1 Low intensity psychological interventions for GAD and mixed anxiety

1.1 Pure self-help vs comparator for pure GAD, mixed anxiety disorders or both populations

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	pure self-help	comparator	Relative (95% CI)	Absolute	Quality	Importance
			Quality assessment					No of patients		Summary of findings		
									Effect			
Non remission - Mixed anxiety population-pure self help vs TAU												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/18 (66.7%)	15/16 (93.8%)	RR 0.71 (0.5 to 1.01)	272 fewer per 1000 (from 469 fewer to 9 more)	HIGH	
								94.5%		274 fewer per 1000 (from 472 fewer to 9 more)		
Anxiety -Mixed anxiety population- Pure bibliotherapy vs Non active control (Better indicated by lower values)												
4	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	86	56	-	SMD 0.76 lower (1.12 to 0.4 lower)	MODERATE	
Anxiety-Pure GAD population- Pure bibliotherapy vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	17	18	-	SMD 1.06 lower (1.77 to 0.35 lower)	HIGH	
Anxiety - combined population-Pure self help vs TAU (Better indicated by lower values)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18	16	-	SMD 0.7 lower (1.4 to 0.01 lower)	MODERATE	
Non remission - Mixed anxiety population-pure self help vs non active control												
2	randomised trials	no serious limitations	no serious inconsistency	serious[3]	no serious imprecision	none	25/39 (64.1%)	35/37 (94.6%)	RR 0.68 (0.53 to 0.87)	303 fewer per 1000 (from 123 fewer to 445 fewer)	MODERATE	
								94.5%		302 fewer per 1000 (from 123 fewer to 444 fewer)		
Anxiety - combined population-Pure self help vs non active control (Better indicated by lower values)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	153	124	-	SMD 0.74 lower (0.99 to 0.49 lower)	MODERATE	
Discontinuation due to any reason - mixed anxiety population- Pure bibliotherapy vs non active control)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[3]	serious[4]	none	2/41 (4.9%)	5/39 (12.8%)	RR 0.5 (0.09 to 2.84)	64 fewer per 1000 (from 117 fewer to 236 more)	LOW	

No	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other	n1	n2	Relative effect (RR)	Absolute	Quality	
								12.7%		64 fewer per 1000 (from 116 fewer to 234 more)		
Anxiety-Pure GAD population- Pure computer mindfulness therapy vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	50	50	-	SMD 0.61 lower (1.01 to 0.21 lower)	HIGH	
Depression - Mixed anxiety population-pure bibliotherapy vs non active control (Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	57	28	-	SMD 0.78 lower (1.27 to 0.3 lower)	MODERATE	
Non remission - Mixed anxiety population-pure self help vs WLC												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	13/21 (61.9%)	20/21 (95.2%)	RR 0.65 (0.46 to 0.92)	333 fewer per 1000 (from 76 fewer to 514 fewer)	HIGH	
								94.5%		331 fewer per 1000 (from 76 fewer to 510 fewer)		
Anxiety - combined population-Pure self help vs WLC (Better indicated by lower values)												
5	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	135	108	-	SMD 0.74 lower (1.01 to 0.48 lower)	MODERATE	
Discontinuation due to any reason - pure GAD population- Pure bibliotherapy vs WLC												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[4]	none	2/19 (10.5%)	1/19 (5.3%)	RR 2 (0.2 to 20.24)	53 more per 1000 (from 42 fewer to 1013 more)	MODERATE	
								27.9%		279 more per 1000 (from 223 fewer to 5368 more)		
Discontinuation due to any reason - pure GAD population- Pure computer mindfulness therapy vs WLC (Copy)												
1	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	32/116 (27.6%)	58/115 (50.4%)	RR 0.55 (0.39 to 0.77)	227 fewer per 1000 (from 116 fewer to 308 fewer)	MODERATE	
								27.9%		126 fewer per 1000 (from 64 fewer to 170 fewer)		
Discontinuation due to any reason - combined population- Pure self help vs non active control												
4	randomised trials	serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	36/187 (19.3%)	64/185 (34.6%)	RR 0.56 (0.4 to 0.78)	152 fewer per 1000 (from 76 fewer to 208 fewer)	LOW	
								27.9%		123 fewer per 1000 (from 61 fewer to 167 fewer)		
Discontinuation due to any reason - combined population- Pure self help vs WLC												
3	randomised	serious[1]	no serious	no serious	no serious	none	34/156	62/155	RR 0.55 (0.37	180 fewer per 1000		

2

	trials		inconsistency	indirectness	imprecision		(21.8%)	(40%)	to 0.82)	(from 72 fewer to 252 fewer)	MODERATE	
								27.9%		126 fewer per 1000 (from 50 fewer to 176 fewer)		
Discontinuation due to any reason - combined population- Pure self help vs WLC (Copy)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	2/20 (10%)	2/18 (11.1%)	RR 0.9 (0.14 to 5.74)	11 fewer per 1000 (from 96 fewer to 527 more)	LOW	
								27.9%		28 fewer per 1000 (from 240 fewer to 1322 more)		

[1] majority completer analysis and unclear bias which may likely inflate the effect size
[2] Unclear attrition bias and completer analysis
[3] different comparison group (WLC and TAU)
[4] 95% confidence interval include no effect
[5] High attrition bias and completer analysis

Economic profile

Stepped care versus minimal intervention							
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Drummond et al. 2009, UK	Minor Limitations [1]	Directly applicable[2]		Unable to calculate [3]	Unable to calculate	Unable to calculate	98% probability of stepped care intervention being cost-effective at UK £20-30,000 threshold- based on 1000 bootstrap samples

[1] Short time horizon; no formal synthesis of incremental costs and effectiveness
[2] Societal perspective including criminal justice costs;
[3] Not possible to calculate ICER with data available. Authors did not report total costs over 6-month period

Appendix 18a

1.2 Guided self help vs comparator for pure GAD, mixed anxiety disorders or both populations

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	guided self help	comparator	Relative (95% CI)	Absolute	Quality	Importance
			Quality assessment						Summary of findings			
							No of patients		Effect			
Anxiety - mixed anxiety population- guided bibliotherapy vs WLC (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	27	33	-	SMD 0.62 lower (1.14 to 0.1 lower)	MODERATE	
Anxiety - mixed anxiety population-guided bibliotherapy vs TAU (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	serious[2]	serious[3]	none	80	44	-	SMD 0.15 higher (0.22 lower to 0.51 higher)	LOW	
Anxiety-pure GAD population-guided CCBT vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	24	21	-	SMD 1.22 lower (1.86 to 0.57 lower)	HIGH	
Anxiety - combined population-guided self help vs non active control (Better indicated by lower values)												
4	randomised trials	serious[1]	serious[4]	serious[2,5]	serious[3]	none	131	98	-	SMD 0.38 lower (0.99 lower to 0.24 higher)	VERY LOW	
Anxiety - combined population-guided self help vs WLC (Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[5]	no serious imprecision	none	51	54	-	SMD 0.89 lower (1.47 to 0.31 lower)	LOW	
Depression - mixed anxiety population-guided bibliotherapy vs WLC (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	27	33	-	SMD 0.44 lower (0.95 lower to 0.08 higher)	LOW	
Depression - mixed anxiety population-guided bibliotherapy vs TAU (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[4]	serious[2]	serious[3]	none	78	44	-	SMD 0.03 higher (0.78 lower to 0.84 higher)	VERY LOW	
Depression-pure GAD population-guided CCBT vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	24	21	-	SMD 0.85 lower (1.46 to 0.23 lower)	HIGH	
Depression - combined population-guided self help vs non active ctrl (Better indicated by lower values)												
4	randomised trials	serious[1]	serious[4]	serious[2,5]	serious[3]	none	129	98	-	SMD 0.31 lower (0.86 lower to 0.25 higher)	VERY LOW	
Depression - combined population-guided self help vs WLC (Better indicated by lower values)												
2	randomised	serious[1]	no serious	serious[5]	no serious	none	51	54	-	SMD 0.63 lower (1.02		

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative effect (RR)	Absolute	Quality	
	trials		inconsistency		imprecision					to 0.23 lower)	LOW	
Worry - mixed anxiety population-guided bibliotherapy vs TAU (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[3]	none	53	26	-	SMD 0.17 higher (0.3 lower to 0.64 higher)	MODERATE	
Worry-pure GAD population-guided CCBT vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	24	21	-	SMD 0.93 lower (1.55 to 0.32 lower)	HIGH	
Non remission - combined population-guided self help vs non active control												
2	randomised trials	serious[1]	very serious[6]	serious[5]	serious[3]	none	53/72 (73.6%)	62/69 (89.9%)	RR 0.71 (0.32 to 1.59)	261 fewer per 1000 (from 611 fewer to 530 more)	VERY LOW	
								86.6%		251 fewer per 1000 (from 589 fewer to 511 more)		
Non remission - mixed anxiety population-guided bibliotherapy vs WLC												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	42/48 (87.5%)	42/48 (87.5%)	RR 1 (0.86 to 1.16)	0 fewer per 1000 (from 122 fewer to 140 more)	MODERATE	
								87.5%		0 fewer per 1000 (from 122 fewer to 140 more)		
Worry -combined population-guided self help vs non active control (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[6]	serious[5]	serious[3]	none	77	47	-	SMD 0.36 lower (1.44 lower to 0.71 higher)	VERY LOW	
Non-remission- pure GAD population-guided CCBT vs WLC												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/24 (45.8%)	20/21 (95.2%)	RR 0.48 (0.31 to 0.75)	495 fewer per 1000 (from 238 fewer to 657 fewer)	HIGH	
								85.7%		446 fewer per 1000 (from 214 fewer to 591 fewer)		
Non-response-pure GAD population-guided CCBT vs WLC												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/24 (62.5%)	21/21 (100%)	RR 0.63 (0.46 to 0.87)	370 fewer per 1000 (from 130 fewer to 540 fewer)	HIGH	
								90.5%		335 fewer per 1000 (from 118 fewer to 489 fewer)		
Discontinuation due to any reason - Mixed anxiety population-guided bibliotherapy vs (WLC												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	21/47 (44.7%)	15/48 (31.3%)	RR 1.4 (0.83 to 2.37)	125 more per 1000 (from 53 fewer to 428 more)	LOW	

							12.9%		52 more per 1000 (from 22 fewer to 177 more)		
Discontinuation due to any reason - Mixed anxiety population-guided bibliotherapy vs TAU											
2	randomised trials	no serious limitations	serious[4]	serious[2]	serious[3]	none	9/96 (9.4%)	6/57 (10.5%)	RR 0.57 (0.03 to 9.99)	45 fewer per 1000 (from 102 fewer to 946 more)	VERY LOW
								12.9%		55 fewer per 1000 (from 125 fewer to 1160 more)	
Discontinuation due to any reason - pure GAD population-guided CCBT vs WLC											
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/24 (25%)	2/21 (9.5%)	RR 2.62 (0.59 to 11.64)	154 more per 1000 (from 39 fewer to 1013 more)	HIGH
								9.5%		154 more per 1000 (from 39 fewer to 1011 more)	
Discontinuation due to any reason - combined population-guided self help vs non active control											
4	randomised trials	no serious limitations[1]	no serious inconsistency	serious[2]	serious[3]	none	36/168 (21.4%)	23/126 (18.3%)	RR 1.42 (0.7 to 2.91)	77 more per 1000 (from 55 fewer to 349 more)	LOW
								12.9%		54 more per 1000 (from 39 fewer to 246 more)	
Discontinuation due to any reason - combined population-guided self help vs WLC											
2	randomised trials	serious[1]	no serious inconsistency	serious[5]	serious[3]	none	27/72 (37.5%)	17/69 (24.6%)	RR 1.5 (0.91 to 2.47)	123 more per 1000 (from 22 fewer to 362 more)	VERY LOW
								12.9%		64 more per 1000 (from 12 fewer to 190 more)	

[1] quasi-RCT
[2] treatment group not comparable (treatment only and treatment plus TAU)
[3] 95% confidence interval include no effect
[4] moderate heterogeneity (50-80%)
[5] different target population (mixed anxiety and pure GAD population)
[6] high heterogeneity (>80%)

Economic profile

Guided bibliotherapy versus waiting list							
Study & country	Limitations	Applicability	Other comments	Increment al cost (£)[1]	Incremental effect	ICER (£/effect)	Uncertainty[1]

Appendix 18a

Guideline analysis UK	Potentially serious limitations [2]	Directly applicable[3]		£83-150	n/a	n/a	£83-150

cCBT versus waiting list for people with GAD

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)[1]	Incremental effect	ICER (£/effect)[1]	Uncertainty[1]
Guideline analysis UK	Minor limitations [4]	Directly applicable[5]		£22.05	0.04	£541/QALY	Probability of cost effectiveness at £20,000/QALY: 93%

1. Costs expressed in 2009 UK pounds
2. 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
3. Cost analysis conducted to assist guideline development; NHS perspective
4. Limited evidence base (1 RCT); intervention currently not available in the UK
5. Analysis conducted to assist guideline development; NHS & personal social services perspective; QALYs estimated based on the generic SF-6D

1.3 Group psychoeducation (CBT) vs comparator for pure GAD, mixed anxiety disorders or both populations

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	group psychoeducation (CBT)	comparator	Relative (95% CI)	Absolute		
Anxiety - mixed anxiety population-psychoeducational group vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25	24	-	SMD 0.34 lower (0.9 lower to 0.23 higher)	MODERATE	
Anxiety-pure GAD population-psychoeducational group vs WLC (Better indicated by lower values)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	22	11	-	SMD 0.7 lower (1.45 lower to 0.04 higher)	LOW	
Anxiety - combined population-psychoeducational group vs WLC (Better indicated by lower values)												
2	randomised trials	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	47	35	-	SMD 0.47 lower (0.92 to 0.02 lower)	LOW	
Depression - mixed anxiety population-psychoeducational group vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	25	24	-	SMD 0.49 lower (1.06 lower to 0.08	HIGH	

											higher)		
Depression- pure GAD population-psychoeducational group vs WLC (Better indicated by lower values)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	22	11	-	SMD 0.51 lower (1.25 lower to 0.22 higher)	LOW	
Depression - combined population-psychoeducational group vs WLC (Better indicated by lower values)												
2	randomised trials	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	47	35	-	SMD 0.5 lower (0.95 to 0.05 lower)	LOW	
Worry - mixed anxiety population-psychoeducational group vs WLC (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25	24	-	SMD 0.36 lower (0.93 lower to 0.2 higher)	MODERATE	
Discontinuation due to any reason-pure GAD population-psychoeducational group vs WLC												
1	randomised trials	very serious[2,4]	no serious inconsistency	no serious indirectness	serious[1]	none	4/26 (15.4%)	0/11 (0%)	RR 4 (0.23 to 68.57)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	
								0%		0 more per 1000 (from 0 fewer to 0 more)		

[1] 95% confidence interval include no effect
[2] quasi-RCT
[3] different target population (pure GAD and mixed anxiety)
[4] high selection bias and completer analysis

Economic profile

Psychoeducational group versus waiting list							
Study & country	Limitations	Applicability	Other comments	Increment al cost (£)[1]	Incremental effect	ICER (£/effect)	Uncertainty[1]
Guideline analysis UK	Potentially serious limitations[2]	Directly applicable[3]		£36-108	n/a	n/a	£36-108

1. Costs expressed in 2009 UK pounds
2. 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
3. Cost analysis conducted to assist guideline development; NHS perspective

1.4 Group CBT vs Group Anxiety Management Training for mixed anxiety populations

	Quality assessment						No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Group CBT	Group Anxiety Management Training	Relative (95% CI)	Absolute		
Discontinuation due to any reason												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	9/25 (36%)	8/24 (33.3%)	RR 1.08 (0.5 to 2.33)	27 more per 1000 (from 167 fewer to 443 more)	MODERATE	
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Anxiety (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25	24	-	SMD 0.16 higher (0.4 lower to 0.72 higher)	MODERATE	
Depression (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25	24	-	SMD 0.1 higher (0.46 lower to 0.66 higher)	MODERATE	
Worry (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	25	24	-	SMD 0.28 lower (0.84 lower to 0.29 higher)	MODERATE	

[1] 95% confidence interval include no effect

1.5 Pure bibliotherapy vs Pure audiotherapy in pure GAD populations

	Quality assessment						No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Pure bibliotherapy	Pure audiotherapy	Relative (95% CI)	Absolute		
Anxiety (Better indicated by lower values)												

| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 11 | 11 | - | SMD 0.55 lower (1.4 lower to 0.31 higher) | MODERATE | |

[1] 95% confidence interval include no effect

1.6 Guided CBT bibliotherapy vs High intensity CBT for mixed anxiety populations

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Guided CBT bibliotherapy	High intensity CBT	Relative (95% CI)	Absolute	Quality	Importance
Discontinuation due to any reason												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	6/53 (11.3%)	9/63 (14.3%)	RR 0.79 (0.3 to 2.08)	30 fewer per 1000 (from 100 fewer to 154 more)	MODERATE	
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Anxiety (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	53	63	-	SMD 0.3 higher (0.07 lower to 0.67 higher)	MODERATE	
Depression (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	53	63	-	SMD 0.25 higher (0.11 lower to 0.62 higher)	MODERATE	
Worry (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	53	63	-	SMD 0.28 higher (0.09 lower to 0.64 higher)	MODERATE	

[1] 95% confidence interval include no effect