1   CCBT for Panic Disorder

1.1   CCBT vs Wait-list control for Panic disorder

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	CCBT	Wait-list control	Relative (95% CI)	Absolute	Quality	Importance
Quality assessment							**Summary of findings**					
							No of patients		**Effect**			
Measure of general anxiety (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	50	-	SMD 1.29 lower (1.72 to 0.86 lower)	⊕⊕⊕⊕ HIGH	
Measure of depression (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	50	-	SMD 0.84 lower (1.39 to 0.29 lower)	⊕⊕⊕⊕ HIGH	
Measure of Quality of Life (psychological) (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	50	-	SMD 0.55 lower (0.95 to 0.15 lower)	⊕⊕⊕⊕ HIGH	
Non Panic free status (clinician and self-report) - Non-Remission (1 mth posttreatment no longer fulfill PD diagnostic criteria)												
2	randomised trials	no serious limitations	very serious[1]	no serious indirectness	serious[2]	none	21/51 (41.2%)	49/51 (96.1%)	RR 0.44 (0.12 to 1.55)	538 fewer per 1000 (from 845 fewer to 528 more)	⊕OOO VERY LOW	
								100%		560 fewer per 1000 (from 880 fewer to 550 more)		
Discontinuation due to any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	5/51 (9.8%)	3/50 (6%)	RR 1.48 (0.2 to 10.79)	29 more per 1000 (from 48 fewer to 587 more)	⊕⊕⊕O MODERATE	
								5.8%		28 more per 1000 (from 46 fewer to 568 more)		

[1] High heterogeneity (>80%)
[2] 95% confidence interval include no effect

Economic profile

Internet Psychiatri versus waiting list							
Study & country	Limitations	Applicability	Other comments	Incremental cost	Incremental effect	ICER (£/effect)[1]	Uncertainty[1]

				(£)[1]			
Guideline analysis (model 3) UK	Minor limitations[2]	Directly applicable[3]	• Time horizon: 1 year	£115.62	0.052	£2,216/QALY	Probability of Internet Psychiatri being cost-effective at £20,000/QALY: 85.3%

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

1.2 CCBT vs information control for Panic disorder

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	CCBT	information control	Relative (95% CI)	Absolute		
Measure of general anxiety (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	31	27	-	SMD 0.1 lower (0.77 lower to 0.58 higher)	⊕⊕⊕O MODERATE	
Measure of panic severity (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[2]	no serious indirectness	no serious imprecision	none	31	27	-	SMD 1.9 lower (3.04 to 0.76 lower)	⊕⊕⊕O MODERATE	
Measure of depression (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	31	27	-	SMD 0.57 lower (1.1 to 0.04 lower)	⊕⊕⊕⊕ HIGH	
Measure of Quality of life (Psychological) (Better indicated by lower values)												
1	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	12	9	-	SMD 0.25 lower (1.12 lower to 0.61 higher)	⊕⊕⊕O MODERATE	
Non "Panic free" status (clinician and self-report) - Non panic free												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/31 (29%)	25/27 (92.6%)	RR 0.32 (0.18 to 0.56)	630 fewer per 1000 (from 407 fewer to 759 fewer)	⊕⊕⊕⊕ HIGH	
								91.7%		624 fewer per 1000 (from 403 fewer to 752 fewer)		
Discontinuation due to any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	3/31 (9.7%)	7/27 (25.9%)	RR 0.42 (0.11 to 1.63)	150 fewer per 1000 (from 231 fewer to 163 more)	⊕⊕⊕O MODERATE	

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| | | | | | | | | | 25% | | 145 fewer per 1000 (from 222 fewer to 157 more) | |

[1] 95% confidence interval include no effect
[2] Moderate heterogeneity (50-80%)

Economic profile

Panic online versus information control

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)[1]	Incremental effect	ICER (£/effect)[1]	Uncertainty[1]
Klein *et al.*, 2006 Australia	Potentially serious limitations[2]	Partially applicable[3]	• Time horizon: 6 weeks • Cost-consequence analysis	£141	See GRADE clinical profile above	Non-Applicable	No statistical analysis of costs
Guideline analysis (model 1) UK	Minor limitations[4]	Directly applicable[5]	• Time horizon: 1 year	£354.96	0.046	£7,599/QALY	Probability of cost effectiveness at £20,000/QALY: 92%

1. Costs converted and uplifted to 2009 UK pounds, using PPP exchange rates (http://www.oecd.org/std/ppp) and the UK HCHS inflation index; assuming study cost year 2004.
2. Short time horizon; intervention costs only considered; various panic, anxiety and cognition outcomes measured (cost-consequence analysis)
3. Australian study; narrow perspective (intervention costs only considered); local prices used; no QALYs estimated but outcome measures considered relevant in guideline systematic review of clinical evidence
4. Limited evidence base (2 RCTs); intervention currently not available in the UK
5. Analysis conducted to assist guideline development; NHS & personal social services perspective; QALYs estimated based on EQ-5D

1.3 CCBT vs any control (WLC or information control) for Panic disorder

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	CCBT	any control (WLC or information control)	Relative (95% CI)	Absolute		
Measure of general anxiety (Better indicated by lower values)												
4	randomised trials	no serious limitations	serious[1]	serious[2]	no serious imprecision	none	82	77	-	SMD 0.7 lower (1.41 lower to 0.01 higher)	⊕⊕OO LOW	
Measure of panic severity (Better indicated by lower values)												
4	randomised trials	no serious limitations	no serious inconsistency	serious[2]	no serious imprecision	none	82	77	-	SMD 1.78 lower (2.26 to 1.31 lower)	⊕⊕⊕O MODERATE	
Measure of depression (Better indicated by lower values)												

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No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	CCBT	Comparator	Relative (95% CI)	Absolute	Quality	Importance
4	randomised trials	no serious limitations	no serious inconsistency	serious[2]	no serious imprecision	none	82	77	-	SMD 0.72 lower (1.05 to 0.4 lower)	⊕⊕⊕O MODERATE	
Measure of Quality of Life - QOL (Psychological) (Better indicated by lower values)												
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	63	59	-	SMD 0.5 lower (0.86 to 0.14 lower)	⊕⊕⊕⊕ HIGH	
Non-Panic free status (clinician and self-report)												
4	randomised trials	no serious limitations	serious[1]	serious[2]	no serious imprecision	none	30/82 (36.6%)	74/78 (94.9%) / 94.6%	RR 0.38 (0.19 to 0.78)	588 fewer per 1000 (from 209 fewer to 768 fewer) / 587 fewer per 1000 (from 208 fewer to 766 fewer)	⊕⊕OO LOW	
Discontinuation due to any reason												
4	randomised trials	no serious limitations	no serious inconsistency	serious[2]	serious[3]	none	8/82 (9.8%)	10/77 (13%) / 14.4%	RR 0.72 (0.22 to 2.4)	36 fewer per 1000 (from 101 fewer to 182 more) / 40 fewer per 1000 (from 112 fewer to 202 more)	⊕⊕OO LOW	

[1] moderate heterogeneity (50-80%)
[2] different comparator
[3] 95% confidence interval include no effect

1.4   CCBT vs Face to Face CBT for Panic disorder

Quality assessment							Summary of findings				Quality	Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	CCBT	Face to Face CBT	Relative (95% CI)	Absolute		
Measure of general anxiety (Better indicated by lower values)												
2	randomised trials	no serious limitations	serious[1]	no serious indirectness	serious[2]	none	67	62	-	SMD 0.11 higher (0.41 lower to 0.62 higher)	⊕⊕OO LOW	
Measure of depression (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	70	63	-	SMD 0.13 higher (0.22 lower to 0.47 higher)	⊕⊕⊕O MODERATE	
Measure of Quality of Life - QOL (Psychological) (Better indicated by lower values)												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	65	62	-	SMD 0.09 higher (0.26 lower to 0.44 higher)	⊕⊕⊕O MODERATE	
Panic free status (clinician and self-report)												

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2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	35/71 (49.3%)	33/64 (51.6%)	RR 0.95 (0.61 to 1.46)	26 fewer per 1000 (from 201 fewer to 237 more)	⊕⊕⊕O MODERATE	
								47.9%		24 fewer per 1000 (from 187 fewer to 220 more)		
Discontinuation due to any reason												
2	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[2]	none	8/71 (11.3%)	5/64 (7.8%)	RR 1.41 (0.48 to 4.2)	32 more per 1000 (from 41 fewer to 250 more)	⊕⊕⊕O MODERATE	
								8.8%		36 more per 1000 (from 46 fewer to 282 more)		

[1] Moderate heterogeneity (50-80%)
[2] 95% confidence interval include no effect

Economic profile

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)[1]	Incremental effect	ICER (£/effect)[1]	Uncertainty[1]
Panic Online (PO) versus face-to-face CBT							
Guideline analysis (model 2) UK	Minor limitations[2]	Directly applicable[3]	• Time horizon: 1 year	-£303.00	-0.023	£126,849/QALY	Probability of PO being cost-effective at £20,000/QALY: 71%
Internet Psychiatri versus face-to-face CBT							
Guideline analysis (model 4) UK	Minor limitations[2]	Directly applicable[3]	• Time horizon: 1 year	-£433.50	0.012	cCBT dominant	Probability of Internet Psychiatri being cost-effective at £20,000/QALY: 95%

1. Costs uplifted to 2009 UK pounds using the UK HCHS inflation index.
2. Limited evidence base (1 RCT); intervention currently not available in the UK
3. Analysis conducted to assist guideline development; NHS & personal social services perspective; QALYs estimated based on EQ-5D

1.5   CCBT versus bibliotherapy

Economic profile

Panic Online versus therapist-assisted self-administered CBT							
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)[1]	Incremental effect	ICER (£/effect)	Uncertainty
Klein *et al.*, 2006 Australia	Potentially serious limitations[2]	Partially applicable[3]	• Time horizon: 6 weeks • Cost-consequence analysis	-£14	See GRADE clinical profile above	Non-Applicable	No significant difference in costs

1. Costs converted and uplifted to 2009 UK pounds, using PPP exchange rates (http://www.oecd.org/std/ppp) and the UK HCHS inflation index; assuming study cost year 2004.
2. Short time horizon; intervention costs only considered; various panic, anxiety and cognition outcomes measured (cost-consequence analysis)
3. Australian study; narrow perspective (intervention costs only considered); local prices used; no QALYs estimated but outcome measures considered relevant in guideline systematic review of clinical evidence

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Fear Fighter (FF) versus face-to-face CBT

Kartenhaler et al., 2006 UK	Minor limitations [2]	Partially applicable[3]	Time horizon: 12 months	-£240	- 0.011QALYs	£22,000/ QALY	Probability threshold of
McCrone et al., 2009 UK	Potentially serious limitations [4]	Partially applicable[5]	Time horizon: 14 weeks Two analyses using: a. main problem ratings b. global phobia ratings	a. -£139 to - £234 b.- £133 to - £234	a. 0.03 b. -0.64	a. FF dominant b. £208-£366/ mean improvement in global phobia rating	

QALYs estimated from data on the self-reported global phobia item; panic symptoms not necessarily captured; short time horizon; resource use estimates based on manufacturers and assumptions

Study population not entirely relevant (people with panic phobia); HRQoL scores taken from European community-based mental health survey; overall state of panic disorder valued

Short time horizon; intervention costs only considered; outcomes measured as improvements in main symptoms & global phobia ratings; potential conflict of interest

Study population not entirely relevant (people with panic or phobic disorder); narrow perspective; no QALYs estimated but outcome measures considered relevant in guideline systematic review of clinical evidence