# Appendix 18b: High-intensity psychological interventions GRADE evidence profiles

CBT versus comparator for GAD	
Applied relaxation versus comparator for GAD	
Psychodynamic therapy versus other comparator for GAD	1
CBT versus waitlist control (subgroup analysis) for GAD	1

## **CBT** versus comparator for **GAD**

			O1:t						Summary o	of findings		
			Quality asses	sment			No. c	f patients		Effect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	СВТ	Comparator	Relative (95% CI)	Absolute	Quality	Importance
Anxiety (	self-rated) - CB	T versus waitli	st control (Better i	ndicated by low	er values)							
10		No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	199	199	-	SMD 0.63 lower (0.83 to 0.42 lower)	⊕⊕⊕⊕ HIGH	
Anxiety (	(self-rated) - CB	T versus applie	ed relaxation (Bett	er indicated by l	ower values)						•	
8	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	154	149	-	SMD 0.01 lower (0.22 lower to 0.23 higher)	⊕⊕⊕O MODERATE	3
Anxiety (	(self-rated) - CB	T versus psych	odynamic therapy	(Better indicate	d by lower value	es)		•		<u>'</u>	!	*
2		No serious limitations	No serious inconsistency	Serious <sup>2</sup>	No serious imprecision	None	64	57	-	SMD 0.45 lower (0.81 to 0.08 lower)	⊕⊕⊕O MODERATE	
Anxiety (	self-rated) - CB	T versus non-d	irective therapy (a	dults) (Better in	dicated by lower	r values)					•	
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	19	18	-	SMD 0.69 lower (1.35 to 0.02 lower)	⊕⊕⊕O MODERATE	3
Anxiety (	(self-rated) - CB	T versus non-d	irective therapy (o	older adults) (Bet	ter indicated by	lower values)					•	
1		No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	13	-	SMD 0.25 lower (0.97 lower to 0.46 higher)	⊕⊕⊕O MODERATE	3
Anxiety (	self-rated) - CB	T versus other	active treatment (a	nxiety managen	nent) (Better ind	icated by lower va	lues)				l	
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	35	16	-	SMD 0.13 lower (0.78 lower to 0.53 higher)	⊕⊕OO LOW	
Anxiety (	self-rated) - CB	T versus other	active treatment (	discussion) (Bett	er indicated by 1	ower values)						
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.13 lower (0.78 lower to 0.53 higher)	⊕⊕OO LOW	
Anxiety (	(clinician-rated)	- CBT versus v	vaitlist control (Be	tter indicated by	lower values)			•		<u>'</u>	!	*
11	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	237	237	-	SMD 1.09 lower (1.33 to 0.84 lower)	⊕⊕⊕O MODERATE	
Anxiety (	(clinician-rated)	- CBT versus a	pplied relaxation	(Better indicated	by lower value	s)						
6	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	131	118	-	SMD 0.15 lower (0.4 lower to 0.1 higher)	⊕⊕OO LOW	

nxiety	(clinician-rated	) - CBT versus	psychodynamic tl	nerapy (Better in	dicated by lowe	r values)					
	trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	64	57	-	SMD 0.46 lower (0.9 to 0.02 lower)	⊕⊕⊕⊕ HIGH
nxiety	(clinician-rated	) - CBT versus	non-directive the	rapy (adults) (Be	tter indicated by	lower values)					
	trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	19	18	-	SMD 0.93 lower (1.61 to 0.25 lower)	⊕⊕⊕O MODERATE
ıxiety	`,	1	non-directive the	- ·	ts) (Better indica		ılues)	T	ı		
	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	13	-	SMD 0.01 lower (0.72 lower to 0.7 higher)	⊕⊕⊕O MODERATE
n-rei	nission - CBT ve	rsus waitlist c	ontrol		•	·	•				
	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	65/130	109/129 (84.5%)	RR 0.62	321 fewer per 1000 (from 211 fewer to 414 fewer)	$\oplus \oplus \oplus \oplus$
							(50%)	81.3%	(0.51 to 0.75)	309 fewer per 1000 (from 203 fewer to 398 fewer)	HIGH
n-res	ponse - CBT ver	sus waitlist co	ntrol								
	Randomised trials	Serious <sup>3</sup>	Serious <sup>4</sup>	No serious indirectness	No serious imprecision	None	64/106	107/113 (94.7%)	RR 0.67	312 fewer per 1000 (from 152 fewer to 445 fewer)	⊕⊕OO
							(60.4%)	93.8%	(0.53 to 0.84)	310 fewer per 1000 (from 150 fewer to 441 fewer)	LOW
on-res	ponse - CBT ver	sus applied re	laxation	•	•	_	1	•		,	,
	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	Serious <sup>5</sup>	Serious <sup>1</sup>	None	53/91	42/87 (48.3%)	RR 1.11	53 more per 1000 (from 68 fewer to 212 more)	⊕000
							(58.2%)	46.7%	(0.86 to 1.44)	51 more per 1000 (from 65 fewer to 205 more)	VERY LOW
n-res	ponse - CBT ver	sus non-direct	tive therapy (adult	rs)							
	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	12/23	16/20 (80%)	RR 0.65	280 fewer per 1000 (from 464 fewer to 16 more)	⊕⊕00
							(52.2%)	72.5%	(0.42 to 1.02)	254 fewer per 1000 (from 421 fewer to 14 more)	LOW
	CPT	sus other activ	ve treatment (enha	nced usual care)			1	L		,	
n-res	ponse - Cb i vei	ous office activ	e eremerrere (errre								

		1		l. 1			(4E E0/)	/F1 (0/)	(0.62 + 1.26)	// 101 ( 1 124 NODER ATE
	trials	limitations	inconsistency	indirectness			(45.7%)	(51.6%)	(0.63 to 1.26)	(from 191 fewer to 134 MODERATE
									_	more)
								62.3%		69 fewer per 1000 (from 231 fewer to 162
								62.5 /0		more)
Anviota	(aliniaian ratad	CRT words (	ther active treatm	ant (anvioty man	agament) (Retter	r indicated by low	or values)			more)
Alixiety	`	<u></u>	1	. ,	1 / (	1	ei vaiuesj		T	
1	trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	35	16	-	SMD 0.59 lower (1.19 ⊕⊕OO
			,							lower to 0.01 higher) LOW
Depressi	on (self-rated) -		aitlist control (Bet	er indicated by l	ower values)					
10	Randomised	No serious	No serious	No serious	No serious	None	201	200		SMD 0.81 lower (1.11 ⊕⊕⊕⊕
	trials	limitations	inconsistency	indirectness	imprecision		201	200	-	to 0.51 lower) HIGH
Depressi	on (clinician-ra	ted) - CBT vers	us waitlist control	(Better indicated	l by lower value	s)				
4		No serious	No serious	No serious	No serious	None				SMD 0.74 lower (1.11 ⊕⊕⊕⊕
	trials	limitations	inconsistency	indirectness	imprecision		94	97	-	to 0.36 lower) HIGH
Dommossi	on (solf mated)	CPT violence on	mliad valavation (l		•					to doo level) Thigh
Depressi	_ `		plied relaxation (l		<u> </u>	h.t.			T	
7	Randomised trials	No serious limitations	No serious	No serious indirectness	Serious <sup>1</sup>	None	141	129	_	SMD 0.18 lower (0.5 ⊕⊕⊕O
			inconsistency							lower to 0.13 higher) MODERATE
Depressi	on (clinician-ra	ted) - CBT vers	us applied relaxat	on (Better indica	ited by lower va	lues)				
3	Randomised	No serious	No serious	Serious <sup>6</sup>	Serious <sup>1</sup>	None	70	60		SMD 0.08 lower (0.4 ⊕⊕OO
	trials	limitations	inconsistency				78	68	-	lower to 0.25 higher) LOW
Depressi	on (clinician-ra	ted) - CBT vers	us non-directive t	nerapy (Better in	dicated by lower	r values)				
1		Serious <sup>3</sup>	No serious	No serious	No serious	None				SMD 0.71 lower (1.38 ⊕⊕⊕O
_	trials		inconsistency	indirectness	imprecision		19	18	-	to 0.05 lower) MODERATE
D	(101 - 1)	CDT			(P	2 - 42 - 4 - 4 1 - 1	1 \			MODERATE
Depressi			her active treatmen		1	1	er vaiues)			
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	35	16	_	SMD 0.76 lower (1.37 ⊕⊕⊕⊕
	triais	IIIIIIIauons	inconsistency	mairectness	imprecision					to 0.15 lower) HIGH
Depressi	on (self-rated)	- CBT versus of	her active treatme	nts- discussion (I	Better indicated	by lower values)				
1	Randomised	Serious <sup>3</sup>	No serious	No serious	Serious <sup>1</sup>	None	10	10		SMD 0.27 lower (0.93 ⊕⊕ <b>OO</b>
	trials		inconsistency	indirectness			18	18	-	lower to 0.39 higher) LOW
Depressi	on (self-rated) -	- CBT versus ps	ychodynamic ther	apy (Better indic	ated by lower va	alues)				
2	,	No serious	No serious	Serious <sup>2</sup>	No serious	None				SMD 0.76 lower (1.21 ⊕⊕⊕O
	trials	limitations	inconsistency	Serious	imprecision	1 10110	64	57	-	( 0000
D			,						ļ	to 0.31 lower) MODERATE
Depressi	_ `		her active treatmen		,		r values)		T	0 T 0 0 1 1 1 1 0 T 1
1	Randomised	No serious	No serious	No serious	Serious <sup>1</sup>	None		<b>5</b> 0		SMD 0.34 lower (0.71
	trials	limitations	inconsistency	indirectness			66	50	-	lower to 0.03 higher) MODERATE
										1.10221111

Worry -	CBT versus wai	tlist control (Be	etter indicated by	lower values)							
9	Randomised trials	No serious limitations	Very serious <sup>7</sup>	No serious indirectness	No serious imprecision	Reporting bias <sup>8</sup>	183	183	-	SMD 1.13 lower (1.58 to 0.68 lower)	⊕OOO VERY LOW
Worry -	CBT versus app	lied relaxation	(Better indicated l	<u>, , , , , , , , , , , , , , , , , , , </u>							
6	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	130	119	-	SMD 0.02 lower (0.27 lower to 0.23 higher)	⊕⊕⊕O MODERATE
Worry -	CBT versus psy	chodynamic th	erapy (Better indic	cated by lower va	alues)						
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	29	28	-	SMD 0.32 lower (0.84 lower to 0.21 higher)	⊕⊕⊕O MODERATE
Worry -	CBT versus oth	er active treatm	ents - enhanced u	sual care (Better	indicated by lov	ver values)	•	•			
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	66	50	-	SMD 0.9 lower (1.29 to 0.52 lower)	⊕⊕⊕⊕ HIGH
QOL - C	BT versus waitl	ist control (Bet	ter indicated by lo	wer values)							
2	Randomised trials	No serious limitations	Serious <sup>4</sup>	Serious <sup>9</sup>	Serious <sup>1</sup>	None	27	28	-	SMD 1.59 lower (3.77 lower to 0.59 higher)	⊕OOO VERY LOW
QOL - C	BT versus psyc	hodynamic the	rapy (Better indica	ted by lower val	ues)						
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	35	29	-	SMD 0.15 lower (0.34 lower to 0.65 higher)	⊕⊕OO LOW
QOL - C	BT versus other	active treatme	nts - enhanced usi	ıal care (SF-12 M	lental) (Better in	dicated by lower v	alues)				
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	66	50	-	SMD 0.47 lower (0.84 to 0.1 lower)	⊕⊕⊕⊕ HIGH
QOL - C	BT versus other	active treatme	nts - discussion gr	oup (QOL-energ	y) (Better indica	ited by lower value	es)				<u> </u>
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.18 lower (0.84 lower to 0.47 higher)	⊕⊕OO LOW
Non-res	ponse - CBT vei	sus non-directi	ive therapy (older	adults)		*					
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	21/26	13/20 (65%)	RR 1.24	156 more per 1000 (from 91 fewer to 520 more)	⊕⊕⊕О
							(80.8%)	72.5%	(0.86 to 1.8)	174 more per 1000 (from 101 fewer to 580 more)	MODERATE
Non-res	ponse - CBT vei	sus other active	e treatment - discu	ssion group							
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	20/26 (76.9%)	19/26 (73.1%)	RR 1.05 (0.77 to 1.44)	37 more per 1000 (from 168 fewer to 322 more)	⊕⊕OO
							(70.970)	62.3%	(0.77 to 1.44)	31 more per 1000 (from 143 fewer to 274	LOW

										more)	
Anxi	ety (clinician-rated	) - CBT versus	other active treatr	nent – discussion	n group (Better i	ndicated by lo	wer values)			, ,	
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.06 lower (0.72 lower to 0.59 higher)	⊕⊕OO LOW
Depr	ession (self-rated)	- CBT versus n	on-directive thera	py (adults) (Bett	er indicated by l	ower values)			+		•
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	19	18	-	SMD 0.9 lower (1.58 to 0.22 lower)	⊕⊕⊕O MODERATE
Depr	ession (self-rated)	- CBT versus n	on-directive thera	py (older adults)	(Better indicate	d by lower val	lues)				
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	13	-	SMD 0.24 higher (0.48 lower to 0.95 higher)	⊕⊕⊕O MODERATE
Depr	ession (clinician-ra	ted) CBT vers	us other active tre	ntments - discuss	sion group (Bette	r indicated by	lower values)				
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.33 lower (0.98 lower to 0.33 higher)	⊕⊕OO LOW
Worr	y - CBT versus nor	n-directive the	rapy (older adults)	(Better indicate	d by lower value	s)			+		•
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	13	-	SMD 0.06 lower (0.78 lower to 0.65 higher)	⊕⊕⊕O MODERATE
Worr	y - CBT versus nor	n-directive the	rapy (adults) (Bette	er indicated by lo	ower values)	<b>!</b>	<u> </u>				,
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	19	18	-	SMD 0.97 lower (1.65 to 0.28 lower)	⊕⊕⊕O MODERATE
Worr	y - CBT versus oth	er active treatr	nents - discussion	group (Better in	dicated by lower	values)					
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.17 lower (0.82 lower to 0.49 higher)	⊕⊕OO LOW
QOL	- CBT versus other	r active treatm	ents - enhanced us	ual care (SF-12 F	hysical) (Better i	indicated by lo	ower values)				<u> </u>
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	66	50	-	SMD 0.02 higher (0.34 lower to 0.39 higher)	⊕⊕⊕O MODERATE
QOL	- CBT versus other	r active treatme	ents - discussion g	roup (QOL-Role	functioning) (Be	etter indicated	by lower value	s)			
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.59 lower (1.26 lower to 0.08 higher)	⊕⊕OO LOW
QOL	- CBT versus other	r active treatme	ents - discussion g	roup (QOL-socia	al role) (Better in	dicated by lov	ver values)			Į.	<b>!</b>
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	18	18	-	SMD 0.11 lower (0.76 lower to 0.54 higher)	⊕⊕OO LOW
Non-	remission - CBT ve	ersus applied r	elaxation			<b>.</b>	, , , , , , , , , , , , , , , , , , ,		<b>.</b>		
4	Randomised trials	No serious limitations	Serious <sup>4</sup>	No serious indirectness	Serious <sup>1</sup>	None	44/81 (54.3%)	47/75 (62.7%)	RR 0.94 (0.63 to 1.41)		⊕⊕OO LOW
								55%		33 fewer per 1000	

		1	_	1					1	1	
										(from 204 fewer to 225	
										more)	
Non-remi	ission - CBT ve	rsus other acti	ve treatment - disc	ussion group							
	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	12/26	13/26 (50%)	RR 0.92	40 fewer per 1000 (from 240 fewer to 315 more)	⊕⊕00
							(46.2%)	50%	(0.52 to 1.63)	40 fewer per 1000 (from 240 fewer to 315 more)	LOW
Discontin	uation due to	any reason - Cl	BT versus waitlist	control							
12	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	43/258	31/258 (12%)	RR 1.4 (0.7	48 more per 1000 (from 36 fewer to 215 more)	$\oplus \oplus \oplus \oplus$
							(16.7%)	8.7%	to 2.79)	35 more per 1000 (from 26 fewer to 156 more)	HIGH
Discontin	uation due to	any reason - Cl	BT versus applied	relaxation							
8	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	21/172	29/162 (17.9%)	RR 0.75	45 fewer per 1000 (from 102 fewer to 55 more)	$\oplus \oplus \oplus \oplus$
							(12.2%)	17.4%	(0.43 to 1.31)	43 fewer per 1000 (from 99 fewer to 54 more)	HIGH
Discontin	uation due to	any reason - Cl	BT versus non-dire	ective therapy							
	Randomised trials	Serious <sup>3,10</sup>	No serious inconsistency	Serious <sup>11</sup>	Serious <sup>1</sup>	None	12/49	9/40 (22.5%)		4 more per 1000 (from 115 fewer to 252 more)	⊕000
							(24.5%)	22.5%	(0.49 to 2.12)	4 more per 1000 (from 115 fewer to 252 more)	VERY LOW
Discontin	uation due to	any reason - Cl	BT versus psychod	lynamic therapy							
	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness <sup>2</sup>	Serious <sup>1</sup>	None	6/69	12/73 (16.4%)	RR 0.54	76 fewer per 1000 (from 130 fewer to 59 more)	⊕⊕⊕О
							(8.7%)	15.4%	(0.21 to 1.36)	71 fewer per 1000 (from 122 fewer to 55 more)	MODERATE
Discontin	uation due to	any reason - Cl	BT versus other ac	tive treatments -	anxiety manage	ment					
1	Randomised trials	Serious <sup>3</sup>	No serious inconsistency	No serious indirectness	Serious <sup>1</sup>	None	4/40 (10%)	6/25 (24%)	RR 0.42 (0.13 to 1.33)	139 fewer per 1000 (from 209 fewer to 79 more) 139 fewer per 1000	⊕⊕OO LOW

Diametic		CP.	T	- traction and						(from 209 fewer to 79 more)		
		<u> </u>	T versus other acti			1	I	1	I			
					No serious imprecision	None	4/70	14/64 (21.9%)	RR 0.26	162 fewer per 1000 (from 55 fewer to 199 fewer)	$\oplus \oplus \oplus \oplus$	
							(5.7%)	24%	(0.09 to 0.75)	178 fewer per 1000 (from 60 fewer to 218 fewer)	HIGH	
Discontin	nuation due to	any reason - CB	T versus other act	ve treatments - c	liscussion group	,		•				
	Randomised trials			No serious indirectness	Serious <sup>1</sup>	None	8/26	8/26 (30.8%)	RR 1 (0.44 to	0 fewer per 1000 (from 172 fewer to 388 more)	⊕⊕00	
							(30.8%)	24%	2.26)	0 fewer per 1000 (from 134 fewer to 302 more)	LOW	

<sup>&</sup>lt;sup>1</sup> 95% confidence interval include no effect

<sup>&</sup>lt;sup>2</sup> Duration for treatment is average of 15 weeks and control is average of 30 weeks

<sup>&</sup>lt;sup>3</sup> High attrition bias and completer analysis

<sup>&</sup>lt;sup>4</sup> Moderate heterogeneity (50-80%)

<sup>&</sup>lt;sup>5</sup> Half of the trials were cognitive therapy while other half were CBT

<sup>&</sup>lt;sup>6</sup> Treatment varies and include: worry exposure, cognitive therapy and manualised CBT

<sup>&</sup>lt;sup>7</sup> High heterogeneity (>80%)

<sup>&</sup>lt;sup>8</sup> Funnel plot inspected (Egger's test p value=0.02)

<sup>&</sup>lt;sup>9</sup> Treatment varies: CBT and acceptance-based behaviour therapy

<sup>&</sup>lt;sup>10</sup> High detection bias

<sup>&</sup>lt;sup>11</sup> The studies target different populations (adults and older adults)

### Health economic profile

Individual	CBT versus wai	ting list					
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental effect	ICER (£/effect)	Uncertainty
Guideline analysis UK	Potentially serious limitations <sup>2</sup>	Directly applicable <sup>3</sup>		£1,125	n/a	n/a	Not estimated
Group CBT	versus waiting	list					
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)¹	Incremental effect	ICER (£/effect)	Uncertainty <sup>1</sup>
Guideline analysis UK	Potentially serious limitations <sup>2</sup>	Directly applicable <sup>3</sup>		£300-350	n/a	n/a	£300-350

<sup>&</sup>lt;sup>1</sup>Costs expressed in 2009 UK pounds

### Applied relaxation versus comparator for GAD

			Quality asses	cm cmt				:	Summary of	findings		
			Quality asses	smem			No. of 1	patients		Effect		Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Applied relaxation	Comparator	Relative (95% CI)	Absolute	Quality	Importance
Anxiety (	self-rated) - ap	plied relaxatior	n versus waitlist c	ontrol (Better inc	dicated by lower	values)						
3			No serious inconsistency	No serious indirectness	No serious imprecision	None	62	59	-	SMD 0.49 lower (0.86 to 0.13 lower)	⊕⊕⊕⊕ HIGH	
Anxiety (	self-rated) - ap	plied relaxatior	versus non-direc	tive therapy (Be	tter indicated by	lower values)		•				
1	Randomised trials		No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	18	18	-	SMD 0.48 lower (1.14 lower to 0.19 higher)	⊕⊕OO LOW	
Anxiety (	clinician-rated	) - applied relax	ation versus wait	list control (Bett	er indicated by	ower values)		•				
3			No serious inconsistency	No serious indirectness	No serious imprecision	None	63	61	-	SMD 1 lower (1.38 to 0.62 lower)	$\oplus \oplus \oplus \oplus$	

<sup>&</sup>lt;sup>2</sup> Simple cost analysis; only intervention costs considered; resource use estimated based on data reported in RCTs included in the guideline systematic review supported by the GDG expert opinion

<sup>&</sup>lt;sup>3</sup>Cost analysis conducted to assist guideline development; NHS perspective

Depression  Depression  Repression  Depression  Repression  Repression  Repression	Randomised rials  n (self-rated) - Randomised rials  n (self-rated) - Randomised rials  n (clinician-ra Randomised	Serious <sup>1</sup> • applied relaxa  No serious  limitations  • applied relaxa  Serious <sup>1</sup>	No serious inconsistency  No serious inconsistency  No serious inconsistency  Ition versus non-consistency  No serious inconsistency  Relaxation versus non-consistency	No serious indirectness ist control (Bette No serious indirectness lirective therapy No serious indirectness	Serious <sup>2</sup> r indicated by lo  No serious imprecision	None None None None	18	18	-	SMD 0.82 lower (1.51 to 0.14 lower)  SMD 0.54 lower (0.98 to 0.1 lower)	HIGH  ⊕⊕OO LOW  ⊕⊕⊕⊕ HIGH	
Depression  Pepression  Repression  Comparison  Repression  Depression  Repression	Randomised rials  n (self-rated) - Randomised rials  n (self-rated) - Randomised rials  n (clinician-ra Randomised	Serious <sup>1</sup> • applied relaxa  No serious limitations  • applied relaxa  Serious <sup>1</sup> ted) - applied 1	No serious inconsistency  tion versus waitli  No serious inconsistency  tion versus non-co  No serious inconsistency	No serious indirectness ist control (Bette No serious indirectness lirective therapy No serious indirectness	Serious <sup>2</sup> r indicated by lo  No serious imprecision  (Better indicate)	None None None None	18		-	to 0.14 lower)  SMD 0.54 lower (0.98	LOW	
Depression  Depression  Depression  R  to  R	Randomised rials  n (self-rated) - Randomised rials  n (clinician-ra Randomised	No serious limitations - applied relaxa Serious <sup>1</sup> ted) - applied 1	No serious inconsistency tion versus non-c No serious inconsistency	No serious indirectness  lirective therapy  No serious indirectness	No serious imprecision  (Better indicate)	None ed by lower valu		40	-	`		
Depression R to Depression R	rials  n (self-rated) - Randomised rials n (clinician-ra Randomised	limitations  - applied relaxa  Serious <sup>1</sup> ted) - applied 1	inconsistency  tion versus non-c  No serious inconsistency	indirectness  lirective therapy  No serious indirectness	imprecision (Better indicate	ed by lower valu		40	-	`		
Depression	Randomised rials n (clinician-ra Randomised	Serious <sup>1</sup> ted) - applied 1	No serious inconsistency	No serious indirectness							шып	
Depression R	rials n (clinician-ra Randomised	ted) - applied 1	inconsistency	indirectness	Serious <sup>2</sup>		es)					
2 R	Randomised		elaxation versus			None	18	18	-	SMD 0.36 lower (1.02 lower to 0.29 higher)	⊕⊕OO LOW	
		No serious		waitlist control (	Better indicated	by lower value	s)					
T.		limitations	Serious <sup>3</sup>	No serious indirectness	Serious <sup>2</sup>	None	53	51	-	SMD 0.47 lower (1.14 lower to 0.2 higher)	⊕⊕OO LOW	
Norry - ap	plied relaxati	on versus wait	list control (Better	r indicated by lo	wer values)	-			•			
	Randomised rials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	54	50	-	SMD 0.7 lower (1.1 to 0.31 lower)	⊕⊕⊕⊕ HIGH	
Vorry - ap	plied relaxati	on versus non-	directive therapy	(Better indicated	d by lower value	es)						
	Randomised rials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	18	18	-	SMD 0.61 lower (1.28 lower to 0.06 higher)	⊕⊕OO LOW	
Non-respon	nse - applied	relaxation vers	us waitlist contro	1		•					•	
R		Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	(11(27.59))	20/20 (100%)	RR 0.39	610 fewer per 1000 (from 280 fewer to 790 fewer)	⊕⊕⊕О	
							6/16 (37.5%)	100%	(0.21 to 0.72)	610 fewer per 1000 (from 280 fewer to 790 fewer)	MODERATE	
Non-respon	nse - applied	relaxation vers	us non-directive t	therapy								
	Randomised rials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	10/23	16/20 (80%)	RR 0.54	368 fewer per 1000 (from 72 fewer to 544 fewer)	$\oplus \oplus \oplus O$	
							(43.5%)	80%	(0.32 to 0.91)	368 fewer per 1000 (from 72 fewer to 544 fewer)	MODERATE	
Discontinu	uation due to	any reason - ap	plied relaxation v	versus waitlist co	ontrol							
		No serious limitations	Serious <sup>3</sup>	No serious indirectness	Serious <sup>2</sup>	None	15/70 (21.4%)	11/71 (15.5%)	RR 2.2 (0.37 to 13.19)	186 more per 1000 (from 98 fewer to 1889 more) 38 more per 1000	⊕⊕OO LOW	

Discontinua	ation due to a	inv reason - apr	olied relaxation ve	ersus non-directi	ve therapy					(from 20 fewer to 390 more)		
1 Ra		Serious <sup>1</sup>	No serious		Serious <sup>2</sup>	None	5/23 (21.7%)	2/20 (10%)	RR 2.17 (0.47 to 10)	117 more per 1000 (from 53 fewer to 900 more) 117 more per 1000 (from 53 fewer to 900 more)	⊕⊕OO LOW	

<sup>&</sup>lt;sup>1</sup> High attrition bias and completer analysis

#### Health economic profile

Applied rela	Applied relaxation versus waiting list											
Study & country												
Guideline analysis UK	Potentially serious limitations <sup>2</sup>	Directly applicable <sup>3</sup>		£1,125	n/a	n/a	Not estimated					

<sup>&</sup>lt;sup>1</sup>Costs expressed in 2009 UK pounds

<sup>&</sup>lt;sup>2</sup> 95% confidence interval include no effect

<sup>&</sup>lt;sup>3</sup> Moderate heterogeneity (50-80%)

<sup>&</sup>lt;sup>2</sup>Simple cost analysis; only intervention costs considered; resource use estimated based on data reported in RCTs included in the guideline systematic review supported by the GDG expert opinion

<sup>&</sup>lt;sup>3</sup>Cost analysis conducted to assist guideline development; NHS perspective

## Psychodynamic therapy versus other comparator for GAD

			Quality asses	cm cm l				Sum	mary of fine	dings			
			Quality asses	smem			No. of pa	tients		Effect		Importance	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Psychodynamic therapy	Other comparator	Relative (95% CI)	Absolute	Quality	Importance	
Anxiety (	Anxiety (self-rated) - psychodynamic versus active control (Better indicated by lower values)												
1	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	29	35	-	SMD 0.18 higher (0.31 lower to 0.67 higher)	⊕⊕OO LOW		
Anxiety (	Anxiety (self-rated) - psychodynamic versus non-directive therapy (Better indicated by lower values)												
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	15	16	-	SMD 0.47 higher (0.24 lower to 1.19 higher)	⊕⊕⊕O moderate		
Anxiety (	clinician-rated	l) - psychodyna	amic versus active	e control (Better	indicated by lo	wer values)							
1	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	29	35	-	SMD 0.08 higher (0.41 lower to 0.57 higher)	⊕⊕OO LOW		
Anxiety (	clinician-rated	l) - psychodyna	amic versus non-c	directive therap	y (Better indicat	ed by lower valu	es)						
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	15	16	-	SMD 0.25 lower (0.95 lower to 0.46 higher)	⊕⊕⊕O MODERATE		
Depressi	on (self-rated)	- psychodynar	nic therapy versu	s active control	(Better indicate	d by lower values	s)					•	
1	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	29	16	-	SMD 0.24 higher (0.38 lower to 0.85 higher)	⊕⊕OO LOW		
Depressi	on (self-rated)	- psychodynar	nic versus non-di	rective therapy	(Better indicate	d by lower values	s)						
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	15	16	-	SMD 0.12 higher (0.58 lower to 0.83 higher)	⊕⊕⊕O MODERATE		
Depressi	on (clinician-r	ated) - psychod	lynamic versus n	on-directive the	rapy (Better ind	icated by lower v	alues)						
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	15	16	-	SMD 0.08 lower (0.78 lower to 0.63 higher)	⊕⊕⊕O MODERATE		
QOL - ps	ychodynamic	therapy versus	active control (B	etter indicated b	y lower values)								
1	Randomised	Serious <sup>1</sup>	No serious	No serious	Serious <sup>2</sup>	None	29	16	-	SMD 0.01 lower	$\oplus \oplus OO$		

	trials		inconsistency	indirectness						(0.62 lower to 0.61 higher)	LOW	
Non-rem	ission - psycho	odynamic vers	us non-directive	therapy								
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	8/15 (53.3%)	14/16 (87.5%)	RR 0.61 (0.37 to	341 fewer per 1000 (from 551 fewer to 9 more)	$\oplus \oplus \oplus \oplus$	
							, , ,	87.5%	1.01)	341 fewer per 1000 (from 551 fewer to 9 more)	HIGH	
Disconti	nuation due to	any reason- p	sychodynamic ve	rsus active cont	rol							
1	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	9/45 (20%)	6/25 (24%)	RR 0.83 (0.34 to	41 fewer per 1000 (from 158 fewer to 257 more)	⊕⊕OO LOW	
							9/ 40 (20%)	24%	2.07)	41 fewer per 1000 (from 158 fewer to 257 more)		
Disconti	nuation due to	any reason- p	sychodynamic ve	rsus non-direct	ive therapy							
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious <sup>2</sup>	None	1 /15 (4 7%)	2/16 (12.5%)	RR 0.53 (0.05 to	59 fewer per 1000 (from 119 fewer to 536 more)	⊕⊕⊕О	
							1/15 (6.7%)	12.5%	5.29)	59 fewer per 1000 (from 119 fewer to 536 more)	MODERATE	

<sup>&</sup>lt;sup>1</sup> High attrition bias and completer analysis <sup>2</sup> 95% confidence interval include no effect

## CBT versus waitlist control (subgroup analysis) for GAD

			01.1.1					s	ummary of	findings		
			Quality asses	sment			No	o. of patients		Effect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	СВТ	Waitlist control (subgroup analysis)	Relative (95% CI)	Absolute	Quality	Importance
Anxiety (	self-rated) - CE	BT versus waitl	ist control (adults	) (Better indicate	d by lower valu	ies)						
7		No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	137	127	1	SMD 0.59 lower (0.85 to 0.33 lower)	⊕⊕⊕⊕ HIGH	
Anxiety (	self-rated) - CE	T versus waitl	ist control (older	adults) (Better in	dicated by lowe	er values)						
2		No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	47	56	-	SMD 0.72 lower (1.12 to 0.32 lower)	⊕⊕⊕⊕ HIGH	
Anxiety (	self-rated) - CE	T versus waitl	ist control (indivi	dual sessions) (E	Better indicated	by lower values)		<u> </u>		,		•
7		No serious limitations¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	141	135	-	SMD 0.56 lower (0.8 to 0.32 lower)	⊕⊕⊕⊕ HIGH	
Anxiety (	self-rated) - CE	T versus waitl	ist control (group	sessions) (Better	indicated by lo	wer values)						
2	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	43	48	-	SMD 0.83 lower (1.26 to 0.39 lower)	⊕⊕⊕O MODERATE	
Anxiety (	clinician-rated	) -CBT versus v	waitlist control (ac	dults) (Better ind	icated by lower	values)						
8		No serious limitations	Serious <sup>2</sup>	No serious indirectness	No serious imprecision	None	175	165	-	SMD 1.14 lower (1.46 to 0.83 lower)	⊕⊕⊕O MODERATE	
Anxiety (	clinician-rated	) - CBT versus	waitlist control (o	lder adults) (Bet	ter indicated by	lower values)						
2		No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	47	56	-	SMD 1.09 lower (1.58 to 0.59 lower)	⊕⊕⊕⊕ HIGH	
Anxiety (	clinician-rated	) - CBT versus	waitlist control (i	ndividual sessio	ns) (Better indic	ated by lower val	ues)					
8	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	179	173	-	SMD 1.08 lower (1.38 to 0.77 lower)	⊕⊕⊕O MODERATE	
Anxiety (	clinician-rated	) - CBT versus	waitlist control (g	roup sessions) (l	Better indicated	by lower values)						
2	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness³	No serious imprecision	None	43	48	1	SMD 1.32 lower (1.78 to 0.86 lower)	⊕⊕⊕O MODERATE	
Depressi	on (self-rated)	- CBT versus w	aitlist control (ad	ults) (Better indi	cated by lower	values)						
7	Randomised	No serious	Serious <sup>2</sup>	No serious	No serious	None	139	128	-	SMD 0.73 lower (1.13	$\oplus \oplus \oplus O$	

2 I	Randomised trials on (self-rated) -	CBT versus w No serious limitations	No serious	der adults) (Bette	imprecision er indicated by I	lower values)	ļ.			,	
t	trials on (self-rated) -		No serious								
Depressio	, ,		inconsistency	No serious indirectness	No serious imprecision	None	47	56	-	SMD 0.84 lower (1.25 to 0.44 lower)	
Depression (self-rated) - CBT versus waitlist control (individual sessions) (Better indicated by lower values)											
		No serious limitations	Serious <sup>2</sup>	No serious indirectness	No serious imprecision	None	143	136	-	SMD 0.7 lower (1.08 to 0.32 lower) MODERATE	
Non-remis	ssion - CBT ve	rsus waitlist co	ontrol (adults)	L		L					
_		No serious limitations	Serious <sup>4</sup>	Serious <sup>3</sup>	No serious imprecision	None	32/65	56/65 (86.2%)	RR 0.62 (0.41 to	327 fewer per 1000 (from 52 fewer to 508 fewer) ⊕⊕OO	
							(49.2%)	81.3%	0.94)	309 fewer per 1000 LOW (from 49 fewer to 480 fewer)	
Depressio	,		aitlist control (gr	<u>, , , , , , , , , , , , , , , , , , , </u>		y lower values)					
	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	43	48	-	SMD 0.96 lower (1.4 to 0.52 lower) MODERATE	
Depressio	n (clinician-ra	ted) - CBT vers	sus waitlist contro	ol (adults) (Better	r indicated by lo	ower values)					
	Randomised trials	Serious <sup>1</sup>	Serious <sup>2</sup>	Serious <sup>3</sup>	No serious imprecision	None	47	41	-	SMD 0.87 lower (1.63 to 0.11 lower) WERY LOW	
Depressio	n (clinician-ra	ted) - CBT vers	sus waitlist contro	ol (older adults) (	Better indicated	d by lower values)					
	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	No serious imprecision	None	47	56	-	SMD 0.59 lower (0.99 to 0.19 lower) MODERATE	
Depressio	n (clinician-ra	ted) - CBT vers	sus waitlist contro	ol (individual ses	ssions) (Better i	ndicated by lower	values)				
	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	Serious <sup>3</sup>	No serious imprecision	None	76	76	-	SMD 0.84 lower (1.26 to 0.42 lower) ⊕⊕OO LOW	
Depressio	n (clinician-ra	ted) - CBT vers	sus waitlist contro	ol (group session	s) (Better indica	ted by lower valu	es)				
	Randomised trials	Serious <sup>1</sup>	No serious inconsistency	No serious indirectness	Serious <sup>5</sup>	None	18	21	-	SMD 0.4 lower (1.04 lower to 0.23 higher) LOW	
Worry - Cl	BT versus wai	tlist control (ac	lults) (Better indi	cated by lower v	alues)					†	
		No serious limitations	Very serious <sup>6</sup>	No serious indirectness	No serious imprecision	None	121	111	-	SMD 1.15 lower (1.81 to 0.5 lower) ⊕⊕OO LOW	
Worry - Cl	BT versus wai	tlist control (ol	der adults) (Bette	r indicated by lo	wer values)						
		No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	47	56	-	SMD 0.89 lower (1.33 to 0.46 lower)	

Worry - 0	Vorry - CBT versus waitlist control (individual sessions) (Better indicated by lower values)											
6	Randomised trials	No serious limitations	Serious <sup>2</sup>	Serious <sup>3</sup>	No serious imprecision	None	125	119	-	SMD 1.16 lower (1.81 to 0.52 lower)	⊕⊕OO LOW	
Worry - 0	Norry - CBT versus waitlist control (group sessions) (Better indicated by lower values)											
2	Randomised trials		No serious inconsistency	No serious indirectness	No serious imprecision	None	43	48	-	SMD 0.85 lower (1.28 to 0.41 lower)	⊕⊕⊕O MODERATE	
Non-rem	ission - CBT ve	ersus waitlist co	ontrol (older adult	s)								
2	Randomised trials	No serious limitations	No serious inconsistency	No serious No serious None indirectness imprecision	33/65	53/64 (82.8%)	RR 0.62	315 fewer per 1000 (from 166 fewer to 439 fewer)	$\oplus \oplus \oplus \oplus$			
							(50.8%)	83.7%	(0.47 to 0.8)	318 fewer per 1000 (from 167 fewer to 444 fewer)	HIGH	
Non-resp	onse - CBT ve	rsus waitlist co	ntrol (adults)									
3	Randomised trials	No serious limitations	Serious <sup>2</sup>	Serious <sup>3</sup>	No serious imprecision	None	19/38	44/46 (95.7%)	RR 0.57	411 fewer per 1000 (from 77 fewer to 612 fewer)	⊕⊕OO	
							(50%)	93.8%	(0.36 to 0.92)	403 fewer per 1000 (from 75 fewer to 600 fewer)	LOW	
Non-resp	onse - CBT ve	rsus waitlist co	ntrol (older adults	;)								
2	Randomised trials	No serious limitations	Serious <sup>2</sup>	No serious indirectness	No serious imprecision	None	41/65	60/64 (93.8%)	RR 0.69 (0.49 to	291 fewer per 1000 (from 19 fewer to 478 fewer)	⊕⊕⊕О	
							(63.1%)	94.2%	`0.98)	292 fewer per 1000 (from 19 fewer to 480 fewer)	MODERATE	

<sup>&</sup>lt;sup>1</sup> High attrition bias and completer analysis
<sup>2</sup> Moderate heterogeneity (50-80%)
<sup>3</sup> Difference in treatment principles
<sup>4</sup> Borderline heterogeneity (45-50%)
<sup>5</sup> 95% confidence interval include no effect

<sup>&</sup>lt;sup>6</sup> High heterogeneity (>80%)