapse (f	ollow-up 24 m	onths)										
								•				
3	randomised			no serious	serious <sup>2</sup>	none	75/116	_	RR 0.89 (0.74	71 fewer per 1000 (from 168	$\oplus$ OOO	CRITICAL
	trials	serious <sup>1</sup>	inconsistency	indirectness			(64.7%)	(64.8%)	to 1.07)	fewer to 45 more)	VERY	
											LOW	
								72.2%		79 fewer per 1000 (from 188		
								/0		fewer to 51 more)		

<sup>&</sup>lt;sup>1</sup> ROB unclear or high across multiple domains in most included studies <sup>2</sup> 95% CI crosses one clinical decision threshold

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## 'Other' psychological interventions versus control for relapse prevention

			Quality asse	essment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Other psychological interventions	Control	Relative (95% CI)	Absolute		

CBASP v	s control - Re	lapse (foll	ow-up 12 months									
1	randomised	very	no serious	no serious	serious <sup>2</sup>	none	1/42	8/40	RR 0.12	176 fewer per 1000	⊕000	CRITICAL
	trials	serious <sup>1</sup>	inconsistency	indirectness			(2.4%)	(20%)	(0.02 to 0.91)	(from 18 fewer to 196	VERY	
										fewer)	LOW	
										176 fewer per 1000		
								20%		(from 18 fewer to 196		
										fewer)		

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## Psychological interventions versus psychological interventions

## **CBT** versus psychoeducation

			Quality asse	ssment			N	o of patients		Effect	<b>Quality</b>	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT Psychoeducation		Relative (95% CI)	Absolute		
Relapse (f	ollow-up 12 m	ionths)										
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	46/90 (51.1%)		RR 0.85 (0.65 to 1.11)	90 fewer per 1000 (from 210 fewer to 66 more)	⊕⊕OO LOW	CRITICAL
								60%		90 fewer per 1000 (from 210 fewer to 66 more)		

<sup>&</sup>lt;sup>1</sup> ROB unclear or high in 1-2 domains

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### IPT versus IPT

Quality assessment	No of patients	Effect Effect	Quality	Importance

<sup>&</sup>lt;sup>1</sup> ROB high or unclear across multiple domains <sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>2</sup> 95% CI crosses one clinical decision threshold

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IPT	IPT	Relative (95% CI)	Absolute					
Relapse - \	elapse - Weekly IPT vs Bi-monthly IPT (follow-up 24 months)														
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	23/43 (53.5%)		RR 1.24 (0.8 to 1.92)	104 more per 1000 (from 86 fewer to 397 more)	⊕⊕OO LOW	CRITICAL			
								43.2%		104 more per 1000 (from 86 fewer to 397 more)					
Relapse - \	Weekly IPT vs	Monthly IP	PT (follow-up 24 mo	nths)											
1	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	23/43 (53.5%)	21/44 (47.7%)	RR 1.12 (0.74 to 1.7)	57 more per 1000 (from 124 fewer to 334 more)	⊕000 VERY LOW	CRITICAL			
								47.7%		57 more per 1000 (from 124 fewer to 334 more)					
Relapse - I	Bi-monthly IPT	vs month	ly IPT (follow-up 24	months)											
1	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	19/44 (43.2%)		RR 0.9 (0.57 to 1.43)	48 fewer per 1000 (from 205 fewer to 205 more)	⊕000 VERY LOW	CRITICAL			
								47.7%		48 fewer per 1000 (from 205 fewer to 205 more)					
<sup>2</sup> 95% CI cr	or unclear acro osses one clinio osses two clinio	cal decision	threshold												

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#### Pharmacological interventions

# Antidepressant versus placebo

	Quality assessment						No of pati	ents		Effect	Quality	Importance	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressant	Placebo	Relative (95% CI)	Absolute			
Relapse- A	apse- All												

48	randomised trials	very serious <sup>1</sup>	 no serious indirectness	no serious imprecision	none	1505/4880 (30.8%)	2216/4225 (52.4%)	RR 0.59 (0.55 to 0.65)	215 fewer per 1000 (from 184 fewer to 236 fewer)	⊕OOO VERY LOW	CRITICAL
							52.4%		215 fewer per 1000 (from 183 fewer to 236 fewer)		

<sup>&</sup>lt;sup>1</sup> ROB low in only one or two domains

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## Antidepressant (full dose) versus antidepressant (half dose)

			Quality ass	essment			No of p	atients		Effect			
											Quality	Importance	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressant (full dose)	Antidepressant (half dose)	Relative (95% CI)	Absolute			
Relapse				ļ									
	randomised trials	very serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	serious <sup>3</sup>	none	155/513 (30.2%)	190/511 (37.2%)	RR 0.81 (0.60 to	71 fewer per 1000 (from 149 fewer to	⊕000 VERY	CRITICAL	
							(55.273)	(01.12.13)	108)	1000 more)	LOW		
TCA (full	dose) versus	TCA (ha	If dose)										
1	randomised	serious4	no serious	no serious	serious <sup>3</sup>	none	110/385	136/382	RR 0.80	71 fewer per 1000	⊕⊕00	CRITICAL	
	trials		inconsistency	indirectness			(28.6%)	(35.6%)	(0.65 to 0.99)	(from 4 fewer to 125 fewer)	LOW		
SSRI (full	SRI (full dose) versus SSRI (half dose)												
	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	45/128 (35.2%)	54/129 (41.9%)	RR 0.73 (0.35 to 1.54)	113 fewer per 1000 (from 272 fewer to 226 more)	⊕000 VERY LOW	CRITICAL	
			tala danata						,	,			

<sup>&</sup>lt;sup>1</sup> ROB high or unclear across multiple domains <sup>2</sup> 12 >50%<80%

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<sup>&</sup>lt;sup>2</sup> I2 >50% <80%

<sup>&</sup>lt;sup>3</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>4</sup> ROB unclear in several domains

Antidepressant versus lithium

			Quality asse	essment			No of pati	ents		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressant	Lithium alone	Relative (95% CI)	Absolute		
Relapse -	Amitriptyline	vs lithium										
				no serious indirectness	serious <sup>2</sup>	none	32/57 (56.1%)	39/50 (78%)	RR 0.72 (0.55 to 0.95)	218 fewer per 1000 (from 39 fewer to 351 fewer)	⊕OOO VERY	CRITICAL
								78%		218 fewer per 1000 (from 39 fewer to 351 fewer)	LOW	

<sup>&</sup>lt;sup>1</sup> ROB high or unclear across multiple domains <sup>2</sup> 95% CI crosses one clinical decision threshold

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Lithium augmentation of antidepressants versus placebo augmentation

			Quality asse	essment			No of patie	nts		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lithium augmentation + AD	Placebo + AD	Relative (95% CI)	Absolute		
Relapse												
3	randomised trials			no serious indirectness	serious <sup>2</sup>	none	19/80 (23.8%)		RR 0.62 (0.35 to 1.12)	(from 268 fewer to 49 more)  146 fewer per 1000	⊕⊕OO LOW	CRITICAL
								38.5%		(from 250 fewer to 46 more)		

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<sup>&</sup>lt;sup>1</sup> ROB high or unclear in several domains <sup>2</sup> 95% CI crosses one clinical decision threshold

1 Risperidone augmentation of antidepressants versus placebo augmentation

		Quality asse	essment		No of patien	ts		Effect	Quality	Importance		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risperidone augmentation + AD	Placebo + AD	Relative (95% CI)	Absolute		
Relapse		'										
1	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	65/122	65/119	RR 0.98	11 fewer per 1000	⊕⊕00	CRITICAL
	trials		inconsistency	indirectness			(53.3%)	(54.6%)		(from 126 fewer to 126 more)  11 fewer per 1000 (from 126 fewer to 126	LOW	
1.000								34.070		more)		

<sup>&</sup>lt;sup>1</sup> ROB unclear across several domains

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5 Antipsychotics versus placebo

		<u> </u>										
			Quality as	sessment			No of patient	S		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antipsychotics versus placebo	Control	Relative (95% CI)	Absolute		
Relapse -	Quetiapine v	ersus pla	cebo									
1	randomised	verv	no serious	no serious	no serious	none	54/387	127/384	RR 0.42	102 fourer per 1000	0000	CRITICAL
		,		indirectness	imprecision	none				192 fewer per 1000 (from 146 fewer to 225 fewer)	LOW	CITIOAL
										192 fewer per 1000		
								33.1%		(from 146 fewer to 225 fewer)		

<sup>&</sup>lt;sup>1</sup> ROB high or unclear across multiple domains

<sup>&</sup>lt;sup>2</sup> OIS not met (<300 events)

## 1 Combination interventions

# 2 Combination psychological plus pharmacological versus pharmacological interventions

			Quality ass	essment			No of pati	ents		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Combination pharm + Psych	Pharm- 12 month	Relative (95% CI)	Absolute		
Imipramir	e + IPT vs Im	ipramine						<u> </u>				
1	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	4/25 (16%)	11/28 (39.3%)	RR 0.41 (0.15 to 1.12)	232 fewer per 1000 (from 334 fewer to 47 more)	⊕000 VERY LOW	CRITICAL
								39.3%		232 fewer per 1000 (from 334 fewer to 47 more)		
MBCT + A	D vs AD	1								,		
1	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	17/33 (51.5%)	20/35 (57.1%)	RR 0.9 (0.58 to 1.4)	57 fewer per 1000 (from 240 fewer to 229 more)	⊕000 VERY LOW	CRITICAL
								57.1%		57 fewer per 1000 (from 240 fewer to 228 more)		
Paroxetin	e + IPT vs pa	roxetine										
1	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	11/28 (39.3%)	16/35 (45.7%)	OR 0.86 (0.42 to 1.4)	37 fewer per 1000 (from 196 fewer to 84 more)	⊕000 VERY LOW	CRITICAL
								45.7%		37 fewer per 1000 (from 196 fewer to 84 more)		
CBT vs A	D vs AD alon	е										
2	randomised trials	very serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	36/88 (40.9%)	42/89 (47.2%)	RR 0.86 (0.62 to 1.21)	66 fewer per 1000 (from 179 fewer to 99 more)	⊕000 VERY LOW	CRITICAL

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#### 31 fewer per 1000 CRITICAL randomised no serious very none 27/66 29/66 RR 0.93 $\oplus$ OOO very no serious trials serious1 inconsistency indirectness serious<sup>3</sup> (40.9%)(43.9%) (0.62 to 1.39) (from 167 fewer to 171 **VERY** more) LOW CBT + AD vs AD CRITICAL 13/23 RR 0.72 (0.3 158 fewer per 1000 serious4 9/22 randomised no serious no serious very none $\oplus$ OOO trials indirectness serious<sup>3</sup> (40.9%)(56.5%)to 1.23) (from 396 fewer to 130 inconsistency **VERY** more) LOW 158 fewer per 1000 56.5% (from 396 fewer to 130 more)

CT + fluoxetine versus fluoxetine alone

## Combination psychological plus pharmacological versus psychological interventions

				,			N. 6 (1)					
			Quality asse	essment			No of patier	nts		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	COMBINATION PHARM + PSYCH	PSYCH-12 month	Relative (95% CI)	Absolute		
CBT + fluc	oxetine vs CE	ЗТ										
		. 1				-		0110	DD 0 =0 (0 0	07.5		ODITION
					,	none	4/11		RR 0.79 (0.3		$\oplus$ OOO	CRITICAL
	trials		inconsistency	indirectness	serious <sup>2</sup>		(36.4%)	(46.2%)	to 2.09)	(from 323 fewer to 503	VERY	
										more)	LOW	
										97 fewer per 1000		
								46.2%		(from 323 fewer to 504		
										more)		
IPT + Imip	ramine vs IP	Т										

<sup>&</sup>lt;sup>1</sup> ROB high or unclear across multiple domains

<sup>&</sup>lt;sup>2</sup> 95% CI crosses one clinical decision threshold

<sup>&</sup>lt;sup>3</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>4</sup> ROB high or unclear across 1-2 domains

1	randomised	very	no serious	no serious	serious⁴	none	4/25	14/26	RR 0.3 (0.11		$\oplus$ OOO	CRITICAL
	trials	serious <sup>3</sup>	inconsistency	indirectness			(16%)	(53.8%)	to 0.78)	(from 118 fewer to 479	VERY	
										fewer)	LOW	
										377 fewer per 1000		
								53.9%		(from 119 fewer to 480		
										fewer)		
PT + noi	triptyline vs l	PT				•					•	
1	randomised	serious1	no serious	no serious	serious4	none	11/29	18/31	RR 0.65	203 fewer per 1000	⊕⊕00	CRITICAL
	trials		inconsistency	indirectness			(37.9%)	(58.1%)	(0.38 to	(from 360 fewer to 81	LOW	
			, , , , , , , , , , , , , , , , , , , ,				(2 2 2 2 )	(====,	1.14)	more)	20	
									,	,		
										203 fewer per 1000		
								58.1%		(from 360 fewer to 81		
										more)		
DT + nai	oxetine vs IP	T								/		
ıı ı · paı	OXCUITE VS II	•										
1	randomised	serious <sup>1</sup>	no serious	no serious	serious4	none	11/28	23/35	RR 0.6 (0.36	263 fewer per 1000	⊕⊕00	CRITICAL
•	trials	ochodo	inconsistency	indirectness	SCHOOS	none	(39.3%)	(65.7%)	to 1)	(from 421 fewer to 0	LOW	ORTHORE
	triais		inconsistency	indirectiness			(00.070)	(00.1 70)	ιο 1)	more)	LOVV	
										111010)		
										263 fewer per 1000		
								65.7%		(from 420 fewer to 0		
								00.1 70		more)		
MDCT ±	nADM vs MB0	 								111010)		
WIDCT TI	IIADIVI VS IVIDO	<b>J</b> 1										
1	randomised	very	no serious	no serious	serious <sup>4</sup>	none	85/121	105/128	RR 0.86	115 fewer per 1000	⊕000	CRITICAL
	trials	serious <sup>3</sup>	inconsistency	indirectness	3611003	HOHE	(70.2%)	(82%)	(0.74 to	(from 8 fewer to 213	VERY	CITIOAL
	uiais	Serious	inconsistency	indirectriess			(10.270)	(02 /0)	0.99)	fewer)	LOW	
									0.99)	iewei)	LOW	
										115 fewer per 1000		
								82%		(from 8 fewer to 213		
								02 /0		•		
		1	1	I		1	1	1		fewer)		İ

<sup>&</sup>lt;sup>1</sup> ROB high or unclear across 1-2 domains

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## Antidepressants plus antipsychotics versus antidepressants plus placebo

Quality assessment	No of patients	Effect	Quality	Importance

<sup>&</sup>lt;sup>2</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>3</sup> ROB high or unclear aoss multiple domains

<sup>4 95%</sup> CI crosses one clinical decision threshold

Other

ADM + antipsychotic

Relative

No of

1

2

3

Risk of

ECT plus antidepressants versus antidepressants (with or without lithium augmentation) 4

			Quality asse	essment			No of patier	nts		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ECT + ADM versus ADM (+/- Li)	Control	Relative (95% CI)	Absolute		
Relapses												
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	4/27 (14.8%)	6/27 (22.2%)	RR 0.65 (0.22 to 1.91)	173 fewer to 202 more)	⊕OOO VERY LOW	CRITICAL
Delenese	FOT L TOA	TO						25.9%		91 fewer per 1000 (from 202 fewer to 236 more)		
Relapses	- ECT + TCA v	ersus 10	A									
1	randomised trials	serious <sup>1</sup>	no serious inconsistency		very serious <sup>2</sup>	none	1/16 (6.3%)	2/17 (11.8%)	RR 0.53 (0.05 to 5.31)	55 fewer per 1000 (from 112 fewer to 507 more)		CRITICAL

CRITICAL

 $\oplus$ OOO

**VERY** 

LOW

Unclear ROB in most domains

<sup>&</sup>lt;sup>2</sup> 95% CI crosses two clinical decision thresholds

								11.8%		55 fewer per 1000 (from 112 fewer to 509 more)	⊕000 VERY LOW	
Relapses -	- ECT + ADM	versus AD	M (+/- Li augment	ation)								
			1	ı	ı	1						
1	randomised	serious <sup>1</sup>	no serious	no serious	very	none	3/11	4/10	RR 0.68 (0.2	128 fewer per 1000 (from	$\oplus$ OOO	CRITICAL
	trials		inconsistency	indirectness	serious <sup>2</sup>		(27.3%)	(40%)	to 2.33)	320 fewer to 532 more)	VERY	
											LOW	l
								400/		128 fewer per 1000 (from		l
								40%		320 fewer to 532 more)		

<sup>&</sup>lt;sup>1</sup> High ROB in one domain and unclear in several others <sup>2</sup> 95% CI crosses two clinical decision thresholds

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#### Light therapy 4

## Which therapy is most effective for relapse prevention of depression with a seasonal pattern/SAD?

									Summary of	findings		
			Quality assessm	ent				_			i e	_
							No of pat	ients		Effect		Importance
				1		1					Quality	importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Relapse Prevention	Control	Relative (95% CI)	Absolute	Quanty	
Leaving st	tudy early for an	y reason - Bright	white light visor vs r	no treatment conti	rol							
1	randomised	no serious	no serious	no serious	very	none		1/10		12 more per 100 (from 7		
_	trials	limitations	inconsistency	indirectness	serious <sup>1</sup>		1/10/22 20()		RR 2.22 (0.29 to	fewer to 163 more)	⊕⊕00	
							4/18 (22.2%)		17.27)		LOW	
								10%		12 more per 100 (from 7 fewer to 163 more)		
Leaving st	tudy early for an	y reason - Bright	white light visor vs o	lim red light visor								
1	randomised	no serious	no serious	no serious	very	none		3/18		6 more per 100 (from 11		
	trials	limitations	inconsistency	indirectness	serious <sup>1</sup>		4/10/22 20/\	(16.7%)	RR 1.33 (0.35 to	fewer to 69 more)	⊕⊕ОО	
							4/18 (22.2%)		5.13)		LOW	
								16.7%		6 more per 100 (from 11 fewer to 69 more)		
Relapse d	uring course of	study (BDI>=13 fo	or 2 consecutive wks	) - Bright white ligh	nt visor vs no	treatment control						

1				no serious indirectness	serious <sup>2</sup>	none	9/18 (50%)	8/10 (80%)	RR 0.63 (0.36 to 1.09)	⊕⊕⊕O MODERATE
Relapse du	iring course of	study (BDI>=13 fo	or 2 consecutive wks	) - Bright white ligh	nt visor vs din	n red light visor				
1				no serious indirectness	serious²	none	9/18 (50%)	4/18 (22.2%) 22.2%	RR 2.25 (0.84 to 5.99)	 ⊕⊕⊕O MODERATE

<sup>&</sup>lt;sup>1</sup> Inconclusive effect size; single study <sup>2</sup> Single study

# Non-light therapy

Is relapse prevention effective for depression with a seasonal pattern/SAD? (Buspirone versus placebo)

								Sur	mmary of findings			
			Quality assessn	nent			No. of pat	ients	Effect			Import
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecis ion	Other considerations	Buspirone- prevention	Placebo	Relative (95% CI)	Absolute	Quality	ance
Relapse F	Prevention - Nur	nber of patients e	xperiencing a recu	ırrence								
3	randomised trial		no serious inconsistency	no serious indirectness	no serious imprecis ion	none	92/542 (17%)	153/5 19 (29.5 %)	RR 0.58 (0.46 to 0.72)	12 fewer per 100 (from 8 fewer to - 16 fewer)	⊕⊕⊕⊕ HIGH	
								31.9%		13 fewer per 100		

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- Access to services (chapter 12)
- 4 Telephone administered psychological interventions versus usual care
- 5 Clinic based telepsychiatry using a video-webcam versus usual care

0		9,01110101	y using a viuc									1
			Quality asses	sment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	<b>Imprecision</b>	Other considerations	Clinic-based telepsychiatry using a video Webcam versus TAU	Control	Relative (95% CI)	Absolute		
Number o	f subjects wi	ho made a	a mental health ap	ppointment (f	ollow-up me	an 6 months; ass	essed with: Not reported)					
	randomised trials		no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	77/80 (96.3%)	29/87 (33.3%)	RR 2.89 (2.14 to 3.9)	630 more per 1000 (from 380 more to 967 more)	⊕OOO VERY LOW	
								33.3%		629 more per 1000 (from 380 more to 966 more)		
Number o	f subjects wl	ho made a	a primary care ap	pointment (fo	llow-up mea	n 6 months; asse	ssed with: Not reported)					
	randomised trials		no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	56/80 (70%)	76/87 (87.4%)	RR 0.8 (0.68 to 0.94)	175 fewer per 1000 (from 52 fewer to 280 fewer)	⊕OOO VERY LOW	
								87.4%		175 fewer per 1000 (from 52 fewer to 280 fewer)		
Number u	sed antidepr	essants (	follow-up mean 6	months; ass	essed with:	Not reported)						
	randomised trials		no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	56/80 (70%)	40/87 (46%)	RR 1.52 (1.16 to 1.99)	239 more per 1000 (from 74 more to 455 more)		

### <sup>6</sup> Non-blind outcome assessment (self-report)

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### Telephone CBT versus enhanced usual care

	Quality assessment							No of patients		Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telephone CBT	Enhanced usual care	Relative (95% CI)	Absolute		
Number re	umber reporting they were staisfied with the treatment provided											

1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none		12/33 6.4%)	RR 1.03 (0.59 to 1.79)	11 more per 1000 (from 149 fewer to 287 more)	⊕000 VERY	CRITICAL
											LOW	
	gh ROB in one dom % CI crosses two c			hers								
957	70 CI CIOSSES (WO C	inical decis	ion thresholds									
Tele	ephone-adm	inistere	d monitoring	intervent	ions vers	us usual care						
Tele	ephone diseas	e manag	gement versus	usual care	<u>,</u>							
	•											
			Quality asses	ssment			No of patient	s		Effect		
											Quality	Importan
	o of Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telephone disease management versus	Contro	Relative (95% CI)	Absolute		
Stu	idles	bias				considerations	usual care		(95% CI)			
Num	nber completing a	t least one	mental health/su	bstance abus	e appointme	nt (follow-up mear	n 4 months; assessed v	vith: Self-r	eport)			
1	randomised	serious <sup>1</sup>	no serious	serious <sup>2</sup>	serious <sup>2,3</sup>	none	19/46	5/51	RR 4.21	315 more per 1000	⊕000	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>2,3</sup>	none	19/46 (41.3%)	5/51 (9.8%	) (1.71 to	(from 70 more to 919	VERY	
1		serious <sup>1</sup>		serious <sup>2</sup>	serious <sup>2,3</sup>	none				(from 70 more to 919 more)		
1		serious <sup>1</sup>		serious <sup>2</sup>	serious <sup>2,3</sup>	none		(9.8%	(1.71 to 10.37)	(from 70 more to 919 more) 315 more per 1000	VERY	
1		serious <sup>1</sup>		serious <sup>2</sup>	serious <sup>2,3</sup>	none			(1.71 to 10.37)	(from 70 more to 919 more)	VERY	
	trials  n-blind outcome as	sessment (s	inconsistency self-report)				(41.3%)	(9.8%	(1.71 to 10.37)	(from 70 more to 919 more)  315 more per 1000 (from 70 more to 918	VERY	
<sup>2</sup> US	trials  n-blind outcome as	sessment (s	inconsistency self-report)			e applicable to all n	(41.3%)	(9.8%	(1.71 to 10.37)	(from 70 more to 919 more)  315 more per 1000 (from 70 more to 918	VERY	
<sup>2</sup> US	trials  n-blind outcome as study with potentia	sessment (s	inconsistency self-report)				(41.3%)	(9.8%	(1.71 to 10.37)	(from 70 more to 919 more)  315 more per 1000 (from 70 more to 918	VERY	
<sup>2</sup> US	trials  n-blind outcome as study with potentia	sessment (s	inconsistency self-report)				(41.3%)	(9.8%	(1.71 to 10.37)	(from 70 more to 919 more)  315 more per 1000 (from 70 more to 918	VERY	

No of patients

Effect

Quality assessment

Quality Importance

Simple collaborative care versus usual ca	are
---	-----

			Quality asse	essment			No of patients			Effect		
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Simple collaborative care versus usual care	Control	Relative (95% CI)	Absolute		
Number v	vho attended	≥1 appoin	tment with menta	l health speciali	st (follow-up	mean 12 months	; assessed with: Databas	se reviev	v)			

Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Close monitoring versus usual care	Control	Relative (95% CI)	Absolute		
ttending prim	ary care v	isits during study	period (follow	v-up mean 6	months; assessed	I with: Case review)					
randomised trials	- ,		serious <sup>2</sup>	serious <sup>3</sup>	none	92/130 (70.8%)	62/93 (66.7%)	RR 1.06 (0.89 to 1.27)	40 more per 1000 (from 73 fewer to 180 more)	⊕OOO VERY LOW	
							66.7%		40 more per 1000 (from 73 fewer to 180 more)		
ho had any M	H care (in	cluding behaviora	l health spec	ialist) during	the study period (	follow-up mean 6 mo	nths; as	sessed with: C	ase review)	•	
randomised trials	- 3		serious <sup>2</sup>	serious <sup>4</sup>	none	43/130 (33.1%)	6/93 (6.5%)	RR 5.13 (2.28 to 11.54)	266 more per 1000 (from 83 more to 680 more)	⊕000 VERY LOW	
							6.5%		268 more per 1000 (from 83 more to 685 more)		
ho started an	antidepre	ssant during the s	study period (	follow-up me	ean 6 months; ass	essed with: Case rev	iew)				
randomised trials			serious <sup>2</sup>	serious <sup>3</sup>	none	21/130 (16.2%)	9/93 (9.7%)	RR 1.67 (0.8 to 3.48)	65 more per 1000 (from 19 fewer to 240 more)	⊕OOO VERY	
							9.7%		65 more per 1000 (from 19 fewer to 241 more)	LOW	
	randomised trials  tho had any Marandomised trials  tho started an randomised	randomised trials very serious trials very very serious trials very very very very very very very very	ttending primary care visits during study  randomised trials  very serious no serious inconsistency  randomised trials  very no serious  randomised very no serious  randomised very no serious	ttending primary care visits during study period (follow randomised trials  very serious no serious inconsistency  randomised very serious no serious inconsistency  randomised trials  very no serious serious serious serious serious serious no serious inconsistency  randomised trials  very serious no serious s	ttending primary care visits during study period (follow-up mean 6  randomised trials very serious inconsistency serious serio	tending primary care visits during study period (follow-up mean 6 months; assessed randomised trials  The had any MH care (including behavioral health specialist) during the study period (follow-up mean 6 months; assessed serious serious none  The had any MH care (including behavioral health specialist) during the study period (follow-up mean 6 months; asserious serious none  The started an antidepressant during the study period (follow-up mean 6 months; asserious serious s	tending primary care visits during study period (follow-up mean 6 months; assessed with: Case review)  randomised trials very serious¹ no serious inconsistency serious² serious³ none 92/130 (70.8%)  randomised trials very serious¹ no serious inconsistency serious² serious³ none 92/130 (70.8%)  randomised trials very serious¹ no serious inconsistency serious² serious² none 43/130 (33.1%)  randomised trials very serious¹ no serious inconsistency serious² serious² serious⁴ none (33.1%)  randomised trials very serious¹ no serious inconsistency serious² serious² none 21/130	tending primary care visits during study period (follow-up mean 6 months; assessed with: Case review)  randomised trials  wery serious¹ inconsistency  no serious serious² serious³ none  serious³ none  92/130 (62/93 (70.8%))  66.7%  ho had any MH care (including behavioral health specialist) during the study period (follow-up mean 6 months; as randomised trials  randomised trials  randomised trials  wery serious¹ inconsistency  no serious serious² serious⁴ none  43/130 (6.5%)  6.5%  ho started an antidepressant during the study period (follow-up mean 6 months; assessed with: Case review)  randomised trials  very no serious inconsistency  serious² serious⁴ none  43/130 (6.5%)  6.5%  ho started an antidepressant during the study period (follow-up mean 6 months; assessed with: Case review)  randomised trials  very no serious inconsistency  serious² serious³ none  21/130 9/93 (16.2%)  9/93 (9.7%)	tending primary care visits during study period (follow-up mean 6 months; assessed with: Case review)  randomised trials  very serious¹  no serious  serious²  serious²  serious³  none  92/130  (66.7%)  (66.7%)  follow-up mean 6 months; assessed with: Case review)  randomised trials  very serious¹  no serious  randomised trials  very serious¹  no serious  serious²  serious²  serious²  serious²  serious⁴  none  43/130  (6.5%)  (6.5%)  follow-up mean 6 months; assessed with: Case review)  randomised trials  very serious¹  no serious  serious²  serious²  serious⁴  none  43/130  (6.5%)  6.5%  follow-up mean 6 months; assessed with: Case review)  randomised very serious¹  randomised trials  very no serious inconsistency  no serious  serious²  serious³  none  21/130  9/93  RR 1.67 (0.8 to 3.48)  to 3.48)	tending primary care visits during study period (follow-up mean 6 months; assessed with: Case review)  randomised trials very serious¹ inconsistency lindirectness limprecision considerations versus usual care versus versus usual care versus usual care versus versus usual care versus versus versus versus usual care versus versus versus versus versus versus usual care versus versus versus versus usual care versus versus versus versus usual care versus versus versus usual care versus versus versus versus usual care versus versus versus versus usual care versus versus versus usual care versus versus versus versus usual care versus versus versus versus usual care versus	tending primary care visits during study period (follow-up mean 6 months; assessed with: Case review)  randomised very serious¹ no serious inconsistency  randomised very serious¹ no serious serious² serious² serious² serious² serious² none  ### Part

<sup>&</sup>lt;sup>1</sup> Outcome assessment was non-blind and there were statistically significant baseline differences between groups (more males, more financial troubles, more subjects with trauma exposure, more with a past history of depression and more with a GAD diagnosis in the intervention group)

<sup>&</sup>lt;sup>2</sup> US study with potential applicability issues and veteran population so may not be applicable to all men

<sup>&</sup>lt;sup>3</sup> 95% CI crosses both line of no effect and threshold for clinically significant benefit (RR 1.25)

<sup>&</sup>lt;sup>4</sup> Events<300

	randomised	serious1	serious <sup>2</sup>	serious <sup>3</sup>	serious4	none	138/357	120/372	RR 1.2 (0.77	65 more per 1000	⊕000	
	trials						(38.7%)	(32.3%)		(from 74 fewer to 277	VERY	
							, ,	,	,	more)	LOW	
										65 more per 1000		
								32.3%		(from 74 fewer to 278		
										more)		
umber v	who have had	l a depres	sion-related prim	nary care visit (f	ollow-up mea	an 12 months; ass	essed with: Database	review)				
	randomised	serious <sup>1</sup>	no serious	serious <sup>3</sup>	serious <sup>5</sup>	none	141/168	106/186	RR 1.47	268 more per 1000	⊕000	
	trials		inconsistency				(83.9%)	(57%)	(1.28 to 1.7)	(from 160 more to 399	VERY	
			·							more)	LOW	
										268 more per 1000		
								57%		(from 160 more to 399		
										more)		
umber c	of patients wh	nose unhe	Ipful medication	s (those potenti	ally exacerba	ting depression) v	vere terminated					
	randomised	serious <sup>6</sup>	no serious	no serious	very	none	23/100	17/75	RR 1.01	2 more per 1000 (from	⊕000	CRITICAL
			inconsistency	indirectness	serious <sup>7</sup>		(23%)	(22.7%)		95 fewer to 172 more)		
	trials											
	triais		·						1.76)		LOW	
	triais		,						1.76)		LOW	
eceived		therapy v	vith a minimally t	herapeutic dosa	age of antide	pressant (follow-u	o mean 12 months; as	sessed wit	,	eview)	LOW	
	≥ 90 days of		•				·		n: Database r	<u> </u>		
	≥ 90 days of	therapy v	vith a minimally t	herapeutic dosa	serious <sup>4</sup>	pressant (follow-u	224/324	182/301	n: Database r	79 more per 1000	⊕000	
	≥ 90 days of		•				·		n: Database r	<u> </u>		
	≥ 90 days of		•				224/324	182/301	RR 1.13 (0.95 to	79 more per 1000 (from 30 fewer to 212	⊕000 VERY	
	≥ 90 days of		•				224/324	182/301	RR 1.13 (0.95 to	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000	⊕000 VERY	
	≥ 90 days of		•				224/324	182/301	RR 1.13 (0.95 to	79 more per 1000 (from 30 fewer to 212 more)	⊕000 VERY	
	≥ 90 days of		•				224/324	182/301 (60.5%)	RR 1.13 (0.95 to	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000	⊕000 VERY	
	≥ 90 days of randomised trials	serious <sup>1</sup>	•				224/324	182/301 (60.5%)	RR 1.13 (0.95 to	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214	⊕000 VERY	
	≥ 90 days of randomised trials	serious <sup>1</sup>	serious <sup>2</sup>	serious <sup>3</sup>	serious <sup>4</sup>	none	224/324 (69.1%)	182/301 (60.5%) 61%	RR 1.13 (0.95 to 1.35)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more)	⊕OOO VERY LOW	CRITICAL
	≥ 90 days of randomised trials	serious <sup>1</sup>	serious <sup>2</sup> tidepressant	serious <sup>3</sup>			224/324 (69.1%)	182/301 (60.5%) 61%	RR 1.13 (0.95 to 1.35)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more)	⊕OOO VERY LOW	CRITICAL
	≥ 90 days of randomised trials	serious <sup>1</sup>	serious <sup>2</sup>	serious <sup>3</sup>	serious <sup>4</sup>	none	224/324 (69.1%)	182/301 (60.5%) 61%	RR 1.13 (0.95 to 1.35)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more)	⊕OOO VERY LOW	CRITICAL
	≥ 90 days of randomised trials	serious <sup>1</sup>	serious <sup>2</sup> tidepressant	serious <sup>3</sup>	serious <sup>4</sup>	none	224/324 (69.1%)	182/301 (60.5%) 61%	RR 1.13 (0.95 to 1.35)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more) 180 more per 1000 (from 33 more to 520	⊕OOO VERY LOW	CRITICAL
umber c	≥ 90 days of randomised trials  of adults start randomised trials	serious <sup>1</sup> ting an an	serious <sup>2</sup> tidepressant	no serious indirectness	serious <sup>4</sup>	none	224/324 (69.1%)	182/301 (60.5%) 61%	RR 1.13 (0.95 to 1.35)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more) 180 more per 1000 (from 33 more to 520	⊕OOO VERY LOW	CRITICAL
umber c	≥ 90 days of randomised trials  of adults start randomised trials	serious <sup>1</sup> ting an an  serious <sup>6</sup>	serious²  tidepressant  no serious inconsistency  psychiatric cons	no serious indirectness	serious <sup>4</sup> serious <sup>5</sup>	none	224/324 (69.1%) 26/100 (26%)	61% 6/75 (8%)	RR 1.13 (0.95 to 1.35) RR 3.25 (1.41 to 7.5)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more) 180 more per 1000 (from 33 more to 520 more)	⊕OOO VERY LOW	
umber c	≥ 90 days of randomised trials  of adults start randomised trials  of patients for randomised	serious <sup>1</sup> ting an an  serious <sup>6</sup>	serious²  tidepressant  no serious inconsistency  psychiatric cons no serious	no serious indirectness ultation was soon	serious <sup>4</sup> serious <sup>5</sup> ught  very	none	224/324 (69.1%) 26/100 (26%)	61% 6/75 (8%)	RR 1.13 (0.95 to 1.35) RR 3.25 (1.41 to 7.5)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more) 180 more per 1000 (from 33 more to 520 more)	⊕OOO VERY LOW	CRITICAL
umber c	≥ 90 days of randomised trials  of adults start randomised trials	serious <sup>1</sup> ting an an  serious <sup>6</sup>	serious²  tidepressant  no serious inconsistency  psychiatric cons	no serious indirectness	serious <sup>4</sup> serious <sup>5</sup>	none	224/324 (69.1%) 26/100 (26%)	61% 6/75 (8%)	RR 1.13 (0.95 to 1.35) RR 3.25 (1.41 to 7.5)	79 more per 1000 (from 30 fewer to 212 more) 79 more per 1000 (from 31 fewer to 214 more) 180 more per 1000 (from 33 more to 520 more)	⊕OOO VERY LOW	

<sup>1</sup> Statistically significant group differences at baseline in Hedrick 2003 (more subjects with previous depression in intervention group)

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## 9 Co-located versus geographically separate services

			Quality as	sessment			No	of patients		Effect			
											Quality	Importance	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Co-located services	Geographically separate services	Relative (95% CI)	Absolute			
Number o	of patient who	o engage	d with treatment	•		'							
	randomised trials				no serious imprecision	none	481/640 (75.2%)	338/657 (51.4%)	RR 1.46 (1.34 to 1.59)	237 more per 1000 (from 175 more to 304 more)	⊕⊕⊕O MODERATE	CRITICAL	
Number o	Number of treatment visits (Better indicated by higher values)												
	trials			no serious indirectness	serious <sup>2</sup>	none	687	703	-	MD 1.28 higher (0.87 to 1.69 higher)	⊕⊕OO LOW	CRITICAL	

<sup>&</sup>lt;sup>1</sup> Unclear ROB in multiple domains

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## Culturally-adapted psychological interventions versus usual care

			Quality asse	ssment		No of patie	nts		Effect			
											Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Culturally- adapted CBT	TAU	Relative (95% CI)	Absolute		

<sup>&</sup>lt;sup>2</sup> I-squared > 50%

<sup>&</sup>lt;sup>3</sup> US study with potential applicability issues and veteran population so may not be applicable to all men

<sup>&</sup>lt;sup>4</sup> 95% CI crosses both line of no effect and threshold for clinically significant benefit (RR 1.25)

<sup>&</sup>lt;sup>5</sup> Events<300

<sup>&</sup>lt;sup>6</sup> Unclear ROB in multiple domains

<sup>&</sup>lt;sup>7</sup> 95% CI crosses two clinical decision thresholds

<sup>&</sup>lt;sup>2</sup> 95% CI crosses one clinical decision threshold

Number	Number of participants stating that they were 'very satisfied' with treatment													
1	randomised	very	no serious	no serious	serious <sup>2</sup>	none	50/69	32/68	RR 1.54 (1.15	254 more per 1000 (from	⊕ООО	CRITICAL		
	trials	serious <sup>1</sup>	inconsistency	indirectness			(72.5%)	(47.1%)	to 2.06)	71 more to 499 more)	VERY			
											LOW			

<sup>&</sup>lt;sup>1</sup> High ROB in multiple domains <sup>2</sup> 95% CI crosses one clinical decision threshold