National Institute for Health and Care Excellence

Version 1.0

Depression in adults: treatment and management

Appendices O-R

NICE Guideline

Appendices

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Draft for Consultation

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Contents

Appendix O: Economic evidence – flow chart 7
Appendix P: Economic evidence – health economic checklists 8
P.1 Service delivery models for people with depression 8
P.1.1 Simple collaborative care 8
P.1.2 Complex collaborative care 13
P.1.3 Medication management 17
P.1.4 Stepped care 20
P.1.5 Integrated care pathways 22
P.2 Interventions for first-line treatment of adults with a new episode of less severe depression 25
P.2.1 Psychological interventions 25
P.2.2 Pharmacological interventions 36
P.2.3 Physical interventions 39
P.2.4 Psychological, pharmacological, physical and combined interventions 41
P.3 Interventions for first-line treatment of adults with a new episode of more severe depression 43
P.3.1 Psychological interventions 43
P.3.2 Pharmacological interventions 49
P.3.3 Combined pharmacological and psychological interventions 54
P.3.4 Physical interventions 57
P.3.5 Psychological, pharmacological and combined interventions 59
P.4 Interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment 60
P.4.1 Psychological interventions 60
P.4.2 Pharmacological interventions 63
P.5 Interventions aimed at preventing relapse in people whose depression has responded to treatment 72
P.5.1 Psychological interventions 72
P.5.2 Psychological, pharmacological and combined interventions 75
Appendix Q: Economic evidence – evidence tables 77
Q.1 Service delivery models for people with depression 77
Q.1.1 Simple collaborative care – references to included studies 77
Q.1.2 Complex collaborative care – references to included studies 81
Q.1.3 Medication management – references to included studies 85
Q.1.4 Stepped care – references to included studies 88
Q.1.5 Integrated care pathways – references to included studies 91
Q.2 Interventions for first-line treatment of adults with a new episode of less severe depression 95
Q.2.1 Psychological interventions – references to included studies 95

Update 2017

Q.2.2 Pharmacological interventions – references to included studies.... 105
Q.2.3 Physical interventions – references to included studies..... 108
Q.3 Interventions for first-line treatment of adults with a new episode of more severe depression..... 110
Q.3.1 Psychological interventions – references to included studies..... 110
Q.3.2 Pharmacological interventions – references to included studies.... 116
Q.3.3 Combined pharmacological and psychological interventions – references to included studies..... 121
Q.3.4 Physical interventions – references to included studies..... 123
Q.4 Interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment..... 124
Q.4.1 Psychological interventions – references to included studies..... 124
Q.4.2 Pharmacological interventions – references to included studies.... 128
Q.5 Interventions aimed at preventing relapse in people whose depression has responded to treatment 134
Q.5.1 Psychological interventions – references to included studies..... 134
Appendix R: Health economic profiles..... 137
R.1 Service delivery models for adults with depression..... 137
R.1.1 Collaborative care..... 137
R.1.2 Medication management..... 140
R.1.3 Stepped care 141
R.1.4 Integrated care pathways..... 142
R.2 First-line treatment of adults with a new episode of less severe depression 143
R.2.1 Psychological interventions..... 143
R.2.2 Pharmacological interventions 147
R.2.3 Physical interventions 148
R.2.4 Psychological, pharmacological, physical and combined interventions 150
R.3 First-line treatment of adults with a new episode of more severe depression 151
R.3.1 Psychological interventions..... 151
R.3.2 Pharmacological interventions 154
R.3.3 Combined pharmacological and psychological interventions..... 155
R.3.4 Physical interventions 157
R.3.5 Psychological, pharmacological, physical and combined interventions 158
R.4 Interventions for adults with depression who responded inadequately or were intolerant to previous treatment 159
R.4.1 Psychological interventions..... 159
R.4.2 Pharmacological interventions 160
R.5 Interventions for relapse prevention..... 161
R.5.1 Psychological interventions..... 161

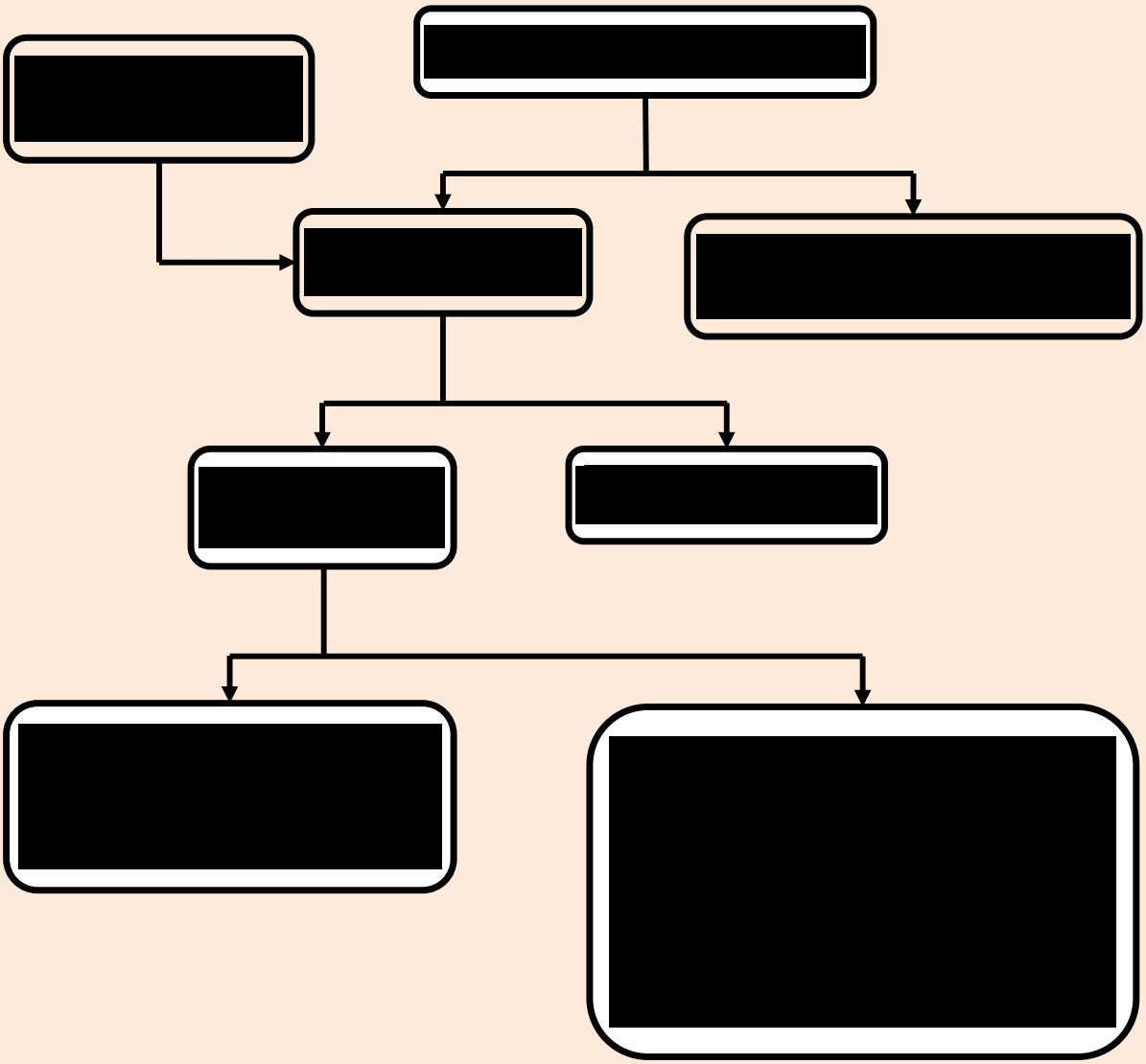
Update 2017

R.5.2 Pharmacological interventions 162
R.5.3 Psychological, pharmacological and combined interventions 165

Update 2017

Appendix O: Economic evidence – flow chart

Figure 1: Flow diagram of economic study selection for review on interventions and services for adults with depression



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Appendix P: Economic evidence – health economic checklists

P.1 Service delivery models for people with depression

P.1.1 Simple collaborative care

Study: Bosanquet K, Adamson J, Atherton K, et al. (2017) CollAborative care for Screen-Positive ElderRs with major depression (CASPER plus): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technology Assessment in press			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Older adults with major depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 18 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	QALYs based on SF-6D (UK tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	18 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=485; at 18 months n=344; cost data available for n=447
2.5	Are the estimates of relative intervention effects from the	Partly	RCT

Update 2017

Study: Bosanquet K, Adamson J, Atherton K, et al. (2017) CollAborative care for Screen-Positive ElderRs with major depression (CASPER plus): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technology Assessment in press			
	best available source?		
2.6	Are all important and relevant costs included?	No	Intervention and primary care costs exclusively considered
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Green C, Richards DA, Hill JJ, et al. (2014) Cost-effectiveness of collaborative care for depression in UK primary care: Economic evaluation of a randomised controlled trial (CADET). PLoS ONE 9(8): e104225.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/**	**Comments**

Update 2017

Study: Green C, Richards DA, Hill JJ, et al. (2014) Cost-effectiveness of collaborative care for depression in UK primary care: Economic evaluation of a randomised controlled trial (CADET). PLoS ONE 9(8): e104225.			
		NA	
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=581
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

1

Study: Lewis H, Adamson J, Atherton K, et al. (2017) CollAborative care and active surveillance for Screen-Positive ElderRs with subthreshold depression (CASPER): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technology Assessment, in press			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Older adults who screened positive for subthreshold depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and	Yes	

Study: Lewis H, Adamson J, Atherton K, et al. (2017) CollAborative care and active surveillance for Screen-Positive ElderRs with subthreshold depression (CASPER): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technology Assessment, in press			
	outcomes used in line with analytical perspectives taken (item 1.4 above).		
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=705; complete data used in base-case economic analysis n=448
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	No	Intervention and primary care costs exclusively considered
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: Attrition was markedly greater in the collaborative care arm			

Update 2017

1

Study: Simon GE, Von Korff M, Ludman EJ, et al. (2002) Cost-effectiveness of a program to prevent depression relapse in primary care. Medical care 40: 941-950.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a history of

Study: Simon GE, Von Korff M, Ludman EJ, et al. (2002) Cost-effectiveness of a program to prevent depression relapse in primary care. Medical care 40: 941-950.			
			recurrent major depression (≥ 3 depressive episodes in the previous 5 years) or dysthymia (continuous depressive symptoms for the past 2 years) that had recovered from a depressive episode following antidepressant treatment in primary care
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	3rd party payer
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Number of depression-free days
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=386; n=315 completed all follow-up assessments and n=377 remained enrolled throughout

Update 2017

Study: Simon GE, Von Korff M, Ludman EJ, et al. (2002) Cost-effectiveness of a program to prevent depression relapse in primary care. Medical care 40: 941-950.			
			follow-up
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Unclear	Probably local data
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; bootstrapping methods employed
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: Analyses of clinical data included only those completing all blinded follow-up assessments; cost analyses included only those remaining enrolled throughout the follow-up period. Participation in follow-up interviews was significantly greater in the intervention group than in usual care, introducing a possibility of bias.			

P.1.21 Complex collaborative care

2

Study: Morriss R, Garland A, Nixon N, et al. (2016) Efficacy and cost-effectiveness of a specialist depression service versus usual specialist mental health care to manage persistent depression: a randomised controlled trial. Lancet Psychiatry 3(9):821-31			
Economic Question: settings for the delivery of care for people with depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with persistent unipolar depression that have received treatment for depression for at least 6 months and currently receive secondary mental healthcare
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS & PSS
1.5	Are all direct effects on individuals included, and are all	Yes	Yes

Update 2017

Study: Morriss R, Garland A, Nixon N, et al. (2016) Efficacy and cost-effectiveness of a specialist depression service versus usual specialist mental health care to manage persistent depression: a randomised controlled trial. Lancet Psychiatry 3(9):821-31			
	other effects included where they are material?		
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 18 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	EK-5D ratings and UK tariff used
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments:			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	18 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=187; completion: 84% at 6 months, 72% at 12 months, 59% at 18 months; all 187 included in ITT analysis
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	national sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Regression conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

1

Study: Goorden M, Vlasveld MC, Anema JR, et al. (2014) Cost-utility analysis of a collaborative care intervention for major depressive disorder in an occupational healthcare setting. Journal of Occupational Rehabilitation, 24(3): 555-62		
Economic Question: service delivery models		
Section 1: Applicability (relevance to specific review	**Yes/ Partly/**	**Comments**

Update 2017

Study: Goorden M, Vlasveld MC, Anema JR, et al. (2014) Cost-utility analysis of a collaborative care intervention for major depressive disorder in an occupational healthcare setting. Journal of Occupational Rehabilitation, 24(3): 555-62			
question and the NICE reference case)		**No/Unclear/ NA**	
1.1	Is the study population appropriate for the review question?	Yes	Sick-listed workers with major depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	Dutch study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare system
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	QALYs based on EQ-5D ratings (Dutch tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments:			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=124
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	Non-psychiatric inpatient costs not considered
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

1

Study: Goorden M, Huijbregts KM, van Marwijk HW, et al (2015) Cost-utility of collaborative care for major depressive disorder in primary care in the Netherlands. Journal of Psychosomatic Research, 79(4), 316-23.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major depression treated in primary care
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	Dutch study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare system (and societal)
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	QALYs based on EQ-5D ratings (Dutch tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments:			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=150; 93 identified by screening and 47 by GP referral; economic analysis based only on n=93 identified by screening
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT (n=93)
2.6	Are all important and relevant costs included?	Yes	Non-psychiatric inpatient costs not considered
2.7	Are the estimates of resource use from the best available	Partly	RCT (n=93)

Update 2017

Study: Goorden M, Huijbregts KM, van Marwijk HW, et al (2015) Cost-utility of collaborative care for major depressive disorder in primary care in the Netherlands. Journal of Psychosomatic Research, 79(4), 316-23.			
	source?		
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

P.1.31 Medication management

2

Study: Bosmans JE, Brook OH, Van Hout HPJ, et al. (2007) Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepressants. PharmacoEconomics 25: 25-37.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression treated in primary care, with a new prescription for a non-tricyclic antidepressant
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	Dutch study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Societal
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 6 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Primary measures adherence to antidepressant treatment and depressive symptoms measured using HSCL
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			

Update 2017

Study: Bosmans JE, Brook OH, Van Hout HPJ, et al. (2007) Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepressants. PharmacoEconomics 25: 25-37.			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	6 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not measured
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=151; completers of both 3- and 6-month follow-ups n=88
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Unclear	Inpatient costs appeared to have been excluded
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: base-case analysis was complete case analysis regardless of assigned treatment. In addition, a per protocol analysis was included. Participants were included in the per protocol analysis if the prescription for antidepressant medication was written out by their GP and they completed all of the follow-up assessments. Participants in the intervention group were excluded from the per protocol analysis if they indicated that they had not watched the intervention videotape or did not receive the 3 coaching contacts. In sensitivity analysis, the mean value per treatment group was imputed for missing values in participants who did not complete all follow-up assessments. Imputation was limited to participants who had completed the baseline assessment (n=135).			

1

Study: Rubio-Valera M, Bosmans J, Fernandez A, et al. (2013) Cost-Effectiveness of a Community Pharmacist Intervention in Patients with Depression: A Randomized Controlled Trial (PRODEFAR Study). PLoS ONE 8(8): e70588.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults initiating treatment with

Update 2017

Study: Rubio-Valera M, Bosmans J, Fernandez A, et al. (2013) Cost-Effectiveness of a Community Pharmacist Intervention in Patients with Depression: A Randomized Controlled Trial (PRODEFAR Study). PLoS ONE 8(8): e70588.			
			antidepressant because of depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	Spanish study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Societal & healthcare
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 6 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	QALYs based on EQ-5D ratings (Spanish tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	6 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=179; N=179; 71% completed at 6 months; n=151 received intervention as allocated
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	Regional sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: base-case analysis was based on intention to treat, with multiple imputation of			

Update 2017

Study: Rubio-Valera M, Bosmans J, Fernandez A, et al. (2013) Cost-Effectiveness of a Community Pharmacist Intervention in Patients with Depression: A Randomized Controlled Trial (PRODEFAR Study). PLoS ONE 8(8): e70588.
missing data. In addition, a per protocol analysis was conducted in which participants who did not receive the intervention were excluded. Also, a complete case analysis was conducted, without the 52 participants who were lost to follow-up at 6 months. Results contradictory, depending on measure of outcome used

P.1.41 Stepped care

2

Study: Mukuria C, Brazier J, Barkham M, et al. (2013) Cost-effectiveness of an improving access to psychological therapies service. British Journal of Psychiatry 202: 220-227.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	People 16-64 years old with a new or recurrent episode of depression or anxiety; >95% of people in IAPT had a primary diagnosis of depression by their GP
1.2	Are the interventions appropriate for the review question?	Yes	IAPT service
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 8 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	SF-6D ratings and predicted EQ-5D ratings after mapping from SF-6D were used (both UK tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cohort study

Update 2017

Study: Mukuria C, Brazier J, Barkham M, et al. (2013) Cost-effectiveness of an improving access to psychological therapies service. British Journal of Psychiatry 202: 220-227.			
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	8 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Prospective cohort study with matched sites, N=403
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Prospective cohort study
2.6	Are all important and relevant costs included?	Partly	Medication costs not considered
2.7	Are the estimates of resource use from the best available source?	Partly	Prospective cohort study
2.8	Are the unit costs of resources from the best available source?	Yes	IAPT financial data and national sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: low response rate at recruitment (403/3391, 11.9%); IAPT service assessed over the first 2 years of establishment, therefore costs associated with learning effects were likely			

Update 2017

1

Study: Ricken R, Wiethoff K, Reinhold T, et al. (2011) Algorithm-guided treatment of depression reduces treatment costs - Results from the randomized controlled German Algorithm Project (GAPII). Journal of Affective Disorders 134: 249-256.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a ICD10 depressive syndrome receiving inpatient care
1.2	Are the interventions appropriate for the review question?	Yes	Stepped care
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	German study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	3rd party payer
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not reported
1.6	Are all future costs and outcomes discounted	NA	Time horizon up to remission or

Study: Ricken R, Wiethoff K, Reinhold T, et al. (2011) Algorithm-guided treatment of depression reduces treatment costs - Results from the randomized controlled German Algorithm Project (GAPII). Journal of Affective Disorders 134: 249-256.			
	appropriately?		drop-out, less than 1 year
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Only remission considered as an outcome
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon up to remission or drop-out, less than 1 year
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not reported
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=148
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted
2.11	Is there any potential conflict of interest?	Unclear	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

P.1.51 Integrated care pathways

2

Study: Pyne JM, Fortney JC, Mouden S, et al. (2015) Cost-effectiveness of on-site versus off-site collaborative care for depression in rural FQHCs. Psychiatric Services 66: 491-499.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults who screened positive for

Update 2017

Study: Pyne JM, Fortney JC, Mouden S, et al. (2015) Cost-effectiveness of on-site versus off-site collaborative care for depression in rural FQHCs. Psychiatric Services 66: 491-499.			
			depression according to a PHQ-9 score ≥10
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare & service users' time & mileage
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 18 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	QALYs based on SF-12/SF-6D (UK tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments:			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	18 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=364; 87% completed at 6 months, 79% at 12 months and 78% at 18 months
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	Regional sources in base-case analyse; national sources in secondary analysis
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain	Yes	Bootstrapping

Update 2017

Study: Pyne JM, Fortney JC, Mouden S, et al. (2015) Cost-effectiveness of on-site versus off-site collaborative care for depression in rural FQHCs. Psychiatric Services 66: 491-499.			
	subjected to appropriate sensitivity analysis?		conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

1

Study: Wiley-Exley E, Domino ME, Maxwell J, et al. (2009) Cost-effectiveness of integrated care for elderly depressed patients in the PRISM-E study. Journal of Mental Health Policy and Economics 12: 205-213+217.			
Economic Question: service delivery models			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults above 65 years of age with depression (major or minor)
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare & service users' and carers' time & mileage
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	See notes
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 6 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	See notes
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: Primary outcome measures were the Center for Epidemiologic Studies Depression Scale (CES-D) score; number of depression-free days (DFD) derived from the 20-item CES-D (score =0 indicated depression-free day, ≥ 16 full symptoms and intermediate severity scores were assigned a value between depression-free and fully symptomatic by linear interpolation); QALYs estimated based on depression-free days (QALY-DFD), using utility weights of health=1, depression=0.59); QALYs estimated based on SF-36 (QALY-SF), using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	6 months
2.3	Are all important and relevant outcomes included?	Partly	See notes on

Update 2017

Study: Wiley-Exley E, Domino ME, Maxwell J, et al. (2009) Cost-effectiveness of integrated care for elderly depressed patients in the PRISM-E study. Journal of Mental Health Policy and Economics 12: 205-213+217.			
			applicability
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=840; within VA n=365, outside VA n=475; individuals with major depression within VA n=214, outside VA n=302
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	national sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: separate analyses undertaken for participants within and outside the Veteran Affairs (VA) system; sub-analyses for people with major depression performed. Contradictory results across sub-analyses			

Update 2017

P.2 Interventions for first-line treatment of adults with a new episode of less severe depression

P.2.1 Psychological interventions

Study: Kendrick T, Simons L, Mynors-Wallis L, et al. (2005) A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study. Health Technology Assessment 9. AND Kendrick T, Simons L, Mynors-Wallis L, et al. (2006) Cost-effectiveness of referral for generic care or problem-solving treatment from community mental health nurses, compared with usual general practitioner care for common mental disorders: Randomised controlled trial. British Journal of Psychiatry 189: 50-59.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with common mental

Study: Kendrick T, Simons L, Mynors-Wallis L, et al. (2005) A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study. Health Technology Assessment 9.
AND
Kendrick T, Simons L, Mynors-Wallis L, et al. (2006) Cost-effectiveness of referral for generic care or problem-solving treatment from community mental health nurses, compared with usual general practitioner care for common mental disorders: Randomised controlled trial. British Journal of Psychiatry 189: 50-59.

			health problems, 75% depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 26 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	26 weeks
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT (N=247; analysis based on n=184)
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted; cost effectiveness planes presented
2.11	Is there any potential conflict of interest?	No	

Update 2017

Study: Kendrick T, Simons L, Mynors-Wallis L, et al. (2005) A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study. Health Technology Assessment 9. AND Kendrick T, Simons L, Mynors-Wallis L, et al. (2006) Cost-effectiveness of referral for generic care or problem-solving treatment from community mental health nurses, compared with usual general practitioner care for common mental disorders: Randomised controlled trial. British Journal of Psychiatry 189: 50-59.			
2.12 Overall assessment: minor limitations			
Other comments:			

1

Study: Simpson S, Corney R, Beecham J (2003) A randomized controlled trial to evaluate the effectiveness and cost-effectiveness of psychodynamic counselling for general practice patients with chronic depression. Psychological Medicine 33: 229-239.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression (BDI 14-40) lasting at least 6 months, with or without comorbid anxiety
1.2	Are the interventions appropriate for the review question?	Yes	Psychodynamic counselling
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Health and social services
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured
1.6	Are all future costs and outcomes discounted appropriately?	NA	time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	BDI and other secondary outcomes
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	1 year
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not measured

Update 2017

Study: Simpson S, Corney R, Beecham J (2003) A randomized controlled trial to evaluate the effectiveness and cost-effectiveness of psychodynamic counselling for general practice patients with chronic depression. Psychological Medicine 33: 229-239.			
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=145; completers n=115
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT, completers n=115
2.8	Are the unit costs of resources from the best available source?	Yes	National sources where available; local costs for intervention
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	Statistical tests undertaken; bootstrapping conducted
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Kaltenthaler E, Brazier J, De Nigris E, et al. (2006) Computerized cognitive behavior therapy for depression and anxiety update: A systematic review and economic evaluation. Health Technology Assessment 10(33).			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression in a primary care setting
1.2	Are the interventions appropriate for the review question?	Yes	cCBT
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	3.5% annually
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and	NA	

Update 2017

Study: Kaltenthaler E, Brazier J, De Nigris E, et al. (2006) Computerized cognitive behavior therapy for depression and anxiety update: A systematic review and economic evaluation. Health Technology Assessment 10(33).			
	appropriately measured and valued?		
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	18 months
2.3	Are all important and relevant outcomes included?	Yes	QALYs estimated
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	analysis of individual-level RCT data
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	analysis of individual-level RCT data and published RCT data; and further assumptions
2.6	Are all important and relevant costs included?	Yes	Crude cost estimates
2.7	Are the estimates of resource use from the best available source?	Partly	Based on manufacturer submissions, published data and further assumptions
2.8	Are the unit costs of resources from the best available source?	Yes	National sources, intervention costs from manufacturers
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA, CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: McCrone P, Knapp M, Proudfoot J, et al. (2004) Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: Randomised controlled trial. British Journal of Psychiatry 185: 55-62		
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression		
Section 1: Applicability (relevance to specific review question and the NICE reference case)	**Yes/ Partly/ No/Unclear/ NA**	**Comments**

Update 2017

Study: McCrone P, Knapp M, Proudfoot J, et al. (2004) Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: Randomised controlled trial. British Journal of Psychiatry 185: 55-62			
1.1	Is the study population appropriate for the review question?	Partly	Adults with depression, mixed depression and anxiety or anxiety
1.2	Are the interventions appropriate for the review question?	Yes	cCBT
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS (& societal)
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL changes based on assumptions
1.6	Are all future costs and outcomes discounted appropriately?	NA	time horizon 8 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	BDI main outcome; QALY estimated based on assumptions around BDI measurements
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	8 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL changes based on assumptions
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=274
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources, intervention cost from manufacturer
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	

Update 2017

Study: McCrone P, Knapp M, Proudfoot J, et al. (2004) Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: Randomised controlled trial. British Journal of Psychiatry 185: 55-62			
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	Statistical tests undertaken; bootstrapping conducted
2.11	Is there any potential conflict of interest?	Yes	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Littlewood E, Duarte A, Hewitt C, et al. (2015) A randomised controlled trial of computerised cognitive behaviour therapy for the treatment of depression in primary care: the Randomised Evaluation of the Effectiveness and Acceptability of Computerised Therapy (REEACT) trial. Health Technol Assess, 19(101).			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Partly	Adults with symptoms of depression
1.2	Are the interventions appropriate for the review question?	Yes	cCBT with support
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS & PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	3.5% annually
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	2 years
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=691; EQ-5D data available for n=416 at 24

Update 2017

Study: Littlewood E, Duarte A, Hewitt C, et al. (2015) A randomised controlled trial of computerised cognitive behaviour therapy for the treatment of depression in primary care: the Randomised Evaluation of the Effectiveness and Acceptability of Computerised Therapy (REEACT) trial. Health Technol Assess, 19(101).			
			months; NHS cost data available for n=580
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical tests undertaken; regression analysis to control for covariates conducted; Cholesky decomposition to account for covariance in costs and QALYs and PSA undertaken
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

1

Study: Phillips R, Schneider J, Molosankwe I, et al. (2014) Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. Psychological Medicine 44: 741-752.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Partly	Adults with depressive symptoms in workplace
1.2	Are the interventions appropriate for the review question?	Yes	cCBT with support
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS (& societal)
1.5	Are all direct effects on individuals included, and are all	Yes	

Update 2017

Study: Phillips R, Schneider J, Molosankwe I, et al. (2014) Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. Psychological Medicine 44: 741-752.			
	other effects included where they are material?		
1.6	Are all future costs and outcomes discounted appropriately?	NA	time horizon 12 weeks for outcomes; 6 weeks for costs
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	No	12 weeks for outcomes; 6 weeks for costs
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=637; completion 56% at 6 weeks & 36% at 12 weeks
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	No	Intervention cost appears to have been omitted
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	Statistical tests undertaken; bootstrapping conducted but no uncertainty results reported
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Very serious limitations			
Other comments: inadequate reporting of results; no incremental analysis conducted (although it is possible to conduct from reported data) and no uncertainty results presented; intervention cost appears to have been omitted			

Update 2017

1

Study: Brabyn S, Araya R, Barkham M, et al. (2016) The second Randomised Evaluation of the Effectiveness, cost-effectiveness and Acceptability of Computerised Therapy trial (REEACT-2): does the provision of telephone support enhance the effectiveness of computer-delivered cognitive behaviour therapy? A randomised controlled trial. Health Technology Assessment, 20(89)			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Partly	Adults with moderate-severe depression
1.2	Are the interventions appropriate for the review question?	Yes	cCBT with and without support
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS & PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=369; complete cost data across the trial period available for n=209
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it	Yes	

Update 2017

Study: Brabyn S, Araya R, Barkham M, et al. (2016) The second Randomised Evaluation of the Effectiveness, cost-effectiveness and Acceptability of Computerised Therapy trial (REEACT-2): does the provision of telephone support enhance the effectiveness of computer-delivered cognitive behaviour therapy? A randomised controlled trial. Health Technology Assessment, 20(89)			
	be calculated from the data?		
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical tests undertaken; regression analysis to control for covariates conducted; Cholesky decomposition to account for covariance in costs and QALYs and PSA undertaken
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

1

Study: Richards DA, Ekers D, McMillan D, et al. (2016) Cost and Outcome of Behavioural Activation versus Cognitive Behavioural Therapy for Depression (COBRA): a randomised, controlled, non-inferiority trial. Lancet, 388(10047):871-80.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major depression
1.2	Are the interventions appropriate for the review question?	Yes	BA CBT
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS & PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	3.5% annually
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			

Update 2017

Study: Richards DA, Ekers D, McMillan D, et al. (2016) Cost and Outcome of Behavioural Activation versus Cognitive Behavioural Therapy for Depression (COBRA): a randomised, controlled, non-inferiority trial. Lancet, 388(10047):871-80.			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	18 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=440; QALYs available for n=309
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT, costs available for n=327)
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical tests including bootstrapping undertaken; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

P.2.21 Pharmacological interventions

2

Study: Kendrick T, Chatwin J, Dowrick C, et al (2009) Randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of selective serotonin reuptake inhibitors plus supportive care, versus supportive care alone, for mild to moderate depression with somatic symptoms in primary care: the THREAD (THREshold for AntiDepressant response) study. Health Technology Assessment 13(22)			
Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depressive symptoms and a baseline HDRS-17 score 12-19
1.2	Are the interventions appropriate for the review question?	Yes	

Study: Kendrick T, Chatwin J, Dowrick C, et al (2009) Randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of selective serotonin reuptake inhibitors plus supportive care, versus supportive care alone, for mild to moderate depression with somatic symptoms in primary care: the THREAD (THREshold for AntiDepressant response) study. Health Technology Assessment 13(22)			
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Health and social services
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 & 26 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	Derived from SF-36; SF-6D UK algorithm used
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	26 weeks
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT, N=220; 12-week completers n=196; 6-month follow-up n=160
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted, CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

1

Study: Peveler R, Kendrick T, Buxton M, et al (2005) A randomised controlled trial to compare the cost-effectiveness of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine. Health Technology Assessment 9(16) **AND Kendrick T, Peveler R, Longworth L, et al (2006) Cost-effectiveness and cost-utility of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine: Randomised controlled trial. British Journal of Psychiatry 188: 337-345.**			
Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a new episode of depression presenting in primary care
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Non-parametric bootstrapping

Update 2017

Study: Peveler R, Kendrick T, Buxton M, et al (2005) A randomised controlled trial to compare the cost-effectiveness of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine. Health Technology Assessment 9(16) **AND Kendrick T, Peveler R, Longworth L, et al (2006) Cost-effectiveness and cost-utility of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine: Randomised controlled trial. British Journal of Psychiatry 188: 337-345.**			
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

P.2.31 Physical interventions

2

Study: Spackman E, Richmond S, Sculpher M, et al. (2014) Cost-effectiveness analysis of acupuncture, counselling and usual care in treating patients with depression: The results of the ACUDep trial. PLoS ONE 9(11): e113726			
Economic Question: physical therapy as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	QALYs estimated using EQ-5D ratings (UK tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT (N=755; at 12 months EQ-5D data n=572; complete

Update 2017

Study: Spackman E, Richmond S, Sculpher M, et al. (2014) Cost-effectiveness analysis of acupuncture, counselling and usual care in treating patients with depression: The results of the ACUDep trial. PLoS ONE 9(11): e113726			
			resource use data n=150; multiple imputation used)
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources; acupuncture cost based on published data
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	One-way SA; multiple imputation and regression analysis of costs and QALYs to account for baseline factors; PSA undertaken and CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: results sensitive to changes in intervention costs and use of complete case analysis			

1

Study: Chalder M, Wiles NJ, Campbell J, et al. (2012) A pragmatic randomised controlled trial to evaluate the cost-effectiveness of a physical activity intervention as a treatment for depression: The treating depression with physical activity (TREAD) trial. Health Technology Assessment 16(10).			
Economic Question: physical therapy as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a recent first or new episode of mild /moderate depression
1.2	Are the interventions appropriate for the review question?	Yes	Exercise
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS & PSS

Update 2017

Study: Chalder M, Wiles NJ, Campbell J, et al. (2012) A pragmatic randomised controlled trial to evaluate the cost-effectiveness of a physical activity intervention as a treatment for depression: The treating depression with physical activity (TREAD) trial. Health Technology Assessment 16(10).			
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	QALYs estimated using EQ-5D ratings (UK tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT (N=361; at 12 months EQ-5D data n=195; complete resource use data n=156)
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	One-way SA; CEACs using bootstrapping
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments: results robust to multiple imputation used in sensitivity analysis; high attrition rates (>50%)			

Update 2017

P.2.41 Psychological, pharmacological, physical and combined interventions

2

Study: Guideline economic analysis
Economic Question: psychological, pharmacological and combined interventions for treatment of new episodes

Study: Guideline economic analysis			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a new episode of less severe depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	Discount rate 3.5%
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: **Directly applicable**			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	12 weeks + 2 years
2.3	Are all important and relevant outcomes included?	Partly	Disutility due to serious (but rare) side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Yes	Review of naturalistic studies
2.5	Are the estimates of relative intervention effects from the best available source?	Yes	Systematic review & NMA
2.6	Are all important and relevant costs included?	Partly	Cost of managing serious (but rare) side effects not considered
2.7	Are the estimates of resource use from the best available source?	Yes	Study based on large UK primary care database,

Update 2017

Study: Guideline economic analysis			
			supplemented by recent resource use data and costs
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: **Minor limitations**			
Other comments:			

P.3 Interventions for first-line treatment of adults with a new episode of more severe depression

P.3.1 Psychological interventions

Update 2017

Study: Horrell L, Goldsmith KA, Tylee AT, et al. (2014) One-day cognitive-behavioural therapy self-confidence workshops for people with depression: Randomised controlled trial. British Journal of Psychiatry 204: 222-233.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**

Study: Horrell L, Goldsmith KA, Tylee AT, et al. (2014) One-day cognitive-behavioural therapy self-confidence workshops for people with depression: Randomised controlled trial. British Journal of Psychiatry 204: 222-233.			
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	No	12 weeks
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT (N=459; economic analysis based on n=375 or 380, depending on outcome used)
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources & published studies
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted, CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: potentially serious limitations			
Other comments:			

Update 2017

1

Study: Holman AJ, Serfaty MA, Leurent BE, et al. (2011) Cost-effectiveness of cognitive behaviour therapy versus talking and usual care for depressed older people in primary care. BMC health services research 11: 33.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Older adults aged ≥ 65 years with depression (BDI ≥14)
1.2	Are the interventions appropriate for the review question?	Yes	CBT
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Health and social services
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured

Study: Holman AJ, Serfaty MA, Leurent BE, et al. (2011) Cost-effectiveness of cognitive behaviour therapy versus talking and usual care for depressed older people in primary care. BMC health services research 11: 33.			
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 10 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	BDI
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	10 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not measured
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=204; analysis on n=167
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	No	Only primary and community healthcare services considered
2.7	Are the estimates of resource use from the best available source?	Partly	RCT, analysis on n=198
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical tests including bootstrapping undertaken; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

Update 2017

1

Study: Hollinghurst S, Peters TJ, Kaur S, et al. (2010) Cost-effectiveness of therapist-delivered online cognitive-behavioural therapy for depression: Randomised controlled trial. British Journal of Psychiatry 197: 297-304.
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

Study: Hollinghurst S, Peters TJ, Kaur S, et al. (2010) Cost-effectiveness of therapist-delivered online cognitive-behavioural therapy for depression: Randomised controlled trial. British Journal of Psychiatry 197: 297-304.			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Partly	Adults with a new episode of depression
1.2	Are the interventions appropriate for the review question?	Yes	individual CBT delivered online
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS (& societal)
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	time horizon 8 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	8 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=297; BDI data for n=210; QALYs for n=165; NHS cost data for n=137
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical tests undertaken; bootstrapping conducted

Update 2017

Study: Hollinghurst S, Peters TJ, Kaur S, et al. (2010) Cost-effectiveness of therapist-delivered online cognitive-behavioural therapy for depression: Randomised controlled trial. British Journal of Psychiatry 197: 297-304.			
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Ekers D, Godfrey C, Gilbody S, et al (2011) Cost utility of behavioural activation delivered by the non-specialist. British Journal of Psychiatry 199: 510-511.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression
1.2	Are the interventions appropriate for the review question?	Yes	Behavioural activation
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 3 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: **Directly applicable**			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	3 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT (N=47, completers n=38)
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources

Update 2017

Study: Ekers D, Godfrey C, Gilbody S, et al (2011) Cost utility of behavioural activation delivered by the non-specialist. British Journal of Psychiatry 199: 510-511.			
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Bootstrapping conducted, CEAC presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: **potentially serious limitations**			
Other comments:			

1

Study: Miller P, Chilvers C, Dewey M, et al. (2003) Counseling versus antidepressant therapy for the treatment of mild to moderate depression in primary care economic analysis. International Journal of Technology Assessment in Health Care 19: 80-90.			
Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major depression
1.2	Are the interventions appropriate for the review question?	Yes	Counselling and antidepressants
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Global outcome, defined using research diagnostic criteria, BDI score and GP notes.
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT & preference trial
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not

Update 2017

Study: Miller P, Chilvers C, Dewey M, et al. (2003) Counseling versus antidepressant therapy for the treatment of mild to moderate depression in primary care economic analysis. International Journal of Technology Assessment in Health Care 19: 80-90.			
			measured
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT (N=103; at 12 months n=81) & preference trial (N=220; at 12 months n=163)
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT & preference trial
2.6	Are all important and relevant costs included?	Partly	Only depression-related costs measured
2.7	Are the estimates of resource use from the best available source?	Partly	RCT (n=103) & preference trial (n=215)
2.8	Are the unit costs of resources from the best available source?	Yes	National sources & local costs for counsellors
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical tests including bootstrapping undertaken; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

Update 2017

P.3.21 Pharmacological interventions

2

Study: Benedict A, Arellano J, De Cock E, Baird J (2010) Economic evaluation of duloxetine versus serotonin selective reuptake inhibitors and venlafaxine XR in treating major depressive disorder in Scotland. Journal of Affective Disorders 120: 94-104.			
Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a new episode of moderate to severe depression treated in primary care
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted	Yes	UK study

Study: Benedict A, Arellano J, De Cock E, Baird J (2010) Economic evaluation of duloxetine versus serotonin selective reuptake inhibitors and venlafaxine XR in treating major depressive disorder in Scotland. Journal of Affective Disorders 120: 94-104.			
	sufficiently similar to the current UK context?		
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Scottish NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 48 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	48 weeks
2.3	Are all important and relevant outcomes included?	Partly	Disutility from side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Meta-analyses of clinical trials
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Meta-analyses of clinical trials - randomisation possibly broken
2.6	Are all important and relevant costs included?	Partly	Cost of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	Expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11	Is there any potential conflict of interest?	Yes	Funded by industry
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

Update 2017

1

Study: Lenox-Smith A, Greenstreet L, Burslem K, Knight C (2009) Cost effectiveness of venlafaxine compared with generic fluoxetine or generic amitriptyline in major depressive disorder in the UK. Clinical Drug Investigation 29: 173-184.

Study: Lenox-Smith A, Greenstreet L, Burslem K, Knight C (2009) Cost effectiveness of venlafaxine compared with generic fluoxetine or generic amitriptyline in major depressive disorder in the UK. Clinical Drug Investigation 29: 173-184.			
Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adult outpatients with major depression
1.2	Are the interventions appropriate for the review question?	Yes	(venlafaxine included but not considered for guideline)
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Side effects not considered
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 24 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	Utility values estimated based on the presumed utilities of a depression-free day and a severely depressed day
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	24 weeks
2.3	Are all important and relevant outcomes included?	Partly	Side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Meta-analysis of RCTs
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Meta-analysis of RCTs; method of synthesis unclear, but randomisation appears to have

Update 2017

Study: Lenox-Smith A, Greenstreet L, Burslem K, Knight C (2009) Cost effectiveness of venlafaxine compared with generic fluoxetine or generic amitriptyline in major depressive disorder in the UK. Clinical Drug Investigation 29: 173-184.			
			been broken
2.6	Are all important and relevant costs included?	Partly	Costs of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	Delphi panel
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11	Is there any potential conflict of interest?	Yes	Funded by industry
2.12 Overall assessment: Very serious limitations			
Other comments:			

1

Study: Wade AG, Toumi I, Hemels MEH (2005) A probabilistic cost-effectiveness analysis of escitalopram, generic citalopram and venlafaxine as a first-line treatment of major depressive disorder in the UK. Current Medical Research and Opinion 21: 631-641.			
Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major depression (baseline MADRS score 18-40)
1.2	Are the interventions appropriate for the review question?	Yes	(venlafaxine was included but not part of RQ)
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS and societal
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Side effects / HRQoL not considered
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 26 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome was measured as % of remission (MADRS score ≤ 12)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	

Update 2017

Study: Wade AG, Toumi I, Hemels MEH (2005) A probabilistic cost-effectiveness analysis of escitalopram, generic citalopram and venlafaxine as a first-line treatment of major depressive disorder in the UK. Current Medical Research and Opinion 21: 631-641.			
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	26 weeks
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not measured
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Meta-analysis of RCTs
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Meta-analysis of RCTs
2.6	Are all important and relevant costs included?	Partly	Cost of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	GP database and expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	SA results not based on incremental analysis
2.11	Is there any potential conflict of interest?	Yes	Funded by industry
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Wade AG, Toumi I, Hemels MEH (2005) A pharmacoeconomic evaluation of escitalopram versus citalopram in the treatment of severe depression in the United Kingdom. Clinical Therapeutics 27: 486-496.			
Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major severe depression (baseline MADRS score ≥ 30)
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted	Yes	UK study

Update 2017

Study: Wade AG, Toumi I, Hemels MEH (2005) A pharmacoeconomic evaluation of escitalopram versus citalopram in the treatment of severe depression in the United Kingdom. Clinical Therapeutics 27: 486-496.			
	sufficiently similar to the current UK context?		
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS and societal
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Side effects / HRQoL not considered
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 26 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome was measured as % of remission (MADRS score ≤ 12)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	26 weeks
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Meta-analysis of RCTs
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Meta-analysis of RCTs
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	Published literature and expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11	Is there any potential conflict of interest?	Yes	Funded by industry
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

Update 2017

P.3.3 Combined pharmacological and psychological interventions

Study: Simon J, Pilling S, Burbeck R, Goldberg D (2006) Treatment options in moderate and severe depression: Decision analysis supporting a clinical guideline. British Journal of Psychiatry 189: 494-501.			
Economic Question: combination therapy as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with moderate / severe depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 15 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	Utilities used to estimate QALYs were derived from service users that valued vignettes using SG
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	Decision tree
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	15 months
2.3	Are all important and relevant outcomes included?	Partly	Side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Yes	Systematic review & meta-analysis
2.5	Are the estimates of relative intervention effects from the best available source?	Yes	Systematic review & meta-analysis
2.6	Are all important and relevant costs included?	Partly	Costs of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	published literature and expert opinion

Update 2017

Study: Simon J, Pilling S, Burbeck R, Goldberg D (2006) Treatment options in moderate and severe depression: Decision analysis supporting a clinical guideline. British Journal of Psychiatry 189: 494-501.			
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	One-way SA; PSA & CEACs
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments: costs and disutility associated with side effects not considered but since drugs were used in both arms of the model, the impact of this omission is considered to be negligible and depends on the difference of treatment discontinuation between the two arms			

1

Study: Koeser L, Donisi V, Goldberg DP, et al. (2015) Modelling the cost-effectiveness of pharmacotherapy compared with cognitive-behavioural therapy and combination therapy for the treatment of moderate to severe depression in the UK. Psychological Medicine, 45(14), 3019-31.			
Economic Question: combination therapy as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with moderate or severe depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	3.5% annually; time horizon 27 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	EQ-5D (UK tariff)
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	Decision tree
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	27 months

Update 2017

Study: Koeser L, Donisi V, Goldberg DP, et al. (2015) Modelling the cost-effectiveness of pharmacotherapy compared with cognitive-behavioural therapy and combination therapy for the treatment of moderate to severe depression in the UK. Psychological Medicine, 45(14), 3019-31.			
2.3	Are all important and relevant outcomes included?	Partly	Side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	NMA of RCTs identified in a database
2.5	Are the estimates of relative intervention effects from the best available source?	Yes	NMA of RCTs identified in a systematic database
2.6	Are all important and relevant costs included?	Partly	Costs of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	published literature based on expert opinion and RCT data
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	One-way SA; PSA & CEACs
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

P.3.41 Physical interventions

2

Study: Greenhalgh J, Knight C, Hind D, et al. (2005) Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: Systematic reviews and economic modelling studies. Health Technology Assessment 9(9).			
Economic Question: physical therapy as first-line treatment for adults with a new episode of depression			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major depression who require hospitalisation
1.2	Are the interventions appropriate for the review question?	Yes	ECT & medication
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Impact of side effects

Study: Greenhalgh J, Knight C, Hind D, et al. (2005) Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: Systematic reviews and economic modelling studies. Health Technology Assessment 9(9).			
			considered only in terms of discontinuation
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	QALYs estimated based on preferences for vignettes using the McSad system valued by Canadian service users with previous depression using SG
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Systematic review and further assumptions
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Systematic review and further assumptions
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	Published literature and expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA; 95% CI reported
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

Update 2017

P.3.5 Psychological, pharmacological and combined interventions

Study: Guideline economic analysis			
Economic Question: psychological, pharmacological and combined interventions for treatment of new episodes			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with a new episode of more severe depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	Discount rate 3.5%
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	12 weeks + 2 years
2.3	Are all important and relevant outcomes included?	Partly	Disutility due to serious (but rare) side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Yes	Review of naturalistic studies
2.5	Are the estimates of relative intervention effects from the best available source?	Yes	Systematic review & NMA
2.6	Are all important and relevant costs included?	Partly	Cost of managing serious (but rare) side effects not considered
2.7	Are the estimates of resource use from the best available source?	Yes	Study based on large UK

Update 2017

Study: Guideline economic analysis			
			primary care database, supplemented by recent resource use data and costs
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

P.4 Interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

P.4.1 Psychological interventions

Update 2017

Study: Scott J, Palmer S, Paykel E, et al (2003) Use of cognitive therapy for relapse prevention in chronic depression: Cost-effectiveness study. British Journal of Psychiatry 182: 221-227.			
Economic Question: psychological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with partially remitted major depression despite adequate clinical treatment
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured
1.6	Are all future costs and outcomes discounted appropriately?	Partly	Annual rate of 6%; time horizon 17 months
1.7	Is QALY used as an outcome, and was it derived using	No	% of relapses

Study: Scott J, Palmer S, Paykel E, et al (2003) Use of cognitive therapy for relapse prevention in chronic depression: Cost-effectiveness study. British Journal of Psychiatry 182: 221-227.			
	NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).		prevented
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	17 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=158
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT, full data on 65% of participants
2.8	Are the unit costs of resources from the best available source?	Partly	National sources; inpatient cost data from local sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEAC presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

1

Study: Hollinghurst S, Carroll FE, Abel A, et al. (2014) Cost-effectiveness of cognitive-behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: Economic evaluation of the CoBalT Trial. British Journal of Psychiatry 204: 69-76.			
Economic Question: psychological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review	Yes	Adults aged 18-

Study: Hollinghurst S, Carroll FE, Abel A, et al. (2014) Cost-effectiveness of cognitive-behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: Economic evaluation of the CoBaIT Trial. British Journal of Psychiatry 204: 69-76.			
	question?		75 years with major depression, who had adhered to antidepressant medication for at least 6 weeks in primary care, but who continued to have significant depressive symptoms
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS for cost-utility analysis; health & social care provider for cost consequence analysis, with service user expenses and productivity losses assessed in additional analyses
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	3.5% annually on costs and outcomes
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	Other outcomes (e.g. response, remission) considered as well
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	3-5 years' follow up
2.3	Are all important and relevant outcomes included?	Yes	

Update 2017

Study: Hollinghurst S, Carroll FE, Abel A, et al. (2014) Cost-effectiveness of cognitive-behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: Economic evaluation of the CoBaIT Trial. British Journal of Psychiatry 204: 69-76.			
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=467
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEAC presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

P.4.21 Pharmacological interventions

2

Study: Olgiati P, Bajo E, Bigelli M, et al. (2013) Challenging sequential approach to treatment resistant depression: cost-utility analysis based on the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial. European Neuropsychopharmacology 23: 1739-1746.			
Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with chronic depression that received second line treatment following non-remission
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	3rd party payer
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 26 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and	Partly	Based on preferences for

Update 2017

Study: Olgiati P, Bajo E, Bigelli M, et al. (2013) Challenging sequential approach to treatment resistant depression: cost-utility analysis based on the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial. European Neuropsychopharmacology 23: 1739-1746.			
	outcomes used in line with analytical perspectives taken (item 1.4 above).		vignettes, elicited from service users in the US/Canada using SG
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	26 weeks
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Large study of series of RCTs
2.5	Are the estimates of relative intervention effects from the best available source?	No	Data for each arm obtained from 2 different studies, thus breaking rules of randomisation
2.6	Are all important and relevant costs included?	Partly	Cost of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	Expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA conducted but no CEAC presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Very serious limitations			
Other comments: only incremental QALYs presented			

1

Study: Nordstrom G, Despiegel N, Marteau F, et al (2010) Cost effectiveness of escitalopram versus SNRIs in second-step treatment of major depressive disorder in Sweden. Journal of Medical Economics 13: 516-526.		
Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment		
Section 1: Applicability (relevance to specific review question and the NICE reference case)	**Yes/ Partly/ No/Unclear/ NA**	**Comments**

Update 2017

Study: Nordstrom G, Despiegel N, Marteau F, et al (2010) Cost effectiveness of escitalopram versus SNRIs in second-step treatment of major depressive disorder in Sweden. Journal of Medical Economics 13: 516-526.			
1.1	Is the study population appropriate for the review question?	Partly	Adults with major depression who initiated antidepressant treatment, with a history of treatment with another antidepressant within the previous 6 months
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	Swedish study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Societal but healthcare costs reported separately
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 6 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	6 months
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Pooled analysis of trial data, for participants who had already received antidepressant therapy – data for duloxetine & venlafaxine pooled together
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Pooled analysis of trial data, for

Update 2017

Study: Nordstrom G, Despiegel N, Marteau F, et al (2010) Cost effectiveness of escitalopram versus SNRIs in second-step treatment of major depressive disorder in Sweden. Journal of Medical Economics 13: 516-526.			
			participants who had already received antidepressant therapy
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	Naturalistic study
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	CEACs presented for escitalopram versus each of the other drugs considered
2.11	Is there any potential conflict of interest?	Yes	Funded by industry
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Benedict A, Arellano J, De Cock E, Baird J (2010) Economic evaluation of duloxetine versus serotonin selective reuptake inhibitors and venlafaxine XR in treating major depressive disorder in Scotland. Journal of Affective Disorders 120: 94-104.			
Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with severe major depression who failed previous treatment with SSRIs
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Scottish NHS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 48 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	

Update 2017

Study: Benedict A, Arellano J, De Cock E, Baird J (2010) Economic evaluation of duloxetine versus serotonin selective reuptake inhibitors and venlafaxine XR in treating major depressive disorder in Scotland. Journal of Affective Disorders 120: 94-104.			
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	48 weeks
2.3	Are all important and relevant outcomes included?	Partly	Disutility from side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Meta-analyses of clinical trials
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Meta-analyses of clinical trials - randomisation possibly broken
2.6	Are all important and relevant costs included?	Partly	Cost of side effects not considered
2.7	Are the estimates of resource use from the best available source?	Partly	Expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11	Is there any potential conflict of interest?	Yes	Funded by industry
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Malone DC (2007) A budget-impact and cost-effectiveness model for second-line treatment of major depression. Journal of Managed Care Pharmacy 13: S8-S18.			
Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with major depression who have failed to achieve remission with SSRIs

Update 2017

Study: Malone DC (2007) A budget-impact and cost-effectiveness model for second-line treatment of major depression. Journal of Managed Care Pharmacy 13: S8-S18.			
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	3rd party payer
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Side effects and HRQoL not considered
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 6 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome measure was probability of remission
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	6 months
2.3	Are all important and relevant outcomes included?	Partly	Side effects and HRQoL not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Baseline data from published trials
2.5	Are the estimates of relative intervention effects from the best available source?	No	review of published trial data and further assumptions – synthesis by naïve addition of data (leading to breaking of randomisation)
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	Analysis of 1,814 persons enrolled in 10 antidepressant studies
2.8	Are the unit costs of resources from the best available source?	Unclear	Medication costs from national sources; other unit costs taken from other studies, unclear

Update 2017

Study: Malone DC (2007) A budget-impact and cost-effectiveness model for second-line treatment of major depression. Journal of Managed Care Pharmacy 13: S8-S18.			
			whether these were national or local
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	Results of sensitivity analysis reported using primarily each intervention's CER and not ICERs.
2.11	Is there any potential conflict of interest?	Yes	
2.12 Overall assessment: Very serious limitations			
Other comments:			

1

Study: Edwards S, Hamilton V, Nherera L, Trevor N (2013) Lithium or an atypical antipsychotic drug in the management of treatment resistant depression: a systematic review and economic evaluation. Health Technology Assessment 17(54).			
Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with treatment-resistant unipolar depression (TRD) defined as failure to respond to at least 2 previous antidepressants in the current episode of depression
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Side effects not considered
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 12 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	

Update 2017

Study: Edwards S, Hamilton V, Nherera L, Trevor N (2013) Lithium or an atypical antipsychotic drug in the management of treatment resistant depression: a systematic review and economic evaluation. Health Technology Assessment 17(54).			
1.9 Overall judgement: Directly applicable			
Other comments: Evidence on lithium derived from people who had failed at least one antidepressant			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	12 months
2.3	Are all important and relevant outcomes included?	Partly	Side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Pooled trial data identified in a systematic review
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Indirect comparison using a common baseline comparator; data on lithium not from TRD population
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	Clinical expert opinion; weighted medication costs were used, based on expert opinion
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Potentially serious limitations			
Other comments:			

1

Study: Taneja C, Papakostas GI, Jing Y, et al (2012) Cost-effectiveness of adjunctive therapy with atypical antipsychotics for acute treatment of major depressive disorder. Annals of Pharmacotherapy 46: 642-649.			
Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review	Yes	Adults with

Update 2017

Study: Taneja C, Papakostas GI, Jing Y, et al (2012) Cost-effectiveness of adjunctive therapy with atypical antipsychotics for acute treatment of major depressive disorder. Annals of Pharmacotherapy 46: 642-649.			
	question?		major depression who responded inadequately to previous antidepressant therapy
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare system
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Side effects and HRQoL not considered
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 6 weeks
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome measure was probability of response
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	No	6 weeks
2.3	Are all important and relevant outcomes included?	Partly	Side effects and HRQoL not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	Pooled published trial data
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	Meta-analysis of published phase 3 clinical trials and indirect comparison using placebo as baseline comparator
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	Administrative databases and assumptions
2.8	Are the unit costs of resources from the best available	Yes	National

Update 2017

Study: Taneja C, Papakostas GI, Jing Y, et al (2012) Cost-effectiveness of adjunctive therapy with atypical antipsychotics for acute treatment of major depressive disorder. Annals of Pharmacotherapy 46: 642-649.			
	source?		sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	Only sensitivity analysis relating to relative effectiveness reported
2.11	Is there any potential conflict of interest?	Yes	
2.12 Overall assessment: Very serious limitations			
Other comments:			

P.5 Interventions aimed at preventing relapse in people whose depression has responded to treatment

P.5.1 Psychological interventions

Study: Kuyken W, Byford S, Taylor RS, et al. (2008) Mindfulness-Based Cognitive Therapy to Prevent Relapse in Recurrent Depression. Journal of Consulting and Clinical Psychology 76: 966-978.			
Economic Question: psychological interventions for relapse prevention			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with three or more previous major depressive episodes, on a therapeutic dose of maintenance antidepressants and currently in full or partial remission
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS; societal perspective
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not measured
1.6	Are all future costs and outcomes discounted appropriately?	NA	Time horizon 15 months
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken	No	% of relapses prevented; number of

Update 2017

Study: Kuyken W, Byford S, Taylor RS, et al. (2008) Mindfulness-Based Cognitive Therapy to Prevent Relapse in Recurrent Depression. Journal of Consulting and Clinical Psychology 76: 966-978.			
	(item 1.4 above).		depression-free days
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Partially applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	15 months
2.3	Are all important and relevant outcomes included?	Partly	HRQoL not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=123
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT, N=123
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEAC presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

Update 2017

1

Study: Kuyken W, Hayes R, Barrett B, et al. (2015) Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. Lancet 386: 63-73.			
Economic Question: psychological interventions for relapse prevention			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with three or more previous major depressive episodes and on a therapeutic dose of

Study: Kuyken W, Hayes R, Barrett B, et al. (2015) Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. Lancet 386: 63-73.			
			maintenance antidepressant
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Health and social services; societal perspective
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	Annual rate of 3.5% used; time horizon 2 years
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Partly	The primary outcome was % of relapse or recurrence; QALYs (based on EQ-5D) were secondary outcome
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	NA	RCT
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	2 years
2.3	Are all important and relevant outcomes included?	Yes	
2.4	Are the estimates of baseline outcomes from the best available source?	Partly	RCT, N=424
2.5	Are the estimates of relative intervention effects from the best available source?	Partly	RCT
2.6	Are all important and relevant costs included?	Yes	
2.7	Are the estimates of resource use from the best available source?	Partly	RCT, N=424
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Statistical analyses conducted; CEACs presented

Update 2017

Study: Kuyken W, Hayes R, Barrett B, et al. (2015) Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. Lancet 386: 63-73.			
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

P.5.21 Psychological, pharmacological and combined interventions

2

Study: Guideline economic analysis			
Economic Question: psychological, pharmacological and combined interventions for relapse prevention			
Section 1: Applicability (relevance to specific review question and the NICE reference case)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
1.1	Is the study population appropriate for the review question?	Yes	Adults with depression that is in remission, at medium or high risk of relapse
1.2	Are the interventions appropriate for the review question?	Yes	
1.3	Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK study
1.4	Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS/PSS
1.5	Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are all future costs and outcomes discounted appropriately?	Yes	Discount rate 3.5%
1.7	Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	NA	
1.9 Overall judgement: Directly applicable			
Other comments: None			
Section 2: Study limitations (level of methodological quality)		**Yes/ Partly/ No/Unclear/ NA**	**Comments**
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	10 years
2.3	Are all important and relevant outcomes included?	Partly	Disutility due to serious (but rare) side effects not considered
2.4	Are the estimates of baseline outcomes from the best available source?	Yes	Review of naturalistic

Update 2017

Study: Guideline economic analysis			
			studies
2.5	Are the estimates of relative intervention effects from the best available source?	Yes	Systematic review & pairwise meta-analysis or NMA, as appropriate
2.6	Are all important and relevant costs included?	Partly	Cost of managing serious (but rare) side effects not considered
2.7	Are the estimates of resource use from the best available source?	Yes	Study based on large UK primary care database, supplemented by recent resource use data and costs
2.8	Are the unit costs of resources from the best available source?	Yes	National sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA conducted; CEACs presented
2.11	Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations			
Other comments:			

1

Update 2017

Appendix Q: Economic evidence – evidence tables

Q.1 Service delivery models for people with depression

Q.1.1 Simple collaborative care – references to included studies

1. Bosanquet K, Adamson J, Atherton K, Bailey D, Baxter C, Beresford-Dent J, Birtwistle J, Chew-Graham C, Clare E, Delgadillo J, Ekers D, Foster D, Gabe R, Gascoyne S, Haley L, Hamilton J, Hargate R, Hewitt C, Holmes J, Keding A, Lewis H, McMillan D, Meer S, Mitchell N, Nutbrown S, Overend K, Parrott S, Pervin J, Richards DA, Spilsbury K, Torgerson D, Traviss-Turner G, Trépel D, Woodhouse R, Gilbody S (2017) CollAborative care for Screen-Positive ElderRs with major depression (CASPER plus): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technology Assessment, in press [**UK**]
2. Green C, Richards DA, Hill JJ, Gask L, Lovell K, Chew-Graham C, et al. (2014) Cost-effectiveness of collaborative care for depression in UK primary care: Economic evaluation of a randomised controlled trial (CADET). PLoS ONE 9(8): e104225. [**UK**]

AND

Richards DA, Bower P, Chew-Graham C, Gask L, Lovell K, Cape J, Pilling S, Araya R, Kessler D, Barkham M, Bland JM, Gilbody S, Green C, Lewis G, Manning C, Kontopantelis E, Hill JJ, Hughes-Morley A, Russell A (2016) Clinical effectiveness and cost-effectiveness of collaborative care for depression in UK primary care (CADET): a cluster randomised controlled trial. Health Technol Assess, 20(14), 1-192.

3. Lewis H, Adamson J, Atherton K, Bailey D, Birtwistle J, Bosanquet K, Clare E, Delgadillo J, et al. (2017) CollAborative care and active surveillance for Screen-Positive ElderRs with subthreshold depression (CASPER): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness. Health Technology Assessment, in press [**UK**]
4. Simon GE, Von Korff M, Ludman EJ, Katon WJ, Rutter C, Unutzer J, Lin EH, Bush T, Walker E (2002) Cost-effectiveness of a program to prevent depression relapse in primary care. Medical care 40: 941-950. [**US, relapse prevention**]

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Bosanquet et al., 2017 UK Cost-utility analysis	Interventions: Simple collaborative care (SCC), using behavioural activation, designed specifically for people aged ≥ 65 with depression, delivered over 8 sessions by a case manager (a primary care mental health / IAPT worker) for an average of 6 sessions over 7-8 weeks. SCC included telephone support, medication management, symptom monitoring and active surveillance, facilitated by a computerised case management. The first session was delivered face-to-face and subsequent sessions via telephone. SCC was provided in addition to usual GP care. Treatment as usual, comprising GP care alone (TAU)	Adults aged ≥ 65 years with major depressive disorder. Exclusion criteria: alcohol dependency; psychotic symptoms; recent suicidal risk/self-harm; significant cognitive impairment Pragmatic, multi-centre open RCT (N=485) Source of efficacy and resource use data: RCT (Bosanquet2017); (N=485; at 18 months n=344; cost data available for n=447) Source of unit costs: national sources	Costs: intervention (case manager's time and supervision, as well as training including manual, supervision, travel and accommodation) and usual primary care (GP appointment, home visits and telephone consultation; practice nurse appointments and telephone consultations) Mean total cost per person (95% CI): SCC: £1,171 (£1,167 to £1176); TAU: £654 (£651 to £658) Adjusted difference £480 (£381 to £579). Primary outcome measure: QALY based on SF-6D ratings (UK tariff) Mean number of QALYs per person (SD): SCC: 0.900 (0.241); TAU: 0.889 (0.224) Adjusted difference 0.019 (95% CI -0.020 to 0.057, p=0.338)	ICER of SCC vs TAU: £26,010/QALY Probability of SCC being cost-effective: 0.39 and 0.55 at WTP £20,000 and £30,000/QALY, respectively. Sensitivity analysis: Including only participants who engaged with 5 or more sessions in the analysis: ICER £9,876/QALY	Perspective: NHS/PSS (intervention and primary care exclusively considered) Currency: GBP£ Cost year: 2012/13 Time horizon: 18 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Green et al., 2014 UK Cost-utility analysis	Interventions: Simple collaborative care in addition to usual primary care (SCC), comprising care managers making 6-12 contacts with service users over 14 weeks; contacts involved education about depression, medication management, behavioural activation and relapse prevention instructions. Care managers provided GPs with advice on medication and regular updates on service user progress including medication adherence. Treatment as usual (TAU), defined as GP care that includes antidepressant treatment and referral for other treatments, including Improving Access to Psychological Therapies (IAPT) services	Adults with depression Multi-centre cluster RCT (N=581) Source of efficacy data: RCT (Richards2013); (data available for n=466) Source of resource use data: RCT (data available for n=447) Source of unit costs: national sources	Costs: intervention (care manager's time and supervision by specialists), staff time (GP, mental health nurse, practice nurse, counsellor, mental health worker, social worker, home care worker, occupational therapist, psychiatrist, psychologist, psychiatric nurse/care coordinator), walk-in-centre, voluntary group, inpatient psychiatric and general stay, A&E, day hospital, other outpatient contact, day care centre, drop-in club; informal care and service user expenses in sensitivity analysis Mean NHS/PSS cost per person (SD): SCC: £1,887 (£3,714); TAU: £1,571 (£2,442) Unadjusted difference: £316 Adjusted difference: £271 (95%CI: -£203 to £886) Primary outcome measure: QALY based on EQ-5D ratings (UK tariff); SF-6D (UK tariff) used in sensitivity analysis Mean number of QALYs per person (SD): SCC: 0.605 (0.261); TAU: 0.554 (0.286) Unadjusted difference: 0.051 Adjusted difference: 0.019 (95%CI: -0.019 to 0.06)	ICER of SCC vs TAU: £14,248/QALY Probability of SCC being cost-effective: 0.58 and 0.65 at WTP £20,000 and £30,000/QALY, respectively. Results robust to multiple imputation of missing data, use of SF-6D utility values, use of alternative SCC costs; SCC dominant using a broader perspective; excluding one participant with an extremely high level of self-reported resource use, ICER became £3,334/QALY and probability of cost effectiveness 0.76 and 0.79 at WTP £20,000 and £30,000 /QALY, respectively	Perspective: NHS/PSS; broader perspective (informal care costs and service user expenses) considered in sensitivity analysis Currency: GBP£ Cost year: 2011 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Simon et al., 2002 US Cost effectiveness analysis	Interventions: Simple collaborative care comprising an educational book and videotape on effective management of depression; 2 visits to a depression prevention specialist including shared decision making on maintenance antidepressant treatment; plus 3 scheduled telephone contacts and 4 personalised mailings for monitoring depressive symptoms and treatment adherence (SCC) Treatment as usual (TAU), including primary care and referral to specialty mental health care	Adults with a history of either recurrent major depression (i.e. at least 3 depressive episodes in the previous 5 years) or dysthymia (depressive symptoms present continuously for the past 2 years) that had recovered from a depressive episode following antidepressant treatment in primary care RCT (Katon2001) Source of efficacy and resource use data: RCT; N=386, n=315 (82%) completed all follow-up assessments; n=377 (98%) remained enrolled throughout the follow-up period Source of unit costs: local data	Costs: medication, staff time, any inpatient and outpatient services for mental health or general medical care Mean total cost cost per person: SCC: $2,691 (95%CI $2,320 to $3,062) TAU: $2,619 (95%CI $2,139 to $3,099) Incremental $13 (95%CI -$584 to $511), after adjustment for gender, age, baseline Hopkins Symptoms Checklist (HSCL) depression score and chronic disease score Primary outcome measure: number of depression-free days, defined as days with a HSCL depression score ≤ 0.5; days with a HSCL score above 0.5 but < 2 were considered 50% depression free Number of depression-free days: SCC: 253.2 (95% CI 241.7 to 264.7) TAU: 239.4 (95% CI 227.3 to 251.4) Incremental 13.9 (95%CI -1.5 to 29.3, p=0.078), after adjustment for gender, age, baseline SCL depression score and chronic disease score	ICER of SCC vs. TAU $1 per depression-free day (95%CI -$134 to $344)	Perspective: 3rd party payer Currency: US$ Cost year: 1998 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Q.1.2 Complex collaborative care – references to included studies

5. Morriss R, Garland A, Nixon N, Guo B, James M, Kaylor-Hughes C, Moore R, Ramana R, Sampson C, Sweeney T, Dalgleish T, NIHR CLAHRC Specialist Mood Disorder Study Group (2016) Efficacy and cost-effectiveness of a specialist depression service versus usual specialist mental health care to manage persistent depression: a randomised controlled trial. Lancet Psychiatry, 3(9), 821-31
6. Goorden M, Vlasveld MC, Anema JR, van Mechelen W, Beekman AT, Hoedeman R, van der Feltz-Cornelis CM, Hakkaart-van Roijen L (2014) Cost-utility analysis of a collaborative care intervention for major depressive disorder in an occupational healthcare setting. Journal of Occupational Rehabilitation, 24(3): 555-62
7. Goorden M, Huijbregts KM, van Marwijk HW, Beekman AT, van der Feltz-Cornelis CM, Hakkaart-van Roijen L (2015) Cost-utility of collaborative care for major depressive disorder in primary care in the Netherlands. Journal of Psychosomatic Research, 79(4), 316-23.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Morriss et al., 2016 UK Cost-utility analysis	Interventions: Complex collaborative care, comprising secondary outpatient specialist depression services offering tailored integrated pharmacological and psychological (CBT, MBCT and compassion focused therapy, as appropriate) treatment within a collaborative care approach for 12-15 months (CCC) Usual secondary mental health care (TAU)	Adults with persistent unipolar moderate or severe depression, with HDRS total≥16, GAF≤60, that have received treatment for depression for at least 6 months and are currently receiving secondary mental healthcare Multi-site single-blind RCT (N=187) Source of efficacy and resource use data: RCT	Costs: primary care (GP surgery and home attendances), practice / district / community psychiatric nurse, psychotherapist, inpatient and outpatient (psychiatric or other) care, A&E attendances, medication Mean total cost per person (95% CI): CCC: £9,315 (£7,547 to £11,084) TAU: £5,869 (£4,501 to £7,238) Incremental total cost (bias-corrected bootstrapped): £3,446 (£1,915 to £5,180) Primary outcome measure: QALYs based on EQ-5D-3L ratings (UK tariff) Mean QALYs per person (95% CI): CCC: 0.753 (0.659 to 0.847) TAU: 0.646 (0.538 to 0.754) Incremental QALYs (bias-corrected bootstrapped): 0.079 (0.007 to 0.149)	ICER of CCC vs. TAU £43,603/QALY Controlling for baseline differences and cluster effects: probability of CCC being cost-effective exceeds 0.50 at WTP of £42,000/QALY	Perspective: NHS and personal social services Currency: GBP£ Cost year: 2014 Time horizon: 18 months Discounting: NA Applicability: directly applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
		(Morriss2016, N=187; 84% completed at 6 months, 72% at 12 months and 59% at 18 months) Source of unit costs: national sources			

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Goorden et al., 2014 The Netherlands Cost-utility analysis	Interventions: Complex collaborative care (CCC) provided by a trained occupational physician – care manager who was guided by a web-based stepped care protocol and received close supervision by a consultant psychiatrist, in addition to treatment as usual. Service users were offered manual guided self-help, 6–12 sessions of problem solving treatment (PST), a workplace intervention and, if considered necessary, antidepressant medication. If symptoms were persistent after 18 weeks of	Sick-listed workers with major depression RCT (N=126) Source of efficacy and resource use data: RCT (Vlasveld2012, N=126) Source of unit costs: national sources	Costs: intervention (occupational physician – care manager's time, training and supervision), staff time (GP, mental health care professional, public and private psychologist/psychiatrist, operational physician, other specialist, paramedic, social worker, alternative medicine practitioner), self-help group, day care, psychiatric inpatient care, medication; productivity losses reported separately Mean total healthcare cost per person: CCC €3,874 (95 %CI €2,778 to €5,718) TAU €4,583 (95 %CI €3,108 to €6,794) Primary outcome measure: QALYs based on EQ-5D ratings (Dutch tariff) Mean total number of QALYs per person:	ICER of TAU vs CCC €14,589/QALY Following bootstrapping and inspection of the cost effectiveness plane: 75% of replications were in the south-west quadrant (CCC less costly and less effective), 21% into the north-west quadrant (CCC dominated), 3% in the south-east quadrant (CCC dominant), and 1% in the north-east quadrant (CCC more costly and	Perspective: healthcare system; productivity losses reported separately Currency: Euro (€) Cost year: 2009 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	treatment, the service users were referred to secondary mental health care. Treatment as usual (TAU), comprising sickness guidance by the company's occupational physician. Both interventions were provided at an occupational healthcare setting. Service users were free to engage in any other treatment as well.		CCC 0.11 (95% CI 0.07 to 0.14) TAU 0.16 (95%CI 0.11 to 0.19) Difference: -0.05 (95%CI -0.11 to 0.00)	more effective). Results not sensitive to day care and psychiatric inpatient care costs.	

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Goorden et al., 2015 The Netherlands Cost-utility analysis	Interventions: Complex collaborative care (CCC) provided by a depression care manager, usually a qualified nurse, who collaborated with a GP and a liaison psychiatrist in order to provide and guide more structured and adherent depression treatment in primary care. Treatment consisted of problem solving, manual guided self-help (both provided by the care	People aged ≥17 years with major depression according to the MINI. Exclusion criteria: being suicidal, psychotic symptoms, dementia, drug or alcohol dependence, already under specialty mental health treatment RCT (N=150; 93	Costs: GP, psychiatric / mental health care practice nurse, psychiatric inpatient care, specialist outpatient care, private psychologist / psychiatrist, occupational physician, other specialist, paramedic, social worker, counselling centre for drugs, alcohol, etc, alternative medicine, self-help group, day care, psychotropic medication Mean total healthcare cost per person: CCC €4,011 (95% CI €,2679 to €,5513) TAU €2,838 (95% CI €,2463 to €,3244) Difference: €1,173 (95% CI, -€216 to €2726)	ICER of TAU vs CCC €53,717/QALY Probability of CCC being cost-effective: 0.20 and 0.70 at WTP €20,000 and €80,000/QALY, respectively.	Perspective: healthcare system; productivity losses reported separately Currency: Euro (€) Cost year: 2013 Time horizon: 12 months Discounting: NA Applicability: partially

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	manager), and, if necessary, antidepressants (prescribed by the GP). Care managers and GPs received training in CCC. Treatment as usual (TAU) in primary care, comprising prescription of antidepressants or referral to psychotherapy	identified by screening and 47 by GP referral) Source of efficacy and resource use data: RCT (Huijbregts 2013, n=93 identified by screeening) Source of unit costs: national sources	Primary outcome measure: QALYs based on EQ-5D ratings (Dutch tariff) Mean total number of QALYs gained per person: CCC 0.07 (95% CI 0.05 to 0.09) TAU 0.05 (95% CI 0.03 to 0.06) Difference: 0.02 (95% CI −0.004 to 0.04)		applicable Quality: potentially serious limitations

Update 2017

Q.1.3 Medication management – references to included studies

8. Bosmans JE, Brook OH, Van Hout HPJ, De Bruijne MC, Nieuwenhuyse H, Bouter LM, Stalman WAB, Van Tulder MW (2007) Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepressants. PharmacoEconomics 25: 25-37.
9. Rubio-Valera M, Bosmans J, Fernandez A, Penarrubia-Maria M, March M, Trave P, Bellon JA, Serrano-Blanco A (2013) Cost-Effectiveness of a Community Pharmacist Intervention in Patients with Depression: A Randomized Controlled Trial (PRODEFAR Study). PLoS ONE 8(8): e70588.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Bosmans et al., 2007 The Netherlands Cost effectiveness analysis	Interventions: Medication management (MM), comprising coaching and education by a pharmacist to improve adherence to antidepressant therapy. This consisted of 3 contacts with the pharmacist (mean duration 13-20 minutes) during which pharmacists gave service users information about the use of antidepressants, plus a take-home video reviewing important facts on depression and antidepressant treatment Treatment as usual (TAU) comprising standard oral and written information that is routinely issued in the	Adults with depression treated in primary care, with a new prescription for a non-tricyclic antidepressant, who had not received antidepressant treatment in the past 6 months RCT (N=151) Source of efficacy and resource use data: RCT (Brook2005, N=151; analysis based on n=88 completers of both 3- and 6-month follow-ups) Source of unit costs: national	Costs: intervention (25-minute take home video, drug coaching contacts at the pharmacy), healthcare and non-healthcare staff time (GP, psychologist, social worker, psychiatrist), other specialist outpatient appointment (homeopath, physiotherapist, community mental healthcare, haptonomist, magnetic therapist, acupuncturist, spiritualist, foot reflex therapist, company doctor), abdominal x-ray, medication, absenteeism from paid labour Mean societal cost per person: MM: €3,275; TAU: €2,961 Mean difference €315 (95%CI –€1,922 to €2,416). Mean direct cost per person: MM: €724; TAU: €712 Mean difference €12 (95%CI not reported). Primary outcome measures: adherence to antidepressant treatment measured using an electronic pill container; depressive symptoms measured using the Hopkins Symptom Checklist (HSCL) Mean adherence per arm:	From a societal perspective: ICER of MM vs. TAU €14,900 per extra person with improvement in adherence €2,550 per point improvement in SCL Probability of MM being cost-effective around 0.65 at WTP of €50,000 per extra person with improvement in adherence. Results robust to per protocol analysis, the price of producing the video-tape, the	Perspective: societal Currency: Euro (€) Cost year: 2002 Time horizon: 6 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	Netherlands when people with depression pick up their prescriptions for antidepressants at the pharmacy	sources	MM: 88%; TAU: 86% Mean difference: 2.1% (95%CI –5.6% to 9.8%) Mean difference in HSCL score per person: –0.15 (95% CI –0.54 to 0.23) favouring MM	method for estimating indirect costs, and imputation of missing data	

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Rubio-Valera et al., 2013 Spain Cost effectiveness and cost-utility analysis	Interventions: Medication management (MM), comprising an educational intervention provided by the pharmacist, focusing on improving service users' knowledge of antidepressant medication, making them aware of the importance of compliance to the medication, reassuring them about possible side-effects, and stressing the importance of carrying out GPs' advice. In service users with a sceptical attitude towards antidepressants, the intervention aimed to reduce stigma. Pharmacists were trained	Adults aged 18-75 years initiating treatment with antidepressants because of depression RCT (N=179) Source of efficacy and resource use data: RCT (Rubio-Valera2012, N=179; 71% completed at 6 months; n=151 received intervention as allocated) Source of unit costs: regional sources	Costs: intervention (pharmacist time, pharmacist training), publicly funded healthcare services (GP, nurse, psychologist, psychiatrist, other medical specialists, social worker, hospital emergency visits, hospital stay, diagnostic tests, medication), privately funded healthcare services (psychiatrist, psychologist, medical specialist, GP), absenteeism from paid labour. Mean societal cost per person: MM: €1,091; TAU: €767 Mean difference €324 (95%CI –€97 to €745). Mean direct cost per person: MM: €444; TAU: €425 Mean difference €49 (95%CI not reported). Primary outcome measures: adherence to antidepressant treatment measured using electronic pharmacy records; remission of depressive symptoms defined as a reduction	Under a healthcare perspective: ICER of MM vs. TAU €962 per extra adherent service user €3,592/QALY TAU dominant in terms of remission Probability of MM being cost-effective 0.71 and 0.76 for WTP €6,000 /adherent service user and €30,000 /QALY, respectively. Using remission, maximum probability of MM being cost-effective 0.46. Results robust to per	Perspective: societal and healthcare Currency: Euro (€) Cost year: 2009 Time horizon: 6 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	for the intervention. Treatment as usual from GP and pharmacist (TAU), comprising filling the prescriptions, addressing service users' questions about medication and giving basic advice about how to take the antidepressant.		in the Patient Health Questionnaire 9-item (PHQ-9) of at least 50%; QALYs based on EQ-5D ratings (Spanish tariff) Incremental probability of adherence per person: 0.04 (95%CI -0.2 to 0.1) Incremental probability of remission per person: -0.01 (95%CI -0.2 to 0.1) Incremental QALYs per person: 0.01 (95%CI -0.02 to 0.03)	protocol or complete case analysis, use of DSM-IV criteria for depression, intervention costs or method for estimating indirect costs.	

Update 2017

Q.1.4 Stepped care – references to included studies

10. Mukuria C, Brazier J, Barkham M, Connell J, Hardy G, Hutten R, Saxon D, Dent-Brown K, Parry G (2013) Cost-effectiveness of an improving access to psychological therapies service. British Journal of Psychiatry 202: 220-227.

11. Ricken R, Wiethoff K, Reinhold T, Schietsch K, Stamm T, Kiermeir J, Neu P, Heinz A, Bauer M, Adli M (2011) Algorithm-guided treatment of depression reduces treatment costs - Results from the randomized controlled German Algorithm Project (GAPII). Journal of Affective Disorders 134: 249-256.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Mukuria et al., 2013 UK Cost effectiveness and cost-utility analysis	Interventions: Stepped care approach: Improving Access to Psychological Therapies (IAPT) service comprising: Step 1 watchful waiting; Step 2 guided self-help including bibliotherapy with support, computerised CBT with support and CBT-based telephone support for problem-solving; Step 3 CBT ± medication. IAPT was provided in addition to treatment as usual Treatment as usual alone (TAU), comprising GP care, primary care counselling and referral to mental health professionals in secondary care. IAPT was evaluated in Doncaster demonstration site. Comparator sites were selected to match IAPT site regarding size & type of population served based on deprivation, ethnicity and age;	People 16-64 years old with a new or recurrent episode of depression or anxiety, who were likely to benefit from psychological therapies. More than 95% of people in IAPT had a primary diagnosis of depression by their GP. Prospective cohort study with matched sites (N=403) Source of efficacy and resource use data: cohort study (N=403; available 8-month cost and QALY data for n=297) Source of unit costs:	Costs: intervention (staff time, training, equipment, facilities and overheads), other mental healthcare (psychiatrist, psychologist, community psychiatric nurse, psychotherapist/ counsellor, other mental health professionals and voluntary sector services), primary and secondary care, social care; medication costs not considered Mean total cost per person (SD): IAPT: £1,190 (£2,193); TAU: £934 (£1,666) Unadjusted difference: £256 (95% CI: -£266 to £779) Adjusted difference: £236 (95%CI: -£214 to £689) Primary outcome measures: proportion of people with a reliable and clinically significant (RCS) improvement on the PHQ-9; QALY based on SF-6D ratings (UK tariff); QALYs based on predicted EQ-5D ratings (UK tariff), estimated from SF-6D using an empirical mapping	ICER of IAPT vs. TAU £9,440 per participant with RCS improvement £29,500/QALY using SF-6D £16,857/QALY using predicted EQ-5D scores Probability of IAPT being cost-effective using SF-6D QALYs: <0.40 at WTP £30,000/QALY; using EQ-5D QALYs: 0.38 and 0.53 at WTP £20,000 and £30,000 / QALY, respectively. Using national unit costs instead of IAPT financial data resulted in an ICER of £3,800 per participant achieving RCS improvement and	Perspective: NHS and social services; productivity losses estimated separately Currency: GBP£ Cost year: 2008/09 Time horizon: 8 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	geographical location; local implementation of 'pathways to work'; ethnic diversity; recent changes in organisational structure. Also, comparator sites were selected based on how well they performed according to average Quality and Outcomes Framework points, a voluntary annual reward and incentive programme for all GPs in England that assesses areas of clinical care, organisation, patient experience & other services.	IAPT data and national sources	function were used in sensitivity analysis Proportion of people with a PHQ-9 RCS significant improvement (95% CI): IAPT: 0.221 (0.164 to 0.278) TAU: 0.205 (0.116 to 0.293) Unadjusted difference: 0.016 (-0.089 to 0.122) Adjusted difference: 0.025 (-0.078 to 0.127) Mean number of SF-6D QALYs per person (95% CI): IAPT: 0.026 (0.018 to 0.033) TAU: 0.018 (0.007 to 0.029) Unadjusted difference 0.007 (-0.006 to 0.021) Adjusted difference 0.008 (-0.005 to 0.021) Mean number of EQ-5D QALYs per person (95% CI): IAPT: 0.038 (0.027 to 0.049) TAU: 0.025 (0.009 to 0.040) Unadjusted difference: 0.013 (-0.007 to 0.033) Adjusted difference: 0.014 (-0.005 to 0.032)	£11,875/QALY using SF-6D	

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Ricken et al., 2011 Germany Cost effectiveness analysis	Interventions: Stepped care comprising a standardised stepwise drug treatment regimen (SC) Treatment as usual (TAU) .	Adults with a depressive syndrome according to ICD-10, with an indication for antidepressant therapy, receiving care in an inpatient setting. Exclusion criteria: organic mental disorders, alcohol or substance dependence, substance-related affective disorders, ongoing prophylactic medication with a mood stabilizer that could not be discontinued, a new antidepressant started within the last 21 days, postpartum depression, pregnancy or breast-feeding, severe general medical illness prohibiting standard antidepressant medication, involuntary court ordered hospitalisation, and/or rejection of psychopharmacology treatment. RCT (N=148) Source of efficacy and resource use data: RCT (Bauer2009, N=148; completers n=103) Source of unit costs: national sources	Costs: medication, hospitalisation Mean hospitalisation cost per person (SD): SC: €10,830 (€8,632); TAU: €15,202 (€12,483), p=0.026 Mean medication cost per person (SD): SC: €155 (€183); TAU: €184 (€216), p=0.188 Primary outcome measures: remission, defined as a Bech–Rafaelsen-Melancholia-Scale (BRMS) score <7 Probability of remission: SC: 0.541; TAU: 0.392 Hazard ratio 2.02, p=0.07	SC dominant	Perspective: 3rd party payer Currency: Euro (€) Cost year: likely 2004 Time horizon: time from enrolment to study endpoint, i.e. dropout or remission Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Q.1.5 Integrated care pathways – references to included studies

12. Pyne JM, Fortney JC, Mouden S, Lu L, Hudson TJ, Mittal D (2015) Cost-effectiveness of on-site versus off-site collaborative care for depression in rural FQHCs. Psychiatric Services 66: 491-499.

13. Wiley-Exley E, Domino ME, Maxwell J, Levkoff SE (2009) Cost-effectiveness of integrated care for elderly depressed patients in the PRISM-E study. Journal of Mental Health Policy and Economics 12: 205-213+217.

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Pyne et al., 2015 US Cost effectiveness and cost-utility analysis	Interventions: On-site, practice-based integrated care, comprising treatment provided by local primary care providers, coordinated by on-site nurse depression care managers; the latter contacted service users either face-to-face or by telephone. Service users could be referred to specialists at off-site locations. Off-site, telemedicine-based integrated care, which used off-site specialists to support local primary care providers. Five types of providers were involved: on-site primary care providers, off-site depression care managers who contacted service users via telephone, a psychologist, a psychiatrist and a clinical pharmacist. At any time service users had access to CBT delivered via interactive video.	Adults who screened positive for depression according to a PHQ-9 score ≥10. Exclusion criteria: schizophrenia, bipolar disorder, acute suicidal ideation Multi-site pragmatic RCT (N=364) Source of efficacy and resource use data: RCT (Dobscha2006, N=364; 87% completed at 6 months, 79% at 12 months and 78% at 18 months) Source of unit costs: regional sources; national sources used in secondary analysis	Costs: intervention (training of depression care managers, education material, interactive video equipment, staff time, telephone line), outpatient visits, inpatient care, emergency room care, medication, service users' time and mileage. Adjusted incremental total cost per person: Off-site vs. on-site $1,146 (95%CI $396 to $1,897); p=0.003. Primary outcome measures: number of depression-free days derived from the 20-item HSCL (score ≤ 0.5 indicated depression-free day, ≥ 1.7 full symptoms and intermediate severity scores were assigned a value between depression-free and fully symptomatic by linear interpolation); QALYs based on SF-12/SF-6D algorithm (UK tariff) Adjusted incremental number of depression-free days per person off-site vs. on-site: 110 (95%CI 80 to 140); p<0.001 Adjusted incremental QALYs per person off-site vs. on-site: 0.04 (95%CI 0.02 to 0.07); p=0.003	ICER of off-site vs. on-site $36,033/QALY using regional costs $28,126/QALY using national costs ICER using depression-free days as the measure of outcome reported only after exclusion of inpatient costs: $10.75 / depression-free day Probability of off-site being cost-effective 0.86 at WTP $50,000/QALY Results sensitive to telephone line charges	Perspective: healthcare & service users' time and mileage Currency: US$ Cost year: 2009 Time horizon: 18 months Discounting: NA Applicability: partially applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Wiley-Exley *et al.*, 2009 US Cost effectiveness and cost-utility analysis	Interventions: Integrated care (IC) comprising collaboration between primary and specialty mental health care; a behavioural health professional was co-located in the primary care setting and the primary care provider continued involvement in the mental health care of the service user Primary care with a specialty referral system (SRS) for referral to a behavioural health provider outside the primary care setting, who had primary responsibility for the mental health needs of the service user. Both service delivery models were assessed within and outside the Veteran Affairs (VA) system.	Adults above 65 years of age with depression (major or minor) Multi-site pragmatic RCT (N=840) Source of efficacy and resource use data: RCT (Krahn2006, N=840; within VA n=365, outside VA n=475; individuals with major depression within VA n=214, outside VA n=302) Source of unit costs: national sources	Costs: outpatient visits, inpatient care, nursing home, rehabilitation, emergency room, medication, service users' and caregivers' time and travel costs. Adjusted incremental total cost per person: All: VA: -$651, p=ns; Non-VA: $46, p=ns Major depression: VA: $877, p=ns; Non-VA: -$380, p=ns Primary outcome measures: Center for Epidemiologic Studies Depression Scale (CES-D) score; number of depression-free days (DFD) derived from the 20-item CES-D (score =0 indicated depression-free day, ≥ 16 full symptoms and intermediate severity scores were assigned a value between depression-free and fully symptomatic by linear interpolation); QALYs estimated based on depression-free days (QALY-DFD), using utility weights of health=1, depression=0.59); QALYs estimated based on SF-36 (QALY-SF), using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG Adjusted incremental CES-D score per person:	Full VA sample: IC is dominant Probability of IC being cost-effective >0.70 for any WTP/QALY-SF Full non-VA sample: IC is dominated when using CES-D, DFD, QALY-DFD. When using QALY-SF, ICER of IC vs. SRS was $94,929/QALY Probability of IC being cost-effective <0.40 for any WTP/QALY-SF Major depression VA sample: ICER of IC vs. SRS: $322/CES-D point change $94/DFD $45,965/QALY-DFD $58,815/QALY-SF Probability of IC being cost-effective <0.50 for WTP of $40,000/QALY-SF and above Major depression non-VA sample:	Perspective: healthcare & service users' and carers' time and travel costs Currency: US$ Cost year: 2002 Time horizon: 6 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
			All: VA: -1.3, p=ns; Non-VA: 2.9, p<0.01 Major depression: VA: -2.8, p<0.05; Non-VA: 3.45, p<0.05 Adjusted incremental DFDs per person: All: VA: 3.89, p=ns; Non-VA: -5.73, p=ns Major depression: VA: 9.29, p=ns; Non-VA: -5.20, p<0.05 Adjusted incremental QALY-DFD per person: All: VA: 0.005, p=ns; Non-VA: -0.016, p<0.05 Major depression: VA: 0.019, p=ns; Non-VA: -0.011, p<0.05 Adjusted incremental QALY-SF per person: All: VA: 0.007, p=ns; Non-VA: 0.0004, p=ns Major depression: VA: 0.015, p=ns; Non-VA: -0.005, p=ns	SRS is dominant in terms of CES-D ICER of SRS vs. IC: $73/DFD $34,167/QALY-DFD $79,590/QALY-SF Probability of IC being cost-effective >0.50 for WTP $50,000/QALY-SF and above	

Q.2 Interventions for first-line treatment of adults with a new episode of less severe depression

Q.2.1 Psychological interventions – references to included studies

Problem solving

14. Kendrick T, Simons L, Mynors-Wallis L, Gray A, Lathlean J, Pickering R, Harris S, Rivero-Arias O, Gerard K, Thompson C (2005) A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study. Health Technology Assessment 9: iii-59.

AND

Kendrick T, Simons L, Mynors-Wallis L, Gray A, Lathlean J, Pickering R, Harris S, Rivero-Arias O, Gerard K, Thompson C (2006) Cost-effectiveness of referral for generic care or problem-solving treatment from community mental health nurses, compared with usual general practitioner care for common mental disorders: Randomised controlled trial. British Journal of Psychiatry 189: 50-59.

Psychodynamic counselling

15. Simpson S, Corney R, Beecham J (2003) A randomized controlled trial to evaluate the effectiveness and cost-effectiveness of psychodynamic counselling for general practice patients with chronic depression. Psychological Medicine 33: 229-239.

Computerised CBT

16. Kaltenthaler E, Brazier J, De Nigris E, Tumur I, Ferriter M, Beverly C, Parry G, Rooney G, Sutcliffe P (2006) Computerized cognitive behavior therapy for depression and anxiety update: A systematic review and economic evaluation. Health Technology Assessment 10(33).

17. McCrone P, Knapp M, Proudfoot J, Ryden C, Cavanagh K, Shapiro DA, Ilson S, Gray JA, Goldberg D, Mann A, Marks I, Everitt B, Tylee A (2004) Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: Randomised controlled trial. British Journal of Psychiatry 185: 55-62.

Computerised CBT with support

18. Littlewood E, Duarte A, Hewitt C, Knowles S, Palmer S, Walker S, Andersen P, Araya R, Barkham M, Bower P, Brabyn S, Brierley G, Cooper C, Gask L, Kessler D, Lester H, Lovell K, Muhammad U, Parry G, Richards DA, Richardson R, Tallon D, Tharmanathan P, White D, Gilbody S; REEACT Team (2015) A randomised controlled trial of computerised cognitive behaviour therapy for the treatment of depression in primary care: the Randomised Evaluation of the Effectiveness and Acceptability of Computerised Therapy (REEACT) trial. Health Technol Assess, 19(101).

19. Phillips R, Schneider J, Molosankwe I, Leese M, Foroushani PS, Grime P, McCrone P, Morriss R, Thornicroft G (2014) Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. Psychological Medicine 44: 741-752.

Update 2017

Computerised CBT with support vs computerised CBT

20. Brabyn S, Araya R, Barkham M, Bower P, Cooper C, Duarte A, Kessler D, Knowles S, Lovell K, Littlewood E, Mattock R, Palmer S, Pervin J, Richards D, Tallon D, White D, Walker S, Worthy G, Gilbody S, on behalf of the REEACT Team (2016) The second Randomised Evaluation of the Effectiveness, cost-effectiveness and Acceptability of Computerised Therapy trial (REEACT-2): does the provision of telephone support enhance the effectiveness of computer-delivered cognitive behaviour therapy? A randomised controlled trial. Health Technology Assessment, 20(89)

Behavioural activation versus cognitive behavioural therapy (CBT)

21. Richards DA, Ekers D, McMillan D, Taylor RS, Byford S, Warren FC, Barrett B, Farrand PA, Gilbody S, Kuyken W, O'Mahen H, Watkins ER, Wright KA, Hollon SD, Reed N, Rhodes S, Fletcher E, Finning K (2016) Cost and Outcome of Behavioural Activation versus Cognitive Behavioural Therapy for Depression (COBRA): a randomised, controlled, non-inferiority trial. Lancet, 388(10047):871-80.

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Kendrick et al., 2005 & 2006a UK Cost-utility analysis	Interventions: Problem-solving treatment provided by nurses Generic community mental health (MH) nurse care Usual GP care	Adults with a new episode of anxiety, depression or reaction to life difficulties with duration of symptoms 4 weeks to 6 months; and a General Health Questionnaire 12-item version (GHQ–12) ≥3. 75% of participants had depression. Exclusion criteria: current psychological treatment or contact with psychiatric services; severe mental disorder or substance misuse; dementia; active suicidal ideas Pragmatic RCT (N=247) (Kendrick2006) Source of efficacy & resource use data: RCT, analysis based on n=184 with clinical data available; cost data available for n=159 Source of unit costs: national sources	Costs: intervention, training & supervision, medication, staff time (GP, practice nurse, counsellor, social worker, psychiatrist, psychologist), outpatient visit, A&E, inpatient care, other hospital contacts For societal perspective: out of pocket expenses and productivity losses Mean total NHS cost per person (SD): Problem solving: £608 (£501) MH nurse care: £569 (£350) GP care: £283 (£300) Adjusted differences vs GP care (95% CI): Problem solving: £325 (£204 to £484) MH nurse care: £286 (£174 to £411) Outcome measure: QALY based on EQ-5D ratings (UK tariff) Mean QALYs gained per person (SD): Problem solving: 0.39 (0.09) MH nurse care: 0.40 (0.07) GP care: 0.40 (0.07) Adjusted differences in QALY vs GP care (95% CI): Problem solving: -0.02 (-0.05 to 0.012) MH nurse care: 0 (-0.03 to 0.03)	Under NHS perspective: usual GP care dominant	Perspective: NHS (and societal) Currency: GBP£ Cost year: 2003 Time horizon: 26 weeks Discounting: NA Applicability: directly applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Simpson et al., 2003 UK Cost effectiveness analysis	Interventions: Psychodynamic counselling (6-12 sessions each lasting 50 min) provided by highly trained, BAC accredited counsellors, who received regular supervision in addition to GP treatment as usual GP treatment as usual (TAU)	Adults aged 18-70 with depression (BDI 14-40) lasting at least 6 months, with or without comorbid anxiety. Exclusion criteria: symptoms of anxiety only; depression lasting >5 years; people 'difficult' or 'hard to treat'; history of drug or alcohol related problems, suicide attempts or psychosis; had seen a counsellor in the last 6 months RCT (Simpson2003, N=145) Source of efficacy and resource use data: RCT (at 12 months n=115 for outcomes and costs) Source of unit costs: local intervention costs; national sources for all other costs	Costs: GPs, practice nurses & counsellors, medication, specialist mental health, hospital, community health and social care services Mean total cost per person (sd): Psychodynamic counselling £1046 (£1728), TAU £1074 (£1509); mean difference -£28, adjusted 95%CI -£597 to £588 Primary outcome measure: BDI Secondary outcome measures: Brief Symptom Inventory (BSI); Inventory for Interpersonal Problems (IIP); Social Adjustment Schedule (SAS); Duke Social Support Scale (DSSS); number of 'cases of depression' defined as BDI≥14 or any of total BSI measures ≥63, or any SAS subcategory ≥2 Outcome results: No significant differences between groups on any of the outcomes at 6 or 12 months, with the exception of BDI-defined cases of depression at 12 months: counselling: 48%; TAU: 64% (p=0.02)	No differences in costs or outcomes between interventions	Perspective: health and social services Currency: GBP£ Cost year: 1998 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Kaltenthaler et al., 2006 UK Cost-utility analysis	Interventions: Computerised CBT – 3 packages examined: Beating the Blues (cCBT1) Cope (cCBT2) Overcoming Depression (cCBT3) Treatment as usual, defined as GP visits, medication and possible referral to a specialist (TAU)	Adults with depression treated in a primary care setting Decision-analytic modelling Source of efficacy data: analysis of RCT individual-level data for cCBT1 and cCBT2; published RCT data for cCBT3; and further assumptions Source of resource use data: manufacturer submissions, published data and other assumptions Source of unit costs: national sources	Costs: intervention (licence fees, computer hardware, screening of patients for suitability, clinical support, capital overheads, training), healthcare costs according to severity of depression (including medication, primary, inpatient and outpatient care) Mean total cost per person: cCBT1: £584 cCBT2: £630 cCBT3: £501 TAU: £437 Outcome measure: QALY estimated based on EQ-5D (UK tariff) Mean QALYs per person cCBT1: 1.10 cCBT2: 1.05 cCBT3: 1.03 TAU: 1.02	ICER vs TAU: cCBT1: £1,801/QALY cCBT2: £7,139/QALY cCBT3: £5,391/QALY Probability of each intervention being cost-effective vs TAU at WTP £30,000/QALY: cCBT1: 0.87 cCBT2: 0.63 cCBT3: 0.54	Perspective: NHS Currency: GBP£ Cost year: likely 2003 Time horizon: 18 months Discounting: 3.5% annually Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
McCrone et al., 2004 UK Cost effectiveness and cost-utility analysis	Interventions: Computerised CBT (Beating the Blues), consisting of a 15min introductory video followed by 8 50min sessions of CBT (cCBT) Treatment as usual (TAU), consisting of a variety of interventions, including discussions with the GP, referral to a counsellor, practice nurse or mental health professional, and treatment of physical conditions.	Adults aged 18-75 years with a diagnosis of depression, mixed depression and anxiety or anxiety disorders, who were not currently receiving face-to-face psychological therapy RCT (Proudfoot2004a, N=274) Source of efficacy and resource use data: RCT (cost data available for n=261) Source of unit costs: national sources, intervention cost from manufacturer	Costs: intervention (programme, computers and overheads), inpatient care (physical and psychiatric), outpatient care, day surgery, A&E, staff time (GP, practice nurse, district nurse, CPN, nurse practitioner, counsellor, clinical psychologist, psychiatrist, health visitor, social worker, physiotherapist, other therapist), psychotropic medication, other services Productivity losses considered in societal perspective Mean total NHS cost per person (SD): cCBT: £397 (£589); TAU: £357 (£575) Mean difference: £40 (90% CI -£28 to £148) Outcome measures: BDI score; number of depression-free days (DFDs) defined based on BDI scores; QALY assuming that a DFD scores 1 and a day with depression scores 0.59 Outcome results: BDI difference: -3.5 (95% CI 0.6–6.4) Number of DFDs (SD): cCBT: 89.7 (74.2); TAU 61.0 (67.1) Difference: 28.4 (95% CI 10.7-45.5). Difference in QALYs: 0.032	ICER of cCBT vs TAU: £11/point improvement on BDI £1/DFD £1,250/QALY Probability of cCBT being cost-effective: 0.14 and 0.81 at WTP zero and £40 per point improvement in BDI, respectively 0.15 and 0.80 at WTP zero and £5 per additional DFD, respectively 0.85 and 0.99 at WTP £5,000 and £15,000 per QALY, respectively	Perspective: NHS (and societal) Currency: GBP£ Cost year: 2000 Time horizon: 8 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Littlewood et al., 2015 UK Cost-utility analysis	Interventions: Computerised, commercially produced CBT (Beating the Blues) with therapist support in addition to treatment as usual (cCBT1) Computerised, free to use cCBT (MoodGYM) with therapist support in addition to treatment as usual (cCBT2) Treatment as usual, comprising GP care with no constraints on the range of treatments that could be accessed (TAU)	Adults with symptoms of depression (PHQ-9 score ≥10) Pragmatic multicentre RCT (Gilbody2015, N=691) Source of efficacy and resource use data: RCT (EQ-5D data available for n=416 at 24 months; NHS cost data available for n=580) Source of unit costs: national sources	Costs: intervention (licence fee, cost of support), GP or nurse visits (including telephone call appointments), out-of-hours GP services, inpatient stays, outpatient visits, other community services (including counsellors, psychologists, psychiatrists, CMHT and IAPT services), depression-related medication (antidepressants, antipsychotics, mood stabilisers, sleeping tablets, anxiety medication) Mean total cost per person (SE): cCBT1: £1,186 (£80) cCBT2: £1,098 (£135) TAU: £1,121 (£62) Adjusted mean differences (95% CI) cCBT1 vs TAU: £104 (-£67 to £275) cCBT2 vs TAU: -£106 (-£262 to £50) Primary outcome measure: QALYs estimated based on EQ-5D (UK tariff) Number of QALYs per person (SE): cCBT1: 1.333 (0.034) cCBT2: 1.356 (0.033) TAU: 1.389 (0.033) Adjusted mean differences (95% CI) cCBT1 vs TAU: -0.044 (-0.117 to 0.030) cCBT2 vs TAU: -0.015 (-0.092 to 0.061)	cCBT1 dominated by TAU TAU vs cCBT2 £6,933/QALY Probability of each intervention being cost effective at WTP £20,000/QALY: cCBT1: 0.038 cCBT2: 0.417 TAU: 0.545 Using SF-6D QALYs: cCBT1 dominated by TAU cCBT2 dominant Probability of each intervention being cost-effective at WTP £20,000/QALY: cCBT1: 0.007 cCBT2: 0.756 TAU: 0.237 Results robust to inclusion of depression-related costs only and to consideration of completers' data only (instead of imputed data analysis) Little evidence of an interaction effect between preference and treatment allocation on outcomes	Perspective: NHS & PSS Currency: GBP£ Cost year: 2012 Time horizon: 2 years Discounting: 3.5% annually Applicability: directly applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Phillips et al., 2014 UK Cost effectiveness and cost-utility analysis	Interventions: Computerised CBT (MoodGYM) comprising 5 1hr modules, usually taken weekly, plus support in the form of telephone interviews (cCBT) 'Attention' control (five websites with general information about mental health)	Adults with depressive symptoms, as measured by PHQ-9 responses, identified via occupational health settings Pragmatic RCT (Phillips2014, N=637) Source of efficacy and resource use data: RCT (for clinical analysis: completion 56% at 6 weeks; 36% at 12 weeks; for cost analysis: completion rates not reported) Source of unit costs: national sources	Costs: hospital (inpatient and outpatient care), community services, staff time (GP, psychiatrist, district nurse, counsellor, occupational health providers, other providers, medication) Intervention cost appears to have been omitted from analysis Productivity losses considered in societal perspective Mean total NHS cost per person (SD): cCBT: £29 (£110); Control: £38 (£125) Outcome measures: Work and Social Adjustment Scale (WSAS); QALYs estimated based on EQ-5D (UK tariff) Outcome results: WSAS difference: -0.470 (95% CI -1.837 to 0.897) QALY: cCBT: 0.082; control: 0.083 at 6 weeks cCBT: 0.167; control: 0.170 at 12 weeks	ICER of control vs cCBT: £3,667/QALY	Perspective: NHS (and societal) Currency: GBP£ Cost year: likely 2010 Time horizon: 12 weeks for outcomes; 6 weeks for costs Discounting: NA Applicability: directly applicable Quality: very serious limitations

Update 2017

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Brabyn et al., 2016 UK Cost-utility analysis	Interventions: Telephone-facilitated computerised CBT (cCBT1) Minimally	Adults with depression, as defined by a PHQ9 score of ≥ 10 and < 3 for item 9 (measuring suicidal thoughts), not currently in receipt of cCBT or specialist psychological therapy;	Costs: intervention (telephone support), community care (GP visits and home visits, nurse, counsellor, psychiatric nurse, other primary care, all day based services), hospital services (inpatient mental health care, inpatient non-mental health care, outpatient	cCBT1 dominant over cCBT2 Probability of cCBT1 being cost effective at WTP £20,000 and £30,000/QALY: 0.55	Perspective: NHS & PSS Currency: GBP£ Cost year: 2013 Time horizon: 12 months

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	supported computerised CBT(cCBT2) In both arms a freely available cCBT program was used (MoodGYM)	antidepressant medication or comorbid physical illness or non-psychotic functional disorders not excluded. Exclusion criteria: actively suicidal, bereaved or given birth within the last year, diagnosis of psychotic depression, primary diagnosis of alcohol or drug abuse Pragmatic multicentre RCT (Brabyn2016, N=369) Source of efficacy and resource use data: RCT (complete cost data across the trial period available for n=209) Source of unit costs: national sources	psychiatrist visit, clinical psychologist, non-mental health outpatient visits) , medication Mean total cost per person (SE): cCBT1: £1,763 (£439) cCBT2: £1,172 (£187) Adjusted cost difference: -£3.42 Primary outcome measure: QALYs estimated based on EQ-5D (UK tariff) Number of QALYs per person (SE): cCBT1: 0.686 (0.019) cCBT2: 0.700 (0.016) Adjusted QALY difference: 0.0026	Results robust to inclusion of mental health-related costs only	Discounting: NA Applicability: directly applicable Quality: minor limitations

Update 2017

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Richards et al., 2016 UK Cost-utility analysis	Interventions: Behavioural activation (20 sessions over 16 weeks, plus 4 booster sessions if participants wanted them)	Adults meeting DSM-IV criteria for major depressive disorder from primary care and psychological therapy services Exclusion criteria: people receiving psychological therapy; alcohol or drug dependence; acutely suicidal or attempted suicide in past 2	Costs: intervention, community health and social care, hospital, medication Mean cost per person (SD): BA: £2,597 (£1,847) CBT £3,251 (£3,041) Difference: -£343 (-£858 to £171) Primary outcome measure: QALY	BA dominant Probability of BA being cost-effective: 0.8 at a WTP of £20,000-£30,000/QALY Results robust	Perspective: NHS & PSS Currency: GBP£ Cost year: 2014 Time horizon: 18 months Discounting:

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	delivered by Band 5 therapists (BA) Cognitive behavioural therapy (20 sessions over 16 weeks, plus 4 booster sessions if participants wanted them) delivered by Band 7 therapists (CBT)	months; cognitive impairment; bipolar disorder or psychosis or psychotic symptoms Non-inferiority RCT (Richards2016, N=440) Source of efficacy and resource use data: RCT (costs available for n=327; outcomes available for n=309) Source of unit costs: national sources	Mean QALY per person (SD): BA: 0.985 (0.422) CBT: 0.935 (0.433) Difference: 0.050 (-0.046 to 0.145)	to imputation of missing data	3.5% annually Applicability: directly applicable Quality: minor limitations

Update 2017

Q.2.2 Pharmacological interventions – references to included studies

SSRIs (fluvoxamine, sertraline, paroxetine, citalopram or escitalopram) plus GP supportive care vs. GP supportive care alone

22. Kendrick T, Chatwin J, Dowrick C, Tylee A, Morriss R, Peveler R, Leese M, McCrone P, Harris T, Moore M, Byng R, Brown G, Barthel S, Mander H, Ring A, Kelly V, Wallace V, Gabbay M, Craig T, Mann A (2009) Randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of selective serotonin reuptake inhibitors plus supportive care, versus supportive care alone, for mild to moderate depression with somatic symptoms in primary care: the THREAD (THREshold for AntiDepressant response) study. Health Technology Assessment 13(22)

TCAs (amitriptyline, dothiepin or imipramine) versus SSRIs (fluoxetine, sertraline or paroxetine) versus lofepramine

23. Peveler R, Kendrick T, Buxton M, Longworth L, Baldwin D, Moore M, Chatwin J, Goddard J, Thornett A, Smith H, Campbell M, Thompson C (2005) A randomised controlled trial to compare the cost-effectiveness of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine. Health Technology Assessment 9(16)

AND

Kendrick T, Peveler R, Longworth L, Baldwin D, Moore M, Chatwin J, Thornett A, Goddard J, Campbell M, Smith H, Buxton M, Thompson C (2006) Cost-effectiveness and cost-utility of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine: Randomised controlled trial. British Journal of Psychiatry 188: 337-345.

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Kendrick et al., 2009 UK Cost effectiveness and cost-utility analysis	Interventions: SSRIs (fluoxetine, fluvoxamine, sertraline, paroxetine, citalopram or escitalopram) plus GP supportive care GP supportive care alone, comprising	Adults with depressive symptoms for ≥ 8 weeks, who had received no antidepressant treatment within the previous 12 months, were not in receipt of counselling or psychological therapies at baseline, had a baseline HAMD17 score 12-19 and at least one	Costs: medication, primary care (face-to-face GP consultations, GP telephone contacts, practice nurse contacts), secondary care (inpatient, outpatient, day patient, accident and emergency), community health services (health visitors, district nurses, counselling or psychological therapists), social care services (social workers, housing workers) Mean (SD) total cost per person: At 12 weeks: SSRI & GP: £341 (£454); GP alone: £388 (£932) Difference adjusted for baseline:	12 weeks SSRI & GP dominates GP alone At zero WTP per unit of reduction on HAMD17, probability of SSRI & GP being cost-effective was 54.9% At a WTP of £20,000–£30,000/QALY, probability of SSRI &	Perspective: health and social care Currency: UK£ Cost year: 2007 Time horizon: 12 and 26 weeks Discounting: NA Applicability: directly applicable

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	consultations at 2, 4, 8 and 12 weeks after the baseline assessment	symptom on the Bradford Somatic Inventory (BSI). Exclusion criteria: significant substance misuse and an Alcohol Use Disorders Identification Test (AUDIT) score ≥ 12 RCT (Kendrick2009, N=220) Source of efficacy & resource use data: RCT (N=220; 12-week completers n=196; 6-month followed-up n=160) Source of unit costs: national sources	-£28 (95%CI -£656 to £117) At 26 weeks: SSRI & GP: £759 (£1730); GP alone: £629 (£1092) Difference adjusted for baseline: £153 (95%CI -£500 to £304) Outcome measures: HAMD17 score; QALY based on SF-36 ratings (UK tariff) Mean (SD) HAMD17 score per person: At 12 weeks SSRI & GP: 8.73 (5.20); GP alone: 11.22 (5.78) At 26 weeks SSRI & GP: 7.92 (5.67); GP alone: 9.73 (5.57) Mean QALYs gained per person: From baseline to 12 weeks SSRI & GP 0.159; GP alone 0.152 Difference adjusting for baseline 0.005 From baseline to 26 weeks SSRI & GP 0.331; GP alone 0.318 Difference adjusted for baseline 0.010	GP being cost-effective was 80-85%. 26 weeks ICER of SSRI & GP vs. GP alone £90/unit of improvement on HAMD17 or £14,854/QALY SSRI & GP has a greater than 0.50 probability of being cost-effective when the WTP exceeds £80 per unit reduction on HAMD17 At a WTP at £20,000–£30,000/QALY, probability of SSRI & GP being cost-effective was 0.65-0.75	Quality: minor limitations

Update 2017

1
2

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Peveler et al., 2005 and Kendrick et al., 2006b UK	Interventions: TCAs (amitriptyline, dothiepin or imipramine)	Adults with a new episode of depression willing to receive antidepressant treatment in primary care, including those with comorbid physical or mental illness.	Costs: GP time (surgery contact, by telephone, home visit), other staff time (practice nurse, district nurse, CPN, counsellor, psychiatrist), day centre, non-psychiatric hospital clinic, A&E, psychiatric and non-	ICERs SSRI vs. TCAs £59/DFW TCAs vs. LOF £183/DFW (TCAs	Perspective: NHS Currency: UK£ Cost year: 2002 Time horizon: 12 months

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Cost effectiveness and cost-utility analysis	SSRIs (fluoxetine, sertraline or paroxetine) Lofepramine (LOF) Treatment lasted 6 months after remission or for at least 12 months if participant had experienced ≥ 2 depressive episodes within the past 5 years.	Exclusion criteria: already taking antidepressants, pregnant, breast-feeding, terminal illness Open-label RCT, with partial preference design (following randomisation, treatment could be prescribed from a different class to the one allocated at random, if participants or their doctor preferred an alternative). (Peveler2005; N=327; entered preference group n=92; followed-up at 12 months n=171) Source of efficacy data: RCT (n=264 for depression-free weeks, n=262 for QALYs) Source of resource use data: RCT (n=324; sub-analysis included for those who provided efficacy data, and used in estimation of ICERs/CEACs) Source of unit costs: national sources	psychiatric in-patient stay Mean total cost per person (95%CI): TCAs £762 (£553 to £1059) SSRIs £875 (£675 to £1355) LOF £867 (£634 to £1521) (p=0.09) Outcome measures: number of depression-free weeks (DFW, defined as a Hospital Anxiety and Depression Scale - Depression subscale (HADS-D) <8) and QALYs based on EQ-5D ratings (UK tariff) Number of depression-free weeks per person (95%CI): TCAs 25.3 (21.3 to 29.0) SSRIs 28.3 (24.3 to 32.2) LOF 24.6 (20.6 to 28.9) p=0.327 Mean QALYs per person, adjusted for baseline (95%CI): TCAs 0.548 (0.481 to 0.606) SSRIs 0.586 (0.523 to 0.641) LOF 0.552 (0.493 to 0.612)	extendedly dominated) SSRI vs. LOF £32/DFW SSRIs vs. LOF £5,686/QALY LOF vs. TCAs £23,250/QALY (LOF extendedly dominated) SSRIs vs. TCAs £2,692/QALY Probability of SSRIs being cost-effective approximately 0.6 at WTP of £20,000/QALY	Discounting: NA Applicability: directly applicable Quality: minor limitations

Update 2017

Q.2.3 Physical interventions – references to included studies

Acupuncture versus counselling versus usual care

24. Spackman E, Richmond S, Sculpher M, Bland M, Brealey S, Gabe R, Hopton A, Keding A, Lansdown H, Perren S, Torgerson D, Watt I, MacPherson H (2014) Cost-effectiveness analysis of acupuncture, counselling and usual care in treating patients with depression: The results of the ACUDep trial. PLoS ONE 9(11): e113726

Exercise versus usual care

25. Chalder M, Wiles NJ, Campbell J, Hollinghurst SP, Searle A, Haase AM, Taylor AH, Fox KR, Baxter H, Davis M, Thorp H, Winder R, Wright C, Calnan M, Lawlor DA, Peters TJ, Sharp DJ, Turner KM, Montgomery AA, Lewis G (2012) A pragmatic randomised controlled trial to evaluate the cost-effectiveness of a physical activity intervention as a treatment for depression: The treating depression with physical activity (TREAD) trial. Health Technology Assessment 16(10).

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Spackman et al., 2014 UK Cost-utility analysis	Interventions: Acupuncture 12 weekly sessions Counselling 12 weekly sessions Treatment as usual (TAU)	Adults with depression (BDI-II score ≥20), who were in contact with primary care services for this reason within the past 5 years, and were continuing to experience moderate to severe depression Open parallel-arm RCT (MacPherson 2013, N=755) Source of efficacy and resource use data: RCT (at 12 months EQ-5D data n=572; complete resource use data n=150; multiple imputation used) Source of unit costs: national sources	Costs: intervention, GP, practice nurse, other health professional, NHS hospital outpatient clinic, hospital ward, hospital mental health unit, other hospital unit, accident and emergency, community mental health nurse, psychologist or psychiatrist, NHS counsellor Mean total cost per person: Acupuncture £1,227; counselling £1,450; TAU £958 Primary outcome measure: QALYs estimated using EQ-5D ratings (UK tariff) QALYs per person: Acupuncture 0.663; counselling 0.666; TAU 0.604 using imputed data and seemingly unrelated regression controlling for the baseline HRQoL	ICER of counselling vs. acupuncture: £71,757/QALY acupuncture vs. TAU £4,560/QALY counselling vs. TAU (when acupuncture is not suitable) £7,935/QALY Probability of cost effectiveness at £20,000/QALY: acupuncture 0.62; counselling 0.36; TAU 0.02 Results sensitive to small changes in intervention costs; results robust to inclusion of depression-related resource use only. In complete case analysis acupuncture dominated counselling.	Perspective: NHS Currency: GBP£ Cost year: 2012 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Chalder et al., 2012 UK Cost-utility analysis	Interventions: Physical activity intervention delivered by a physical activity facilitator plus GP treatment as usual GP treatment as usual (TAU), which may include antidepressant medication, counselling or referral to secondary mental health services	Adults 18-69 years of age, with a recent first or new episode of mild/moderate depression (BDI score ≥14), who were not taking antidepressants at the time of assessment or had been prescribed antidepressants within 4 weeks of assessment but had had an antidepressant-free period of 4 weeks prior to that Pragmatic, multicentre RCT (N=361, excluded from clinical analysis due to high attrition rates) Source of efficacy and resource use data: RCT (at 12 months EQ-5D data n=195; complete resource use data n=156; multiple imputation used in sensitivity analysis) Source of unit costs: national sources	Costs: intervention (physical activity facilitator's time), primary care professionals' time (GP, practice nurse, phlebotomist, health visitor, district nurse, midwife, nurse practitioner, mental health worker, counsellor, community psychiatric nurse, physiotherapist), paramedic, A&E, outpatient care, walk-in centre, NHS Direct out-of-hours care, medication, productivity losses Mean total service cost per person: Physical activity £ 646; TAU £350 Difference: £296 (95%CI £202 to £390) Primary outcome measure: QALYs estimated using EQ-5D ratings (UK tariff) QALYs per person: Physical activity: 0.809; TAU 0.795 Difference 0.014 (95%CI -0.033 to 0.061)	Under NHS & PSS perspective: Using completers' data: ICER of physical activity vs. TAU: £20,834/QALY Probability of physical activity being cost-effective at £20,000 and £30,000/QALY: 0.49 and 0.57, respectively Using imputed data: ICER of physical activity vs. TAU £19,394/QALY Probability of physical activity being cost-effective at £20,000 and £30,000/QALY: 0.50 and 0.60, respectively	Perspective: NHS & PSS (and societal) Currency: GBP£ Cost year: 2009 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Q.3 Interventions for first-line treatment of adults with a new episode of more severe depression

Q.3.1 Psychological interventions – references to included studies

Psychoeducation

26. Horrell L, Goldsmith KA, Tylee AT, Schmidt UH, Murphy CL, Bonin EM, Beecham J, Kelly J, Raikundalia S, Brown JSL (2014) One-day cognitive-behavioural therapy self-confidence workshops for people with depression: Randomised controlled trial. British Journal of Psychiatry 204: 222-233.

Cognitive behavioural therapy (CBT)

27. Holman AJ, Serfaty MA, Leurent BE, King MB (2011) Cost-effectiveness of cognitive behaviour therapy versus talking and usual care for depressed older people in primary care. BMC health services research 11: 33.

28. Hollinghurst S, Peters TJ, Kaur S, Wiles N, Lewis G, Kessler D (2010) Cost-effectiveness of therapist-delivered online cognitive-behavioural therapy for depression: Randomised controlled trial. British Journal of Psychiatry 197: 297-304.

Behavioural activation

29. Ekers D, Godfrey C, Gilbody S, Parrott S, Richards DA, Hammond D, Hayes A (2011) Cost utility of behavioural activation delivered by the non-specialist. British Journal of Psychiatry 199(6): 510-1.

Counselling versus antidepressants

30. Miller P, Chilvers C, Dewey M, Fielding K, Gretton V, Palmer B, Weller D, Churchill R, Williams I, Bedi N, Duggan C, Lee A, Harrison G (2003) Counseling versus antidepressant therapy for the treatment of mild to moderate depression in primary care economic analysis. International Journal of Technology Assessment in Health Care 19: 80-90.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Horrell et al., 2014 UK Cost effectiveness and cost-	Interventions: Psychoeducational one-day self-confidence workshop Wait list	Adults with depression, as indicated by a BDI≥14 No exclusion criteria in relation to antidepressants or concurrent	Costs: intervention (venue, advertising, workshop materials, volunteer time, staff time including training, preparation, administration, delivering the intervention and volunteer time), medication, primary care, outpatient and inpatient care, specialist mental health and community-based services such as social work and alternative	Psychoeducation dominant in terms of BDI-II change scores and DFDs; Less costly and less effective in terms of QALYs; ICER of WL	Perspective: NHS (and societal) Currency: GBP£ Cost year: 2011 Time horizon: 12 weeks

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
utility analysis		psychological therapy Multicentre open RCT (N=459; completers n=382) (Horrell2014) Source of efficacy & resource use data: RCT; cost effectiveness analysis based on n=380; cost-utility analysis based on n=375 Source of unit costs: national sources and other published studies	therapy For societal perspective: productivity losses Mean total NHS cost per person (95% CI): Psychoeducation: £834, WL: £841 (-£286 to -£278) Outcome measures: Change in BID-II number of depression-free days (DFD) calculated based on BDI-II scores: a full DFD was assigned for BDI <10 and no DFD for BDI >28, with scores in between weighted proportionally QALY based on EQ-5D ratings (UK tariff) Mean change in BDI-II (SD): Psychoeducation: 9.47 (10.91); WL: 3.51 (8.32) Difference (95% CI): 5.96 (4.01 to 7.91) Additional depression-free days (SD): Psychoeducation: 28.85 (31.16); WL: 9.62 (24.99) Difference: 19.23 (13.56 to 24.90) QALYs gained (SD): Psychoeducation: 0.007 (0.06); WL: 0.010 (0.61) Difference: -0.003 (-0.01 to 0.012)	vs pychoeducation: £2,333/QALY Psychoeducation and WL had similar costs and QALYs Probability of psychoeducation being cost-effective: 0.30, 0.80 and 0.99 at WTP zero, £30 and £70 per BDI point improvement 0.90 at WTP £14 per DFD gained 0.50 at WTP of £19,500/QALY, max 0.56 irrespective of WTP per QALY gained	Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

1
2

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Holman et al., 2011 UK Cost	Interventions: Cognitive behavioural therapy (12	Older adults aged ≥ 65 years with depression (BDI ≥14) and, if on an antidepressant, a stable dose of medication for at least 8 weeks	Costs: intervention (CBT) and community health service costs (contacts with GP's, practice and district nurses, health visitors, psychiatrists, clinical	ICER of CBT vs. TAU £120 /additional point reduction	Perspective: health and social services (only primary and

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
effectiveness analysis	sessions) in addition to treatment as usual (CBT) Treatment as usual (TAU)	prior to randomization Single-blind RCT (Serfaty2009, N=204) Source of efficacy and resource use data: RCT (at 10 months n=198 for costs, n=167 for outcomes) Source of unit costs: national sources	psychologists, occupational therapists, physiotherapists, community psychiatric nurses and general counsellors); medication not considered but likely similar between groups; secondary care not considered Mean cost difference per person: £427 (95% CI: £56 to £787, p < 0.001) Primary outcome measure: BDI-II Mean BDI-II difference per person: 3.6 (95%CI: 0.7 to 6.5, p = 0.018)	in BDI-II Probability of CBT being cost-effective: 0.90 at a WTP of £270 /point reduction in BDI-II	community healthcare services considered) Currency: GBP£ Cost year: 2008 Time horizon: 10 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

1

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Hollinghurst et al., 2010 UK Cost effectiveness and cost-utility analysis	Interventions: Computerised CBT delivered online using real-time therapist interaction through written messaging comprising up to 10 55min sessions (CBT)	Adults aged 18-75 years who were identified in primary care as having a new episode of depression, defined by a BDI score ≥14 and an ICD–10 diagnosis of depression using the Revised Clinical Interview Schedule (CIS–R) RCT (Kessler2009,	Costs: intervention, staff time (GP, practice nurse, counsellor, health visitor, occupational health therapist, psychiatrist, phlebotomist, physiotherapist), walk-in centre, NHS Direct, A&E, inpatient and outpatient care, medication Personal expenses (private sector healthcare, over-the-counter drugs, social and domestic help, travel costs and out-of-pocket loss of earnings) and productivity losses considered in societal perspective	Complete data: ICER of CBT vs WL: £3,528/extra person recovering £17,173/QALY Probability of CBT being cost-effective: 0.56 and 0.71 at WTP £20,000 & £30,000/QALY, respectively Imputed missing data:	Perspective: NHS (and societal) Currency: GBP£ Cost year: 2007 Time horizon: 8 months Discounting: NA Applicability:

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	Waiting list (WL)	N=297) Source of efficacy and resource use data: RCT (BDI data available for n=210; QALYs available for n=165; NHS cost data available for n=137) Source of unit costs: national sources	Mean total NHS cost per person (SD): CBT: £764 (£380); WL: £295 (£359) Mean difference: £469 (95% CI £342 to £597) Outcome measures: BDI; recovery based on BDI score <10; QALYs estimated based on EQ-5D (UK tariff) Outcome results: BDI score: CBT 14.7 (11.6); WL 22.2 (15.2) Difference: -6.2 (-9.3 to -3.9) % of people recovered: CBT 42%, WL 26% Difference 16.5% (3.7% to 29.2%) QALYs: CBT 0.530 (0.099); WL 0.496 (0.126) Difference 0.034 (-0.001 to 0.069)	ICER of CBT vs WL: £10,083/QALY Probability of CBT being cost-effective: 0.94 and 0.98 at WTP £20,000 & £30,000/QALY, respectively	directly applicable Quality: potentially serious limitations

1

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Ekers *et al.*, 2011 UK Cost effectiveness and cost-utility analysis	Interventions: Behavioural activation (BA), delivered over 12 hourly sessions by 2 mental health nurses on post qualification pay bands with no previous formal therapy training; therapists	Adults with depression (confirmed by the revised Clinical Interview Schedule - CIS-R), on stable or no antidepressant medication for 6 weeks, attending general practice or primary care mental health services Pragmatic RCT (N=47; completers n=38) (Ekers2011)	Costs: intervention: therapist time, supervision & training costs spread over 3 years; 2 scenarios employed, based on 2 estimates of workload according to Improving Access to Psychological Therapy (IAPT) service specifications: 65 treatments/year in a depression-specific role (scenario A) or 33 treatments/year treating depression and anxiety (scenario B); primary (general & mental health) care, secondary (general & mental health) care, community and social services, medication Cost differences adjusted for baseline:	Scenario A ICER of BA vs. TAU • £9.45 per BDI-II point reduction • £5,006/QALY At a WTP of £20,000/QALY, probability of BA being cost-effective was 0.98 Scenario B ICER of BA vs. TAU • £11.04 per BDI-II point reduction	Perspective: NHS & PSS Currency: GBP£ Cost year: 2009 Time horizon: 3 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	received 5-day training and 1 hour clinical supervision fortnightly Treatment as usual (TAU) comprising GP care or primary care by mental health workers	<u>Source of efficacy & resource use data:</u> RCT, based on participants' primary care records and self-completed questionnaires <u>Source of unit costs:</u> national sources	Scenario A: £149 (95%CI -£56 to £355) Scenario B: £175 (95%CI -£31 to £380) Imputed, bias-corrected costs – scenario A: BA: £583 (95%CI £442 to £771) TAU: £413 (95%CI £279 to £560) Imputed, bias-corrected costs – scenario B: BA: £609 (95%CI £473 to £797) TAU: £413 (95%CI £284 to £587) <u>Outcome measure:</u> BDI score; QALY based on EQ-5D ratings (UK tariff) Mean change in BDI-II: -15.78 (95% CI -24.55 to -7.02) Mean bias-adjusted QALYs gained: BA: 0.05 (95%CI 0.04 to 0.07) TAU: 0.02 (95%CI 0.00 to 0.03)	• £5,756/QALY At a WTP of £20,000/QALY, probability of BA being cost-effective was 0.97	

1

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Miller et al., 2003 UK Cost effectiveness analysis	Interventions: Generic psychological therapy comprising 6 weekly 50-minute sessions (counselling) Routinely prescribed antidepressant drugs, comprising dothiepin (150 mg)	Adults aged 18-70 years who met diagnostic criteria for major depression (assessed by their GP). Exclusion criteria: psychosis, suicidal tendencies, postnatal depression, recent bereavement, drug or alcohol misuse RCT (Bedi2000, N=103); people refusing randomisation but agreeing to participate in the	Costs: intervention (counselling, medication), depression-related GP visits, psychiatric inpatient & outpatient care Mean cost (SD) per person: RCT Counselling: £302 (£38) AD: £344 (£62); p=0.777 Preference trial: Counselling: £336 (£25) AD: £263 (£34) p =0.005	RCT: ICER of AD vs. counselling £263/ extra person with a good global outcome Probability of counselling being cost-effective: 0.25 and 0.10 at a WTP of £500 and £2,000 per extra person with a good global outcome, respectively Sensitivity analysis:	Perspective: NHS (only depression-related costs considered) Currency: UK£ Cost year:1995 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: potentially

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	taken at night, fluoxetine (20 mg) taken once daily or lofepramine (140–210 mg) taken daily in divided doses, or a different drug if it was judged necessary by GP (AD)	patient preference trial were given the treatment of their choice (N=220) Source of efficacy data: RCT (at 12 months n=81) and preference trial (at 12 months n=163) Source of resource use data: RCT (at 12 months n=103) and preference trial (at 12 months n=215) Source of unit costs: national sources and local costs for counsellors	Primary outcome measure: global outcome, assessed by a psychiatrist blind to treatment allocation, using the research diagnostic criteria (RDC), BDI score and GP notes. The outcome was good if the person responded to treatment within 8 weeks and then remained well % of people with good global outcome: RCT Counselling: 25%, AD: 41%, p=0.196 Preference trial: Counselling: 36%, AD: 28%, p=0.191	assuming missing data were good: probability of counselling being cost-effective increases for any WTP; assuming missing data were poor: probability of counselling being cost-effective slightly increases for WTP<£1,500 and decreases for WTP >£1,500. Preference trial: ICER of counselling vs. AD £912/ extra person with a good global outcome	serious limitations

Update 2017

Q.3.21 Pharmacological interventions – references to included studies

SSRIs versus mirtazapine [versus duloxetine and venlafaxine XR that were not part of the guideline decision problem]

31. Benedict A, Arellano J, De Cock E, Baird J (2010) Economic evaluation of duloxetine versus serotonin selective reuptake inhibitors and venlafaxine XR in treating major depressive disorder in Scotland. Journal of Affective Disorders 120: 94-104.

Fluoxetine versus amitriptyline [versus venlafaxine XR that was not part of the guideline decision problem]

32. Lenox-Smith A, Greenstreet L, Burslem K, Knight C (2009) Cost effectiveness of venlafaxine compared with generic fluoxetine or generic amitriptyline in major depressive disorder in the UK. Clinical Drug Investigation 29: 173-184.

AND

Lenox-Smith A, Conway P, Knight C (2004) Cost effectiveness of representatives of three classes of antidepressants used in major depression in the UK. PharmacoEconomics 22: 311-319 (updated by Lenox et al. 2009)

Escitalopram versus citalopram [versus venlafaxine XR that was not part of the guideline decision problem]

33. Wade AG, Toumi I, Hemels MEH (2005) A probabilistic cost-effectiveness analysis of escitalopram, generic citalopram and venlafaxine as a first-line treatment of major depressive disorder in the UK. Current Medical Research and Opinion 21: 631-641.

34. Wade AG, Toumi I, Hemels MEH (2005) A pharmacoeconomic evaluation of escitalopram versus citalopram in the treatment of severe depression in the United Kingdom. Clinical Therapeutics 27: 486-496.

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Benedict et al., 2010 UK Cost-utility analysis	Interventions: SSRIs Mirtazapine (Duloxetine and venlafaxine also included but not considered here as they were not part of review question)	Adults with moderate to severe major depression defined by a HAMD17 score ≥19, having a new treatment episode in primary care Decision-analytic modelling Source of efficacy data: meta-analyses of clinical trials - randomisation likely broken Source of resource use data: expert opinion Source of unit costs: national sources	Costs: medication, A&E Visits, GPs, psychiatrists, hospitalisation Mean total cost per person: SSRIs £486 Mirtazapine £516 Outcome measure: QALY estimated based on EQ-5D ratings (UK tariff) Number of QALYs per person: SSRIs 0.656 Mirtazapine 0.654	SSRIs dominated mirtazapine PSA favouring duloxetine which is not part of the guideline decision problem Results sensitive to changes in efficacy (response / relapse) and utility values	Perspective: Scottish NHS Currency: UK£ Cost year: likely 2003 Time horizon: 48 weeks Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Lenox-Smith et al., 2009 UK Cost-utility analysis	Interventions: Fluoxetine Amitriptyline (Venlafaxine also included but not considered here as it was not part of review question)	Adult outpatients with major depression Decision-analytic modelling Source of efficacy data: pooled data from meta-analysis for fluoxetine versus amitriptyline; a single RCT for amitriptyline vs. venlafaxine; method of synthesis unclear, but most likely randomisation was broken Source of resource use data: Delphi panel Source of unit costs: national sources	Costs: medication, lab testing, clinical examinations, community psychiatric nursing, inpatient and outpatient services, staff time (GP, psychiatrist, psychologist), psychotherapy Mean total cost per person: Fluoxetine £1539 Amitriptyline £1558 Outcome measure: QALY estimated based on the presumed utilities of a depression-free day and a severely depressed day Mean QALY gains per person Fluoxetine 0.090 Amitriptyline 0.085	Fluoxetine dominates amitriptyline Results robust to changes in costs. Results sensitive to the value of the utility gain associated with a depression-free day	Perspective: NHS Currency: GBP£ Cost year: 2006 Time horizon: 24 weeks Discounting: NA Applicability: partially applicable Quality: very serious limitations

Update 2017

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Wade et al., 2005a (probabilistic …) UK Cost effectiveness analysis	Interventions: Escitalopram Citalopram (Venlafaxine XR included but not part of decision problem)	Adults with major depression with baseline MADRS score between 18-40 Decision-analytic modelling Source of efficacy data: meta-analysis of head-to-head RCTs	Costs: study medication, staff time (GP, psychiatrist, hospitalisation, community services, attempted suicide; sick leave Mean (range) total NHS cost per person: Escitalopram: £465 (£436-£493) Citalopram: £544 (£514-£573) Outcome measure: % of remission,	Escitalopram dominates citalopram Results robust under different scenarios (changes in rates of remission, relapse, discontinuation, unit costs)	Perspective: NHS (and societal) Currency: GBP£ Cost year: 2003 Time horizon: 26 weeks Discounting: NA Applicability:

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
		between escitalopram and citalopram; and between escitalopram and venlafaxine XR Source of resource use data: General Practice Research Database, published literature and expert opinion Source of unit costs: national sources	defined as MADRS score ≤ 12 % of remission: mean (range) Escitalopram: 63.5% (61.5%-65.4%) Citalopram: 58.2% (56.3%-60.3%)		partially applicable Quality: potentially serious limitations

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Wade et al., 2005b (severe depression) UK Cost effectiveness analysis	Interventions: Escitalopram Citalopram	Adults with major severe depression with baseline MADRS score ≥ 30 Decision-analytic modelling Source of efficacy data: published meta-analysis of RCTs Source of resource use data: published literature and expert opinion Source of unit costs: national sources	Costs: study medication, GP and psychiatrist visits, inpatient psychiatric hospitalizations, treatment discontinuation, treatment-emergent AEs, attempted suicide. Sick leave Mean (range) total NHS cost per person: Escitalopram: £422 (£404-£441) Citalopram £454 (£436-£471) Outcome measures: % of remission, defined as MADRS score ≤ 12, and % remission without switch % of remission: mean (range) Escitalopram: 53.7% (50.3%-57.5%) Citalopram: 48.7% (45.8%-51.7%) % of remission without switch: mean	Escitalopram dominates citalopram Results robust to changes in drug-specific probabilities and cost data PSA: Escitalopram was dominant in >99.8% of iterations	Perspective: NHS (and societal) Currency: GBP£ Cost year: 2003 Time horizon: 26 weeks Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
			(range) Escitalopram: 41.7% (37.5 %-46.3%) Citalopram: 30.8% (27.5%-34.6%)		

Update 2017

Q.3.3 Combined pharmacological and psychological interventions – references to included studies

CBT plus antidepressant (fluoxetine) versus antidepressant alone

35. Simon J, Pilling S, Burbeck R, Goldberg D (2006) Treatment options in moderate and severe depression: Decision analysis supporting a clinical guideline. British Journal of Psychiatry 189: 494-501.

36. Koeser L, Donisi V, Goldberg DP, McCrone P (2015) Modelling the cost-effectiveness of pharmacotherapy compared with cognitive-behavioural therapy and combination therapy for the treatment of moderate to severe depression in the UK. Psychological Medicine, 45(14), 3019-31.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Simon et al., 2006 UK Cost effectiveness and cost-utility analysis	Interventions: Combination therapy comprising 16 sessions of CBT lasting 50min each and antidepressant therapy (Combo) Antidepressant therapy alone, comprising fluoxetine 40mg daily for 3 months and standard outpatient care (AD)	Adults with moderate depression and adults with severe depression Decision-analytic modelling (decision tree) Source of efficacy data: systematic literature review & meta-analysis of RCTs Source of resource use data: published literature and expert opinion Source of unit costs: national sources	Costs: intervention (clinical psychologist's time for CBT, antidepressant medication, dispensing fee, outpatient care with consultant psychiatrist or specialist registrar), subsequent depression treatment over 12months Mean total cost per person: Combo £1,297; AD £660; difference £637 Outcome measures: Probability of successful treatment (remission and no relapse over 12 months) with remission defined as HRSD-17 ≤ 6 or HRSD-24 ≤ 8 QALYs estimated based on vignettes valued by service users using SG Outcome results: Probability of successful treatment: Combo 0.29; AD 0.14; difference 0.16 QALYs per person with severe depression: Combo 0.63; AD: 0.52; difference 0.11 QALYs per person with moderate depression Combo 0.89; AD 0.84; difference 0.04	ICER of Combo vs AD: £4,056 per additional successfully treated person (95% CI £1,400 to £18,300) Moderate depression: £14,540/QALY (95%CI £4,800 to £79,400/QALY) Probability of Combo being cost-effective at WTP £30,000/QALY 0.88 Severe depression: £5,777/QALY (95% CI £1,900 to £33,800/QALY) Probability of Combo being cost-effective at WTP £30,000/QALY 0.97 Results sensitive to changes in relative efficacy (in terms of	Perspective: NHS Currency: GBP£ Cost year: 2003 Time horizon: 15 months Discounting: NA Applicability: partially applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
				remission, relapse)	

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Koeser et al., 2015 UK Cost-utility analysis	Interventions: Antidepressant therapy alone, comprising citalopram 20mg daily for 15 months and standard outpatient care (AD) Cognitive Behavioural Therapy (CBT) comprising 16 acute + 2 booster sessions for responders, each lasting 50 min Combination therapy comprising CBT and AD treatment (Combo)	Adults with moderate or severe major depression Decision-analytic modelling (decision tree) Source of efficacy data: systematic screening of database containing RCTs that compare psychological treatments (single or combined) for adults with depression with a control intervention; NMA Source of resource use data: published literature that reported expert opinion and analysis of RCT data Source of unit costs: national sources	Costs: intervention (clinical psychologist's time for CBT, antidepressant medication, dispensing fee, outpatient care with consultant psychiatrist or specialist registrar), service use associated with remission, response, no response Mean total cost per person: AD: £3,645 CBT: £4,418 Combo: £5,060 Outcome measures: QALYs estimated based on EQ-5D (UK tariff) Mean total QALYs per person: AD: 1.236 CBT: 1.274 Combo: 1.274	Combo dominated by CBT ICER of CBT vs AD: £20,039/QALY Probability of being best at WTP £25,000/QALY: CBT: 0.43 AD: 0.37 Combo: 0.20 Results sensitive to changes in inclusion criteria for RCTs for acute and follow-up treatment and to use of SF-6D values	Perspective: NHS Currency: GBP£ Cost year: 2012 Time horizon: 27 months Discounting: 3.5% annually Applicability: directly applicable Quality: minor limitations

Update 2017

Q.3.43 Physical interventions – references to included studies

ECT versus SSRIs, SNRIs, or SSRIs & lithium

37. Greenhalgh J, Knight C, Hind D, Beverley C, Walters S (2005) Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: Systematic reviews and economic modelling studies. Health Technology Assessment 9(9).

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Greenhalgh et al., 2005 UK Cost-utility analysis	Interventions: Electroconvulsive therapy (ECT), TCAs, SSRIs, SNRIs and lithium augmentation (Li) combined in 8 strategies of 3 lines of therapy plus maintenance therapy of SSRI unless otherwise specified: 1. SNRI, SSRI, Li 2. ECT, SSRI, Li; ECT maintenance in ECT 3. ECT, SSRI, Li; Lithium & TCA maintenance in ECT 4. SNRI, ECT, Li; Lithium & TCA maintenance in ECT 5. ECT, SSRI, Li 6. SNRI, SSRI, ECT; Lithium & TCA maintenance in ECT 7. SNRI, ECT, Li; ECT maintenance in ECT	Adults with major depressive disorder who require hospitalisation Decision-analytic modelling (decision tree) Source of efficacy data: systematic literature review of RCTs and published meta-analyses, and further assumptions Source of resource use data: published literature and expert opinion Source of unit costs: national sources	Costs: intervention (ECT, medication, hospitalisation), continued care for non-responders (nursing home placement with psychiatric provision), maintenance treatment (laboratory testing, contacts with GP, psychiatrist and psychiatric nurse) Mean total cost per person (95% CI): Strategy 1. £11,400 (£9,349 to £13,718) Strategy 2. £15,354 (£13,445 to £17,361) Strategy 3. £10,997 (£9,080 to £13,045) Strategy 4. £10,592 (£8,874 to £12,435) Strategy 5. £11,022 (£9,016 to £13,069) Strategy 6. £13,939 (£11,161 to £17,049) Strategy 7. £12,591 (£10,678 to £14,497) Strategy 8. £14,548 (£11,680 to £17,717) Primary outcome measure: QALYs estimated based on preferences for vignettes using the McSad health state classification system valued by service users with previous depression in Canada using SG	Strategies 1, 2, 3, 6, 7, and 8 dominated ICER of Strategy 5 vs. strategy 4: £6,232/QALY Results modestly sensitive to use of alternative utility values; results robust to small changes in costs and suicide rates	Perspective: NHS Currency: GBP£ Cost year: 2001 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	8. SNRI, SSRI, ECT; ECT maintenance in ECT		Mean total QALYs per person (95% CI): Strategy 1. 0.490 (0.453 to 0.526) Strategy 2. 0.458 (0.422 to 0.493) Strategy 3. 0.424 (0.389 to 0.459) Strategy 4. 0.470 (0.431 to 0.508) Strategy 5. 0.539 (0.498 to 0.579) Strategy 6. 0.489 (0.452 to 0.524) Strategy 7. 0.486 (0.449 to 0.522) Strategy 8. 0.494 (0.459 to 0.529)		

Q.4 Interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

Update 2017

Q.4.1 Psychological interventions – references to included studies

Cognitive behavioural therapy (CBT) as an adjunct to pharmacotherapy

38. Scott J, Palmer S, Paykel E, Teasdale J, Hayhurst H (2003) Use of cognitive therapy for relapse prevention in chronic depression: Cost-effectiveness study. British Journal of Psychiatry 182: 221-227.

39. Hollinghurst S, Carroll FE, Abel A, Campbell J, Garland A, Jerrom B, Kessler D, Kuyken W, Morrison J, Ridgway N, Thomas L, Turner K, Williams C, Peters TJ, Lewis G, Wiles N (2014) Cost-effectiveness of cognitive-behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: Economic evaluation of the CoBalT Trial. British Journal of Psychiatry 204: 69-76.

AND

Wiles N, Thomas L, Abel A, Barnes M, Carroll F, Ridgway N, Sherlock S, Turner N, Button K, Odondi L, Metcalfe C, Owen-Smith A, Campbell J, Garland A, Hollinghurst S, Jerrom B, Kessler D, Kuyken W, Morrison J, Turner K, Williams C, Peters T, Lewis G (2014) Clinical effectiveness and cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: The CoBalT randomised controlled trial. Health Technology Assessment 18(31).

AND

Wiles NJ, Thomas L, Turner N, Garfield K, Kounali D, Campbell J, Kessler D, Kuyken W, Lewis G, Morrison J, Williams C, Peters TJ, Hollinghurst S (2016) Long-term effectiveness and cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: follow-up of the CoBalT randomised controlled trial. Lancet Psychiatry, 3(2), 137-44.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Scott et al., 2003 UK Cost effectiveness analysis	Interventions: Cognitive therapy (16 sessions in 20 weeks plus 2 booster sessions) in addition to antidepressants (minimum dose equivalent to ≥ 125mg of amitryptiline) and clinical management (30-min appointments with a psychiatrist every 4 weeks during 20 weeks and every 8 weeks during the 48-week follow-up) (CT & AD) Antidepressants and clinical management alone (AD)	Outpatients 21-65 years that met DSM-III-R criteria for major depression, who were in an episode within the past 18 months but not in the past 2 months. At randomisation they had residual symptoms over at least 8 weeks with HAMD ≥ 8 and BDI ≥ 9. Exclusion criteria: past history of bipolar disorder; current history of significant Axis I or II comorbidity; currently receiving formal psychotherapy; having previously received CT for > 5 sessions. RCT Source of efficacy data: RCT (Paykel1999); (N=158) Source of resource use data: RCT (full data for 65% of participants) Source of unit costs: national & local inpatient cost data	Costs: CT, medication, clinical management, inpatient care, day hospital, GP, social worker, community psychiatric nurse, therapist/counsellor, group therapy, marital therapy. Mean cost per person: CT & AD: £1898 AD: £1119 Cost difference: £779 (95% CI £387 to £1170) Primary outcome measure: percentage of relapses Cumulative relapse rates: CT & AD: 29% AD: 47% Adjusted HR 0.51 (95% CI 0.32-0.93)	ICER of CT & AD vs AD: £4328 per relapse prevented £4667 using mean imputation £5028 using non-parametric multiple imputation £7056 using only the 65% of subjects in the complete case analysis Probability of CT & AD being cost-effective 0.60 and 0.80 at WTP of £6000 and £8500 per relapse prevented, respectively Probability sensitive to method of missing data imputation	Perspective: NHS/PSS Currency: GBP£ Cost year: 1999 Time horizon: 17 months Discounting: 6% Applicability: partially applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Hollinghurst et al., 2014; Wiles et al., 2016 UK Cost consequence and cost-utility analysis	Interventions: Cognitive behavioural therapy comprising 12-18 sessions lasting about an hour each, taking place at a GP surgery or a similar location, in addition to treatment as usual (CBT) Treatment as usual alone, comprising GP care, including antidepressant treatment as judged appropriate by the person's GP or a referral as required (TAU)	Adults aged 18-75 years with major depression, who had adhered to antidepressant medication for at least 6 weeks in primary care, but who continued to have significant depressive symptoms; people had a BDI-II score of at least 14 or more and an ICD-10 diagnosis of depression using the Revised Clinical Interview Schedule (CIS-R) RCT (Wiles2013, N=469) Source of efficacy data and resource use data: RCT (NHS and PSS cost and QALY data available for n=368 at 12 months; follow-up data available for n= 248) Source of unit costs: national sources	Costs: medication, primary and community mental and general health care, specialist (secondary) mental health care, personal out-of-pocket expenditure such as travel costs, use of private therapies and over-the-counter medications; productivity losses AT 12 MONTHS Mean total cost per person (SD): NHS/PSS cost: CBT £1614 (£1100); TAU £763 (£697); difference: £850 (95%CI £683 to £1017) Personal expenditure: CBT £80 (£12), TAU £127 (£35); difference -£47 (95%CI -£120 to £25) Out-of-pocket expenses: CBT £694 (£4,824), TAU £517 (£2,464); difference £176 (95%CI -£662 to £1014) Lost productivity: CBT £1,067 (£3,887), TAU £1,102 (£3,529); difference -£36 (95%CI -£797 to £726) AT 3-5 YEARS Mean annual NHS/PSS cost (SD): CBT £885 (£938); TAU £604 (£904); difference: £281 (95%CI £32 to £531) Outcome measures: response (reduction of at least 50% in BDI-II score); BDI-II score; remission (BDI-II <10; SF-12 mental and physical subscales; EQ-5D; QALYs estimated using EQ-5D & SF-6D ratings (latter in sensitivity analysis) (UK tariff) AT 12 MONTHS Response: CBT 55.3%, TAU %31.3; OR 2.89 (95%CI 2.03 to 4.10) BDI-II score (mean, SD): CBT 17.0 (14.0), TAU 21.7 (12.9); difference -5.1 (-7.1 to -3.1) Remission: CBT 39.6%, TAU 18.2%; OR 2.74	AT 12 MONTHS ICER of CBT vs. TAU £14,911/QALY Probability of CBT being cost-effective 0.74 and 0.91 at WTP of £20,000/QALY and £30,000/QALY, respectively Results robust to changes in psychologist unit costs and exclusion of hospitalisation costs. Results sensitive to use of SF-6D instead of EQ-5D, with ICER rising at £29,626/QALY Analysis of completers' data (instead of imputation of missing data): ICER £18,361/QALY AT 3-5 YEARS ICER of CBT vs. TAU £5,374/QALY Probability of CBT being cost-effective at a WTP of	Perspective: NHS/PSS for cost-utility analysis; health and social care provider for cost consequence analysis, with service user expenses and productivity losses assessed in additional analyses Currency: GBP£ Cost year: 2010 for endpoint data; 2013 for follow-up data Time horizon: 12 months; follow-up analysis 3-5 years (median 45.5 months, interquartile range 42.5 to 51.1) Discounting: 3.5% annually Applicability: directly applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
			(95%CI 1.82 to 4.13) SF-12 mental sub-scale (mean, SD): CBT 39.1 (14.6), TAU 35.4 (12.8); difference 4.8 (2.7 to 6.9) SF-12 physical sub-scale (mean, SD): CBT 44.6 (13.2), TAU 41.1 (13.5); difference -0.7 (95%CI -2.1 to 0.8) QALYs: CBT 0.62 (0.22), TAU 0.56 (0.25); difference 0.053 (95%CI 0.019 to 0.087) AT 3-5 YEARS Response: CBT 43%, TAU 27%; OR 2.09 (95%CI 1.19 to 3.67) BDI-II score (mean, SD): CBT 19.2 (13.8), TAU 23.4 (13.2); difference -3.6 (-6.6 to -0.6) Remission: CBT 28%, TAU 18%; OR 1.77 (95%CI 0.93 to 3.39) SF-12 mental sub-scale (mean, SD): CBT 38.7 (12.1), TAU 34.6 (11.8); difference 3.5 (0.7 to 6.3) SF-12 physical sub-scale (mean, SD): CBT 42.2 (13.8), TAU 39.2 (13.5); difference 0.9 (95%CI -0.2 to 3.8) Mean annual QALYs: CBT 0.60 (0.17), TAU 0.54 (0.20); difference 0.052 (95%CI 0.003 to 0.102)	£20,000/QALY and £30,000/QALY: 0.92 and 0.95, respectively	

Update 2017

Q.4.21 Pharmacological interventions – references to included studies

Continuation of current treatment (citalopram) versus switching to another antidepressant (venlafaxine, sertraline) or augmentation with bupropion

40. Olgiati P, Bajo E, Bigelli M, Montgomery S, Serretti A, group CEAP (2013) Challenging sequential approach to treatment resistant depression: cost-utility analysis based on the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial. European Neuropsychopharmacology 23: 1739-1746.

Escitalopram versus duloxetine and venlafaxine

41. Nordstrom G, Despiegel N, Marteau F, Danchenko N, Maman K (2010) Cost effectiveness of escitalopram versus SNRIs in second-step treatment of major depressive disorder in Sweden. Journal of Medical Economics 13: 516-526.

Duloxetine versus venlafaxine XR and mirtazapine

42. Benedict A, Arellano J, De Cock E, Baird J (2010) Economic evaluation of duloxetine versus serotonin selective reuptake inhibitors and venlafaxine XR in treating major depressive disorder in Scotland. Journal of Affective Disorders 120: 94-104.

Various antidepressants (generic SSRIs including citalopram, fluoxetine and paroxetine, escitalopram, paroxetine controlled release, sertraline, and venlafaxine extended release)

43. Malone DC (2007) A budget-impact and cost-effectiveness model for second-line treatment of major depression. Journal of Managed Care Pharmacy 13: S8-S18.

Augmentation with lithium or atypical antipsychotics (including combination of olanzapine / fluoxetine)

44. Edwards S, Hamilton V, Nherera L, Trevor N (2013) Lithium or an atypical antipsychotic drug in the management of treatment resistant depression: a systematic review and economic evaluation. Health Technology Assessment 17(54).

45. Taneja C, Papakostas GI, Jing Y, Baker RA, Forbes RA, Oster G (2012) Cost-effectiveness of adjunctive therapy with atypical antipsychotics for acute treatment of major depressive disorder. Annals of Pharmacotherapy 46: 642-649.

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Olgiati et al., 2013 US Cost-utility analysis	Interventions: Different strategies for non-remitters: A. Continuation of current treatment (citalopram) for 13 weeks B. Choice to: a. switch to sertraline or venlafaxine for 13 weeks or b. augment with bupropion for 13 weeks Remitters (HAMD17<7) continued treatment with citalopram for another 13 weeks	Adult outpatients with chronic depression, with a HAMD17 ≥ 14, who were treated with citalopram for 13 weeks and received 2nd line treatment following no remission; exclusion criteria: indications for hospital treatment such as psychotic symptoms, suicidal risk or inpatient detoxification for alcohol / substance dependence; obsessive compulsive disorder, eating disorder Decision-analytic modelling Source of efficacy data: data for A taken from RCT (Wade2006); data for B taken from a study comprising series of RCTs (Rush2006/STAR*D), thus breaking randomisation rules Source of resource use data: expert opinion Source of unit costs: national sources	Costs: medication, primary care, outpatient visits, community mental health services Mean total cost per person: Strategy A: $724 Strategy B: $800 Strategy Ba: $809 Strategy Bb: $849 Outcome measure: QALY estimated based on service Canadian/US users' preferences for vignettes Incremental number of QALYs per person: Strategy B versus strategy A: 0.007 Strategy Ba versus strategy A: 0.006 Strategy Bb versus strategy A: 0.008	ICER of strategy B versus strategy A: Deterministic analysis: $11,481/QALY Probabilistic analysis: $10,665/QALY (95%CI: $6,498 to $14,832) ICER of strategy Ba versus strategy A: $14,738/QALY ICER of strategy Bb versus strategy A: $15,458/QALY Results robust to changes in utility scores and the probability of remission after 3 months of citalopram (strategy A)	Perspective: 3rd party payer Currency: US$ Cost year: 2011 Time horizon: 26 weeks Discounting: NA Applicability: partially applicable Quality: very serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Nordström et al., 2010 Sweden Cost effectiveness and cost-utility analysis	Interventions: Escitalopram Duloxetine Venlafaxine extended release (XR)	Adults with major depression who initiated treatment with one of the assessed interventions in primary care, who had had a history of treatment with another antidepressant within the previous 6 months Decision-analytic modelling Source of efficacy data: pooled analysis of trial data, including only participants who had already received antidepressant therapy prior to randomisation – data for duloxetine and venlafaxine pooled together Source of resource use data: cohort study conducted in 56 primary care centres in Sweden over 6 months Source of unit costs: national sources	Costs: medication, staff time (GP, psychiatrist, other doctors e.g. neurologist, cardiologist, psychotherapist, counsellor, psychologist, nurse), hospitalisation, treatment of side effects, indirect costs (sick leave) Mean total healthcare cost per person: Escitalopram €973 Duloxetine €990 Venlafaxine €1,014 Outcome measures: probability of remission (defined as a MADRS total score ≤ 12) achieved after 8 weeks of treatment and sustained until the end of 6 months; QALY estimated based on EQ-5D ratings (UK tariff) Probability of remission: Escitalopram: 50.1% Duloxetine: 33.6% Venlafaxine: 33.6% Mean QALYs per person: Escitalopram 0.322 Duloxetine 0.297 Venlafaxine 0.298	Escitalopram dominant over duloxetine and venlafaxine Considering healthcare costs only: probability of escitalopram being cost-effective at WTP £20,000/QALY (€22,080/QALY) 0.981 and 0.985 compared with duloxetine and venlafaxine, respectively Results robust to changes in remission rates, relapse rates, number of GP visits, or incidence of nausea	Perspective: societal; healthcare costs reported separately Currency: Euros(€) Cost year: 2009 Time horizon: 6 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Benedict et al., 2010 UK Cost-utility analysis	Interventions: Duloxetine Venlafaxine XR Mirtazapine	Adults with severe major depression defined by a HAMD17 score ≥25, who failed previous SSRI treatment and were referred to mental health specialists in secondary care Decision-analytic modelling Source of efficacy data: meta-analyses of clinical trials - randomisation possibly broken Source of resource use data: expert opinion Source of unit costs: national sources	Costs: medication, A&E Visits, GPs, psychiatrists, hospitalisation Mean total cost per person: Duloxetine £1,622 Venlafaxine XR £1,667 Mirtazapine £1,640 Outcome measure: QALY estimated based on EQ-5D ratings (UK tariff) Number of QALYs per person: Duloxetine 0.637 Venlafaxine XR 0.632 Mirtazapine 0.629	Duloxetine dominates venlafaxine XR and mirtazapine Probability of duloxetine being cost-effective at WTP £20,000/QALY: approximately 0.80 Results robust to sensitivity analysis	Perspective: Scottish NHS Currency: GBP£ Cost year: likely 2003 Time horizon: 48 weeks Discounting: NA Applicability: directly applicable Quality: potentially serious limitations

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Malone, 2007 US Cost effectiveness analysis	Interventions: Generic SSRIs (citalopram, fluoxetine, paroxetine, weighted according to market share) Escitalopram Paroxetine controlled release [CR]	Adults with major depression who failed to achieve remission with SSRIs Decision-analytic modelling Source of efficacy data: review of published trial data and further assumptions – synthesis by naïve addition of data (leading to breaking of randomisation) Source of resource use data:	Costs: medication, physician visits, laboratory tests, inpatient mental health care Mean total healthcare cost per person: Generic SSRIs $3,095 Escitalopram $3,127 Paroxetine CR $3,206 Sertraline $3,178 Venlafaxine $3,172	Paroxetine CR and sertraline dominated by other options ICER of venlafaxine XR vs. generic SSRIs $2,073 per person achieving remission ICER of escitalopram vs. generic SSRIs $3,566 / additional person remitting [extendedly	Perspective: 3rd party payer Currency: US$ Cost year: not reported, likely 2005 Time horizon: 6 months Discounting: NA Applicability: partially applicable

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	Sertraline Venlafaxine extended release [XR]	analysis of 1,814 persons enrolled in 10 antidepressant studies Source of unit costs: medication costs from national sources; other unit costs taken from other studies, unclear whether these were national or local	Outcome measure: probability of remission (defined as a HDRS score ≤ 7 or a MADRS total score ≤ 10) Probability of remission: Generic SSRIs 18.5% (weighted average) Escitalopram 19.4% Paroxetine CR 17.7% Sertraline 19.5% Venlafaxine XR 22.2%	dominated] Results of sensitivity analysis reported using primarily each intervention's CER and not ICERs.	Quality: very serious limitations

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Edwards et al., 2013 UK Cost-utility analysis	Interventions: An atypical antipsychotic drug (AAP) as an adjunct to an SSRI Lithium as an adjunct to an SSRI	Adults with treatment-resistant depression (TRD) defined as failure to respond to at least 2 previous antidepressants in the current episode of depression Decision-analytic modelling Source of efficacy data: systematic review and indirect comparison using 6 RCTs comparing olanzapine + fluoxetine vs. fluoxetine alone in people with TRD and 1 RCT comparing lithium + fluoxetine vs. fluoxetine alone in people who had failed at least one antidepressant; a common class effect was assumed for the SSRIs and the AAPs. Data on lithium taken from population that had failed to respond to 1 previous SSRI (so not a TRD population)	Costs: medication (weighted costs according to expert opinion; it was estimated that AAP comprises 30% aripiprazole, 30% olanzapine, 20% quetiapine, and 20% risperidone; and an SSRI comprises 20% citalopram, 20% escitalopram, 30% fluoxetine, and 30% sertraline), healthcare professional time (GP, CMHT, CRHTT), hospitalisation and monitoring (laboratory testing) Mean total cost per person: AAP £5,644; Lithium £4,739 Outcome measure: QALYs estimated using EQ-5D	Augmentation with lithium dominates augmentation with AAP Probability of lithium being dominant 1 Results sensitive to efficacy of augmentation strategies and discontinuation rates; robust under different assumptions regarding resource use, as well as under changes in remission and relapse risk at follow-up	Perspective: NHS/PSS Currency: GBP£ Cost year: 2011 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations Other comments: a fixed baseline MADRS score was assumed; change in MADRS scores at endpoint

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
		Source of resource use data: mainly clinical expert opinion, length of hospitalisation taken from national hospital episode statistics Source of unit costs: national sources	ratings (UK tariff) Mean QALYs per person: AAP 1.225; Lithium 1.253		assumed to have a normal distribution in order to estimate proportions of people in response, no response, and remission states

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Taneja et al., 2012 US Cost effectiveness analysis	Interventions: Aripiprazole 2-20 mg /day and antidepressant therapy (ARI) Quetiapine 150 mg /day or 300 mg /day and antidepressant therapy (QUE) Fixed-dose combination of olanzapine 6, 12, or 18 mg /day with fluoxetine 50 mg /day (OLZ/FLUO) Antidepressant therapy alone (AD)	Adults with major depression who responded inadequately to previous antidepressant therapy Decision-analytic modelling Source of efficacy data: meta-analysis of published phase III clinical trials and indirect comparison using placebo as baseline comparator Source of resource use data: administrative databases and assumptions Source of unit costs: national sources	Costs: medication, outpatient care for depression, treatment of adverse events Mean total healthcare cost per person: ARI $847 QUE 150 mg/day $541 QUE 300 mg/day $672 OLZ/FLUO $791 AD $192 Outcome measure: probability of response (defined as at least 50% reduction in MADRS total score) Probability of response: ARI 49% QUE 150 mg/day 34% QUE 300 mg/day 38% OLZ/FLUO 45% AD 30%	QUE 150 & 300 mg/day and OLZ/FLUO extendedly dominated ICER of ARI vs. AD $3,447 per person responding Results sensitive to changes in relative effectiveness	Perspective: healthcare system Currency: US$ Cost year: 2011 Time horizon: 6 weeks Discounting: NA Applicability: partially applicable Quality: very serious limitations

Update 2017

Q.5 Interventions aimed at preventing relapse in people whose depression has responded to treatment

Q.5.1 Psychological interventions – references to included studies

46. Kuyken W, Byford S, Taylor RS, Watkins E, Holden E, White K, et al (2008) Mindfulness-Based Cognitive Therapy to Prevent Relapse in Recurrent Depression. Journal of Consulting and Clinical Psychology 76: 966-978.

47. Kuyken W, Hayes R, Barrett B, Byng R, Dalgleish T, Kessler D, et al (2015) Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. Lancet 386: 63-73.

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Kuyken et al., 2008 UK Cost effectiveness analysis	Interventions: Mindfulness - based cognitive therapy with support to taper or discontinue antidepressant treatment, comprising 8 x 2 hour group sessions over consecutive weeks, with 4 follow-up sessions in the following year (MBCT-TS) Maintenance antidepressant treatment plus medication adherence	Adults with ≥ 3 previous major depressive episodes, on a therapeutic dose of maintenance antidepressants over the last 6 months, and currently either in full or partial remission from the most recent episode. Exclusion criteria: organic brain damage, comorbid diagnoses of current substance dependence, current/past psychosis, bipolar disorder, persistent antisocial behaviour, persistent self -injury requiring clinical management/therapy, unable to engage with MBCT for physical, practical, or other reasons, formal concurrent psychotherapy Pragmatic single-blind parallel 2-group RCT Source of efficacy data: RCT (Kuyken2008); (N=123,	Costs: MBCT-TS, medication, hospital (inpatient, outpatient, emergency department) and community health and social services (e.g., primary care, social work, complementary therapies), plus productivity losses. Mean NHS/PSS cost per person: MCBT-TS: $2076, AD: $1577 Mean societal cost per person (SD): MCBT-TS: $3373 ($4002), AD: $2915 ($4838); difference $457 (95%CI -$1130 to $2043, p=0.87) Primary outcome measure: time to and % of relapse/recurrence Secondary outcomes: severity/duration of relapses/recurrences, severity of residual depressive symptoms, number of comorbid psychiatric diagnoses, quality of life using the WHO Quality of Life instrument (WHOQOL-BREF). Percentage of people relapsing:	ICER of MCBT-TS vs AD: $439/additional relapse or recurrence prevented and $23/depression-free day (NHS/PSS perspective) $962 /additional relapse or recurrence prevented and $50 /depression-free day (societal perspective) Probability of MBCT-TS being cost-effective at zero willingness to pay for preventing an additional relapse /recurrence: 0.42;	Perspective: NHS/PSS (and societal) Currency: international $ Cost year: 2006 Time horizon: 15 months Discounting: NA Applicability: partially applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	monitoring (AD)	completers n=115) Source of resource use data: RCT (N=123, completers=115) Source of unit costs: national sources	MBCT-TS: 47%; ADs: 60% Hazard ratio 0.63 (95%CI 0.39 to 1.04, p=0.07) Difference in secondary outcomes: MBCT-TS more effective than AD in reducing residual depressive symptoms and psychiatric comorbidity and in improving quality of life in the physical and psychological domains.	probability of MBCT-TS exceeds 0.50 at willingness to pay ≥ $1,000 per relapse / recurrence averted (societal perspective)	

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Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
Kuyken et al., 2015 UK Cost effectiveness and cost-utility analysis	Interventions: Mindfulness - based cognitive therapy with support to taper or discontinue antidepressant treatment, comprising 8 x 2.25 hour group sessions, normally over consecutive weeks, with 4 refresher sessions offered roughly every 3 months for the following year	Adults with ≥ 3 previous major depressive episodes, in full or partial remission from their most recent episode, and on a therapeutic dose of maintenance antidepressants Exclusion criteria: current major depressive episode, comorbid diagnoses of current substance misuse, organic brain damage, current or past psychosis including bipolar disorder, persistent antisocial behaviour, persistent self-injury needing clinical	Costs: MBCT-TS, medication, inpatient & outpatient care, A&E, ambulance, staff time (GP, practice nurse, district nurse, health visitor, community psychiatric nurse, midwife, community psychiatrist, clinical psychologist, occupational therapist, physiotherapist, counselling, art/drama/music therapist, chiropodist, dietician, social worker, support worker), advice service, day centre Plus out-of-pocket expenses and productivity losses Mean health and social care cost per person (SD): MCBT-TS: £2485 (£4077), AD: £2360 (£4206); difference £124 (95%CI -£750 to £973, p=0.80). Mean societal cost per person (SD): MCBT-TS: £3204 (£4012), AD: £2755 (£4465); difference £449 (95%CI -£842 to £1286, p=0.68) Primary outcome measure: time to and % of relapse/recurrence Secondary outcomes: depression-free days	Using primary outcome: ICER of MCBT-TS vs AD: £4,955 (NHS/PSS perspective) or £10,604 (societal perspective) per additional relapse or recurrence averted Using QALYs, MBCT-TS is dominated by AD Using any of the outcomes, the probability of	Perspective: NHS/PSS (and societal) Currency: GBP£ Cost year: 2012 Time horizon: 2 years Discounting: 3.5% Applicability: directly applicable Quality: minor limitations

Update 2017

Study Country Study type	Intervention details	Study population Study design Data sources	Costs and outcomes: description and values	Results: Cost-effectiveness	Comments
	(MBCT-TS) Maintenance antidepressant treatment plus GP support in maintaining a therapeutic level of medication over 2 years (AD)	management or therapy, formal concurrent psychotherapy. Pragmatic single-blind parallel 2-group RCT Source of efficacy data: RCT (Kuyken2015); (N=424, completers=366) Source of resource use data: RCT (N=424, completers=248) Source of unit costs: national sources	recorded by the depression module of the Structured Clinical Interview for DSM–IV (SCID), residual depressive symptoms assessed by the GRID-HAMD and the BDI, psychiatric and medical comorbidity using the relevant SCID modules and the Medical Symptom Checklist (MSCL), respectively, quality of life using the WHO Quality of Life instrument (WHOQOL-BREF) and the EQ-5D-3L (used to estimate QALYs) Percentage of people relapsing: MBCT-TS: 44%; ADs: 47% Hazard ratio 0.89 (95%CI 0.67 to 1.18, p=0.43) Difference in secondary outcomes: no statistically significant differences QALYs: MBCT-TS: 1.49; ADs: 1.53	MBCT-TS being cost-effective did not exceed 0.49 (NHS/PSS perspective) or 0.52 (societal perspective)	

Update 2017

Appendix R: Health economic profiles

R.1 Service delivery models for adults with depression

R.1.1 Collaborative care

Table 1: Clinical / economic question: simple collaborative care in addition to TAU versus TAU for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Bosanquet et al., 2017 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcome: QALY	£490	0.019	£26,535	Probability of intervention being cost-effective: 0.39 and 0.55 at WTP £20,404 and £30,606/QALY, respectively. Including only participants who engaged with 5 or more sessions in the analysis, ICER fell at £10,075/QALY
Green et al., 2014 UK	Minor limitations[4]	Directly applicable[5]	Outcome: QALY	£287	0.019	£15,092	Probability of intervention being cost-effective: 0.58 and 0.65 at WTP £21,185 and £31,778/QALY, respectively Results robust to multiple imputation of missing data, use of SF-6D utility values, use of alternative intervention costs
Lewis et al., 2017 UK	Potentially serious limitations[6]	Directly applicable[7]	Outcome: QALY	£429	0.044	£9,827	Probability of intervention being cost-effective: 0.92 and 0.97 at WTP £20,404 and £30,606/QALY, respectively. Accounting for the true observed intervention contact rate (rather than the expected that was used in the base-case analysis), ICER fell at £3,395/QALY

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis conducted alongside RCT (N=485; at 18 months n=344; cost data available for n=447); national unit costs used; statistical analyses conducted; CEACs presented; consideration of intervention and primary care costs only
3. UK study; NHS & PSS perspective; QALY estimates based on SF-6D (UK tariff)

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**

4. Time horizon 12 months; analysis conducted alongside RCT (N=581; data available for cost analysis n=447); national unit costs used; statistical analyses conducted; CEACs presented.
5. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)
6. Time horizon 12 months; analysis conducted alongside RCT (N=705; complete data used in base-case economic analysis n=448); national unit costs used; statistical analyses conducted; CEACs presented; high attrition that was markedly greater in the collaborative care arm; consideration of intervention and primary care costs only
7. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)

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2 **Table 2: Clinical / economic question: simple collaborative care versus TAU aiming at preventing relapse in adults with depression**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Simon et al., 2002 US	Potentially serious limitations[2]	Partially applicable[3]	Outcome: number of depression-free days (days with a Hopkins Symptoms Checklist (HSCL) depression score ≤ 0.5; days with a HSCL score above 0.5 but < 2 considered 50% depression free)	£13.91	13.9	£1.1	ICER 95% CI: -£143 to £368

Notes:

1. Costs converted and uplifted to 2015 UK pounds using purchasing power parity (PPP) exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=386, n=377 used for cost analysis and n=315 used for clinical analysis); local prices used; statistical analyses conducted, including bootstrapping; analyses of clinical data included only those completing all blinded follow-up assessments; cost analyses included only those remaining enrolled throughout the follow-up period; participation in follow-up interviews was significantly greater in the intervention group than in usual care, introducing a possibility of bias.
3. US study; 3rd party payer perspective; no QALYs estimated

3

Update 2017

Table 3: Clinical / economic question: complex collaborative care versus secondary mental health care for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Morriss et al., 2016 UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	£3,477	0.079	£43,993	Controlling for baseline differences and cluster effects: probability of complex collaborative care being cost-effective exceeds 50% at WTP of £42,376/QALY

Notes:
1. Costs uplifted to 2015 UK pounds using the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis conducted alongside RCT (N=187; 84% completed at 6 months, 72% at 12 months and 59% at 18 months); national unit costs used; statistical analyses conducted; CEACs presented.
3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)

Table 4: Clinical / economic question: complex collaborative care in addition to TAU versus TAU for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Goorden et al., 2014 The Netherlands	Minor limitations[2]	Partially applicable[3]	Occupational setting Outcome: QALY	-£644	-0.05	£13,233	Following bootstrapping and inspection of the cost effectiveness plane: in 75% of replications collaborative care less costly and less effective; in 21% collaborative care dominated; in 3% collaborative care dominant; in 1 % collaborative care more costly and more effective
Goorden et al., 2015 The Netherlands	Potentially serious limitations[4]	Partially applicable[3]	Primary care setting Outcome: QALY	£1089	0.02	£49,894	Probability of CCC being cost-effective: 0.20 and 0.70 at WTP £18,576 and £74,304/QALY, respectively.

Notes:
1. Costs converted and uplifted to 2015 UK pounds using PPP exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=126); national unit costs used.
3. Dutch study; healthcare system perspective; QALY based on EQ-5D ratings but Dutch tariff

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
4. Time horizon 12 months; analysis conducted alongside RCT (N=150; 93 identified by screening and 47 by GP referral; economic analysis based only on n=93 identified by screening); national unit costs used; CEACs presented							

R.1.21 Medication management

Table 5: Clinical / economic question: medication management in addition to TAU versus TAU for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Bosmans et al., 2007 The Netherlands	Potentially serious limitations[2]	Partially applicable[3]	Outcomes: Adherence Difference in HSCL score	£324	0.021 -0.15	£15,314/ extra adherence £2,621/point improvement in HSCL	Probability of intervention being cost-effective around 0.65 at WTP of £51,391 per extra person with improvement in adherence
Rubio-Valera et al., 2013 Spain	Potentially serious limitations[4]	Partially applicable[5]	Outcomes: Adherence Remission QALY	£44	0.04 -0.01 0.01	£863/extra adherence Dominated using remission as an outcome £3,224/QALY	Probability of intervention being cost-effective 0.71 and 0.76 for WTP £5,385 /adherent service user and £26,927/QALY, respectively. Using remission, maximum probability of intervention being cost-effective was 0.46
Notes: 1. Costs converted and uplifted to 2015 UK pounds using PPP exchange rates and the UK HCHS index (Curtis & Burns, 2015). 2. Time horizon 6 months; no consideration of HRQoL outcomes; analysis conducted alongside RCT (N=151; economic analysis based on n=88 completers of both 3- and 6-month follow-up); national unit costs used; CEACs presented. 3. Dutch study; societal perspective; no QALY outcome 4. Time horizon 6 months; analysis conducted alongside RCT (N=179; 71% completed at 6 months; n=151 received intervention as allocated); regional unit costs used; CEACs presented; contradictory results depending on the outcome measure used 5. Spanish study; healthcare perspective; QALYs based on EQ-5D ratings, Spanish tariff							

Update 2017

R.1.31 Stepped care

Table 6: Clinical / economic question: stepped care in addition to TAU versus TAU for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Mukuria et al., 2013 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcomes: proportion with reliable and clinically significant improvement on PHQ-9 QALY - SF-6D (UK tariff) QALY - predicted EQ-5D (UK tariff), estimated from SF-6D using empirical mapping	£259	0.025 0.008 0.014	£10,363/ improved participant £32,384/ QALY (SF-6D) £18,504/ QALY (predicted EQ-5D)	Probability of IAPT being cost-effective using SF-6D QALYs: <0.40 at WTP £32,933/QALY; using EQ-5D QALYs: 0.38 and 0.53 at WTP £21,955 and £32,933/QALY, respectively. Using national unit costs instead of IAPT financial data: £4,171/improved participant; £13,036/QALY using SF-6D
Ricken et al., 2011 Germany	Potentially serious limitations[4]	Directly applicable[5]	Outcome: probability of remission, defined as a Bech–Rafaelsen-Melancholia-Scale (BRMS) score <7	-£4,170	0.15	Dominant	Difference in costs p<0.05; difference in effect p=0.07

Notes:

1. Costs converted and uplifted to 2015 UK pounds using PPP exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 8 months; prospective cohort study with matched sites (N=403); low response rate at recruitment (403/3,391, 11.9%); IAPT service was assessed over the first 2 years of establishment, therefore costs associated with learning effects were likely; IAPT financial data used – results sensitive to the use of national unit costs; CEACs presented.
3. UK; NHS and social service perspective; QALY based on SG-6D (UK tariff); QALYs based on predicted EQ-5D ratings (UK tariff), estimated from SF-6D using an empirical mapping function, used in sensitivity analysis
4. Time horizon from enrolment to study endpoint, i.e. drop-out or remission; consideration of hospitalisation and medication costs only; analysis conducted alongside RCT (N=148; completers n=103); national unit costs used.
5. German study; 3rd party payer perspective; no QALYs used, but intervention dominant so judgements on cost effectiveness were straightforward

Update 2017

R.1.41 Integrated care pathways

Table 7: Clinical / economic question: off-site versus on-site integrated care (primary care liaison) for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Pyne et al., 2015 US	Minor limitations[2]	Partially applicable[3]	Outcome: QALY Study included number of free days as an outcome measure, however, this analysis did not include inpatient costs, hence ICER not reported here	£823	0.04	£25,875/QALY (regional costs) £20,197/QALY (national costs)	Probability of off-site being cost-effective 0.86 at a cost effectiveness threshold of £35,905/QALY

Notes:
1. Costs converted and uplifted to 2015 UK pounds using PPP exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis conducted alongside RCT (N=364); unit costs from regional sources; national sources used in sensitivity analysis; bootstrapping conducted, CEACs presented
3. US study; health care provider perspective including service users' time and mileage; QALYs based on SF-12/SF-6D algorithm (UK tariff)

Table 8: Clinical / economic question: integrated care versus primary care with referral system to specialist care for adults with depression

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Wiley-Exley et al., 2009 US	Potentially serious limitations[2]	Partially applicable[2]	Separate analyses for: Full (major and minor depression) VA sample Full non-VA sample Major depression VA sample Major depression non-VA sample Outcomes used: CES-D score; number of depression-free days derived from CES-D; QALYs estimated based	-£580 £41 £781 -£339	0.007 0.0004 0.015 -0.005	Dominant £84,566/QALY £52,395/QALY £70,902/QALY (less effective, less costly)	Probability of IC being cost-effective: >0.70 for any WTP/QALY <0.40 for any WTP/QALY <0.50 for WTP of £35,600/QALY and above >0.50 for WTP £44,500/QALY and above

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
			on depression-free days, using utility weights of health=1, depression=0.59; QALYs estimated based on SF-36, using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG. Only results for the latter presented here.				

Notes:

1. Costs converted and uplifted to 2015 UK pounds using PPP exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 6 months; analysis conducted alongside multi-site pragmatic RCT (N=840 with major or minor depression, assessed within and outside the Veteran Affairs (VA) system.; within VA n=365, outside VA n=475; individuals with major depression within VA n=214, outside VA n=302); national unit costs; bootstrapping conducted, CEACs presented
3. US study; health care provider perspective including service users' time and mileage; QALYs based on SF-36, using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG.

Update 2017

R.2 First-line treatment of adults with a new episode of less severe depression

R.2.1 Psychological interventions

Table 9: Clinical / economic question: problem solving versus treatment as usual

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty[1]**
Kendrick et al., 2005 & 2006	Minor limitation[2]	Directly applicable[3]	Outcome: QALY	£446	-0.02	Problem solving dominated by TAU	Significant difference in costs; non-significant difference in effects; majority of bootstrapped iterations showed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty[1]**
UK							problem solving being dominated by TAU

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 26 weeks; analysis conducted alongside RCT (N=247; analysis based on n=184 with clinical data available; cost data available for n=159); national unit costs used; statistical analyses conducted; cost effectiveness planes presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)

1 **Table 10: Clinical / economic question: psychodynamic counselling versus treatment as usual**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty[1]**
Simpson et al. 2003 UK	Potentially serious limitation[2]	Partially applicable[3]	Primary outcome: change on the BDI; various other scales used as secondary outcomes	-£47	Non-reported	Similar costs and outcomes between interventions	Non-significant difference in costs and outcomes

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=145; cost and outcome data at 12 months available for n=115); local prices used for intervention, national unit costs used for other cost elements; statistical analyses (including bootstrapping) conducted; costs and outcomes not combined/summarised in a cost effectiveness measure; no uncertainty around cost effectiveness suggested.
3. UK study; NHS and social services perspective; QALY was not used as an outcome

2 **Table 11: Clinical / economic question: computerised CBT (with minimal support) versus treatment as usual**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Kaltenthaler	Potentially	Partially	Outcome: QALY	From £88	From 0.01	From £2,470 to	Probability of cCBT being cost-effective

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
et al., 2006 UK	serious limitation[2]	applicable[3]	3 commercially produced computerised CBT packages assessed	to £265 (depending on package)	to 0.08 (depending on package)	£9,791 (depending on package)	at WTP £41,146/QALY: 0.54-0.87 (depending on package)
McCrone et al., 2003 UK	Potentially serious limitation[4]	Partially applicable[5]	Outcomes: BDI score number of depression-free days (DFDs) QALY	£62	-3.5 28.4 0.032	£17 / BDI unit change £2 / DFD £1,944 / QALY	Probability of cCBT being cost-effective: 0.14 and 0.81 at WTP zero and £62 per point improvement in BDI, respectively 0.15 and 0.80 at WTP zero and £8 per additional DFD, respectively 0.85 and 0.99 at WTP £7,775 and £23,324 per QALY, respectively
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 18 months; analysis based on decision-analytic economic modelling; efficacy data based on analysis of individual-level RCT data, published RCT data and further assumptions; resource use data based on manufacturer submissions, published data and other assumptions; manufacturer prices used for intervention, national unit costs used for other cost elements; sensitivity analyses, including PSA conducted; CEACs presented 3. UK study; NHS perspective; QALY estimated based on EQ-5D ratings (UK tariff) 4. Time horizon 8 months; analysis conducted alongside RCT (N=274, cost data available for n=261); manufacturer prices used for intervention, national unit costs used for other cost elements; statistical analyses (including bootstrapping) conducted; QALY estimates based on assumption around BDI measurements. 5. UK study; NHS perspective; DFDs and QALY estimated based on assumptions around BDI measurements and around the utility of DFDs, respectively							

Update 2017

1 **Table 12: Clinical / economic question: computerised CBT with support versus treatment as usual**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Littlewood *et al.*, 2015 UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY 2 computerised CBT programmes assessed (one commercially produced, the other	£108 -£110 (depending on package)	-0.044 -0.015 (depending on package)	cCBT package 1 dominated cCBT package 2 less costly, less effective £7,193	Probability of each intervention being cost effective at WTP £20,000/QALY: cCBT package 1 0.038; cCBT package 2 0.417; TAU: 0.545 Using SF-6D QALYs:

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
			freely available)				cCBT package 1 dominated by TAU; cCBT package 2 dominant Probability of each intervention being cost-effective at WTP £20,000/QALY: cCBT package 1 0.007; cCBT package 2 0.756; TAU: 0.237 Results robust to inclusion of depression-related costs only and to consideration of completers' data only (instead of imputed data analysis) Little evidence of an interaction effect between preference and treatment allocation on outcomes
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 2 years; analysis conducted alongside RCT (N=691; at 24 months EQ-5D data available for n=416 and NHS cost data available for n=580); national unit costs used; statistical analyses including regression analysis to control for covariates conducted; Cholesky decomposition conducted to account for covariance in costs and QALYs; CEACs presented; deterministic sensitivity analysis conducted 3. UK study; NHS & PSS perspective; QALY estimated based on EQ-5D ratings (UK tariff)							

1 **Table 13: Clinical / economic question: computerised CBT with support versus computerised CBT (with minimal support)**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Brabyn *et al.*, 2016 UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY A freely available computerised CBT programme was used in both arms	-£3	0.003	Computerised CBT with support dominant	Probability of computerised CBT with support being cost effective 0.55 at WTP both £20,000 and £30,000/QALY Results robust to inclusion of mental health-related costs only
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 12 months; analysis conducted alongside RCT (N=369; complete cost data across the trial period available for n=209); national unit costs used;							

Economic evidence profile
statistical analyses including regression analysis to control for covariates conducted; Cholesky decomposition conducted to account for covariance in costs and QALYs; CEACs presented; deterministic sensitivity analysis conducted 3. UK study; NHS & PSS perspective; QALY estimated based on EQ-5D ratings (UK tariff)

Table 14: Clinical / economic question: behavioural activation versus CBT

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Richards *et al.*, 2016 UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	-£346	0.050	Behavioural activation dominant	Probability of behavioural activation being cost-effective 0.8 at a WTP both £20,000 and £30,000/QALY Results robust to imputation of missing data
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 18 months; analysis conducted alongside RCT (N=440; costs available for n=327; QALYs available for n=309); national unit costs used; statistical analyses including bootstrapping conducted; CEACs presented; deterministic sensitivity analysis conducted 3. UK study; NHS & PSS perspective; QALY estimated based on EQ-5D ratings (UK tariff)							

R.2.2 Pharmacological interventions

Table 15: Clinical / economic question: SSRIs added to supportive care versus supportive care alone

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty[1]**
Kendrick *et al.*, 2009 UK	Minor limitations[2]	Directly applicable[3]	Outcomes: HAMD17 and QALY	12 weeks -£33 26 weeks £180	12 weeks -2.49 0.005 26 weeks -1.81 0.010	12 weeks: SSRIs & supportive care dominant 26 weeks: £106/HAMD17 reduction in score £17,429/QALY	Probability of SSRI plus supportive care being cost-effective >0.50 at WTP £94/HAMD17 unit reduction; 0.65-0.70 at WTP £20,000-£30,000 /QALY

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty[1]**
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 12 and 26 weeks; analysis conducted alongside RCT (N=220; 12-week completers n=196; 6-month follow-up n=160); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented. 3. UK study; NHS and social care perspective; QALY estimates based on SF-36/SF-6D (UK tariff)							

1 **Table 16: Clinical / economic question: TCAs versus SSRIs versus lofepramine**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty[1]**
Peveler *et al.*, 2005; Kendrick et al., 2006b UK	Minor limitations[2]	Directly applicable[3]	Outcomes: number of DFWs, defined as a HADS-D score <8; QALY	Versus lofepramine: TCAs: -£149 SSRIs: £11	Versus lofepramine: DFWs: TCAs: 0.7 SSRIs: 3.7 QALYs: TCAs: -0.004 SSRIs: 0.034	SSRIs vs lofepramine £45/DFW (TCAs extendedly dominated) SSRIs vs TCAs £3,821/QALY (lofepramine extendedly dominated)	Probability of SSRIs being cost-effective 0.6 at WTP £20,000/QALY
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 12 months; analysis conducted alongside an open label RCT (N=327; entered preference group n=92; followed-up at 12 months n=171); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented.. 3. UK study; NHS perspective; QALY estimates based on EQ-5D ratings (UK tariff)							

R.2.32 Physical interventions

3 **Table 17: Clinical / economic question: acupuncture versus counselling versus treatment as usual**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Spackman *et al.*, 2014 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcome: QALY	Versus counselling: -£231 Versus TAU: £279	Versus counselling: -0.003 Versus TAU: 0.059	Versus TAU: £4,731 Counselling extendedly dominated	Probability of cost effectiveness at WTP £20,000/QALY: acupuncture 0.62, counselling 0.36, TAU 0.02 Results sensitive to small changes in intervention costs; results robust to inclusion of depression-related resource use only. In complete case analysis acupuncture dominated counselling.
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 12 months; analysis conducted alongside RCT (N=755; at 12 months EQ-5D data available for n=572; complete resource use data for n=150; multiple imputation used); acupuncture cost based on published data, for all other costs national unit costs used; statistical analyses conducted, including multiple imputation and regression analysis of costs and QALYs to account for baseline factors; PSA undertaken and CEACs presented; one way sensitivity analysis undertaken 3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)							

Update 2017

Table 18: Clinical / economic question: exercise versus treatment as usual

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Chalder *et al.*, 2012 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcome: QALY	£325	0.014	£22,871	Probability of cost effectiveness at £20,000 and £30,000/QALY: 0.49 and 0.57, respectively Using imputed data: ICER £21,290/QALY Probability of cost effectiveness at £20,000 and £30,000/QALY: 0.50 and 0.60, respectively
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 12 months; analysis conducted alongside RCT (N=361; at 12 months EQ-5D data n=195; complete resource use data n=156); national							

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
unit costs used; statistical analyses conducted, including bootstrapping; PSA undertaken and CEACs presented; one way sensitivity analysis undertaken 3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)							

R.2.41 Psychological, pharmacological, physical and combined interventions

2 **Table 19: Clinical / economic question: various interventions**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost / 1000 people (£)[1]**	**Incremental effect / 1000 people**	**NMB (£) per person[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	Versus pill placebo: Cital -50,274 Mirtaz -101,239 BA 767,091 Coping with Dep 86,317 CBT ind 804,296 CBT group -86,000 IPT 832,720 PDPT 814,333 Counsell 924,908 cCBT + support 19,874 cCBT -14,879 Psychoed -4,299 Exercise -91,696 CBT ind +cital 918,525 IPT +cital 826,497 PDPT +cital 919,265 Exercise + sert	Versus pill placebo: Cital 29.4 Mirtaz 41.6 BA 48.2 Coping with Dep 23.0 CBT ind 50.5 CBT group 40.1 IPT 36.8 PDPT 32.1 Couns 35.6 cCBT+ sup 25.1 cCBT 17.4 Psychoed 20.6 Exercise 32.7 CBT ind + cital 17.4 IPT + cital 50.3 PDPT+cital 36.4 Exerc+sertr 22.9	Mirtazapine 31,816 CBT group 31,770 Exercise 31,628 Citalopram 31,522 cCBT + sup 31,365 Exercise + sertraline 31,311 Psychoed 31,300 Coping with Dep 31,257 cCBT 31,245 CBT indiv 31,089 BA 31,079 IPT + cital 31,063 Pill placebo 30,883 IPT 30,787 PDPT 30,710 PDPT +cital 30,692 Counselling 30,671 CBT ind + cital 30,313	Probability of cost effectiveness at WTP £20,000/QALY: mirtazapine 0.45; CBT group 0.27; exercise 0.08; citalopram 0.03; cCBT with support 0.02; exercise + sertraline 0.02; psychoeducation 0.07; coping with Depression group 0.01; cCBT 0.01; CBT individual 0.00; BA 0.00; IPT + citalopram 0.02; pill placebo 0.00; IPT 0.00; PDPT 0.00; PDPT + citalopram 0.00; counselling 0.01; CBT individual + citalopram 0.00 Results of individual psych interventions sensitive to utility values, cost of relapse and unit cost of therapist

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost / 1000 people (£)[1]**	**Incremental effect / 1000 people**	**NMB (£) per person[1]**	**Uncertainty[1]**
				30,005			

Notes:
1. Costs uplifted to 2016 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Decision-analytic hybrid model, time horizon 12 weeks + 2 years; relative effects based on guideline systematic review and NMA; baseline effects derived from review of naturalistic studies; resource use based on published data supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs and CEAF presented
3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)

R.3 First-line treatment of adults with a new episode of more severe depression

R.3.1 Psychological interventions

Update

Table 20: Clinical / economic question: psychoeducational workshop versus wait list

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Horrell *et al.*, 2014 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcomes: BDI-II scores, number of depression-free days (DFDs), QALY	-£7	5.96 19.23 -0.003	Not reported (not possible to estimate as reported costs and outcomes were not adjusted for baseline differences)	Probability of psychoeducation being cost-effective: 0.30, 0.80 and 0.99 at WTP zero, £32 and £74 per BDI-II point improvement, respectively; 0.90 at WTP £15/DFD gained; 0.50 at WTP £20,656/QALY, max probability 0.56, irrespective of WTP per QALY gained

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 3 months; analysis conducted alongside RCT (N=459, completers n=382); national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)

Table 21: Clinical / economic question: individual CBT versus treatment as usual

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Holman *et al.*, 2011 UK	Potentially serious limitations[2]	Partially applicable[3]	CBT delivered online using real-time therapist interaction through written messaging Outcome: change in BDI-II score	£487	3.6	£137	Probability of CBT being cost-effective 0.90 at WTP £308 per point reduction in BDI-II.

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 10 months; analysis conducted alongside RCT (N=204, at endpoint available cost data for n=198, available outcome data for n=167).); only primary and community service costs considered; secondary care costs omitted; national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; health and social services perspective; QALY not used as an outcome

Table 22: Clinical / economic question: individual CBT delivered online versus wait list

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Hollinghurst *et al.*, 2010 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcomes: % of recovery (BDI <10), QALY	£550	16.5% 0.034	£20,150	Probability of computerised CBT being cost-effective: 0.56 and 0.71 at WTP £20,000 and £30,000/QALY, respectively. After imputation of missing data: ICER £11,831/QALY Probability of computerised CBT being cost-effective: 0.94 and 0.98 at WTP £20,000 and £30,000/QALY, respectively.

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 8 months; analysis conducted alongside RCT (N=297; BDI data available for n=210; QALYs available for n=165; NHS cost data available for n=137); national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)

Table 23: Clinical / economic question: behavioural activation versus treatment as usual

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Ekers *et al.*, 2011 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcomes: change in BDI-II score; QALY Intervention delivered by nurses with no previous training 2 scenarios: therapists delivering 65 treatments/year in a depression-specific role (A) or 33 treatments/year treating depression and anxiety (B)	A: £164 B: £192 Imputed values: A: £187 B: £215	BDI -15.78 QALY 0.03	A: £10/BDI-II point reduction £5,495/QALY B: £12/BDI-II point reduction £6,319/QALY	Probability of behavioural activation being cost-effective at WTP £20,000/QALY 0.98 (A) or 0.97 (B)

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 3 months; analysis conducted alongside RCT (N=47, completers n=38); primary, secondary and community care costs considered; national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS and personal social services perspective; QALY estimates based on EQ-5D (UK tariff)

Table 24: Clinical / economic question: counselling versus antidepressants (AD)

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Miller *et al.*, 2003 UK	Potentially serious limitations[2]	Partially applicable[3]	Outcome: % of people with good 'global outcome', reflecting response to treatment within 8 weeks and remaining well	RCT: -£77 Preference trial: £134	RCT: -16% Preference trial: 8%	RCT: AD vs counselling £483 Preference trial: counselling vs AD £1,675	RCT: probability of counselling being cost-effective 0.25 and 0.10 at WTP £918 and £3,674 /extra person with good global outcome, respectively Assuming missing data reflected good outcomes, probability of counselling being cost-effective increased at any WTP Assuming missing data represented poor outcomes, probability of counselling being cost-effective slightly increased for WTP < £2,755 /good global outcome and decreased for WTP> £2,755 /good global outcome

Notes:

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 12 months; analysis conducted alongside RCT (N=103, at 12 months efficacy data for n=81 and resource data for n=103) and preference trial (N=220; at 12 months efficacy data for n=163 and resource use data n=215); only depression-related costs considered; national unit costs used except for counsellors, where local costs were used; statistical analyses conducted including bootstrapping, CEACs presented. 3. UK study; NHS perspective; QALY not used as an outcome							

R.3.21 Pharmacological interventions

2 Table 25: Clinical / economic question: SSRIs versus mirtazapine

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Benedict *et al.*, 2010 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcome: QALY	-£41	0.002	SSRIs dominant	Probabilistic analysis favoured duloxetine, which was not part of decision problem for this review question Results sensitive to efficacy and utility data
Notes: 1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Time horizon 48 weeks; analysis based on decision-analytic modelling; efficacy data derived from meta-analyses of clinical trials with randomisation possibly broken; disutility and costs due to side effects not considered; resource use estimates based on expert opinion; national unit costs used; funded by industry 3. UK study; Scottish NHS perspective; QALYs based on EQ-5D (UK tariff)							

3 Table 26: Clinical / economic question: escitalopram versus citalopram

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Wade *et al.*, 2005a	Potentially serious	Directly applicable[3]	Population: adults with moderate-to-severe	-£108	5.3%	Escitalopram dominant	Results robust under different scenarios (changes in rates of remission, relapse,

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
UK	limitations[2]		depression Outcome: % of remission				discontinuation, unit costs)
Wade *et al.*, 2005b UK	Potentially serious limitations[4]	Directly applicable[3]	Population: adults with severe depression Outcome: % of remission	-£44	5%	Escitalopram dominant	Results robust to changes in drug-specific probabilities and cost data PSA: Escitalopram dominant in >99.8% of iterations

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 26 weeks; analysis based on economic modelling, efficacy data from pooled RCTs; resource use data based on a general practice database, expert opinion and published studies; national unit costs used; statistical analyses conducted including PSA, funded by industry, side effects not considered in estimation of costs
3. UK study; NHS perspective; QALY not used as an outcome but intervention dominant (so no further judgements on cost effectiveness required)
4. Time horizon 26 weeks; analysis based on economic modelling, efficacy data from pooled RCTs; resource use data based on a general practice database, expert opinion and published studies; national unit costs used; statistical analyses conducted including PSA, funded by industry.

Update 2017

R.3.31 Combined pharmacological and psychological interventions

Table 27: Clinical / economic question: combination therapy (CBT and fluoxetine) versus antidepressant therapy (fluoxetine)

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Simon *et al.*, 2006 UK	Minor limitations[2]	Partially applicable[3]	Population: adults with moderate or severe depression Outcomes: % of successful treatment (remission and no relapse over 12 months, remission defined as HAMD17 ≤ 6 or HAMD24 ≤ 8); QALY	£874	% successful treatment: 16% QALYs - moderate depression 0.04 - severe depression 0.11	£5,563 /extra successfully treated person £19,942/QALY for moderate depression £7,923/QALY for severe depression	95% CIs: £1,920 to £25,099 /extra successfully treated person £6,583 to £108,901/QALY for moderate depression £2,606 to 446,358/QALY for severe depression Results sensitive to changes in relative efficacy (remission and relapse). Probability of Combo being cost-

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
							effective at WTP £41,000/QALY 0.88 for moderate depression and 0.97 for severe depression

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis based on economic modelling, efficacy data from systematic review and meta-analysis; resource use data based on expert opinion and published studies; national unit costs used; PSA conducted, CEACs presented; side effects not considered in estimation of costs or QALYs
3. UK study; NHS perspective; QALYs generated based on vignettes valued by service users using standard gamble techniques

Table 28: Clinical / economic question: combination therapy (CBT and citalopram) versus CBT versus antidepressant therapy (citalopram)

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Koeser *et al.*, 2015 UK	Minor limitations[2]	Directly applicable[3]	Population: adults with moderate or severe depression Outcome: QALY	Vs citalopram: CBT £802 Combo £1,468	Vs citalopram: CBT 0.038 Combo 0.038	Combo dominated by CBT CBT vs citalopram: £20,791	Probability of CBT, citalopram, Combo being cost-effective at WTP £26,000/QALY: 0.43, 0.37 and 0.20, respectively Results sensitive to changes in inclusion criteria for RCTs for acute and follow-up treatment Using SF-6D values: ICER of CBT vs citalopram £33,805/QALY

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 27 months; analysis based on economic modelling, efficacy data from systematic review and network meta-analysis; resource use data based on published estimates of expert opinion and analysis of RCT data; PSA conducted, CEACs presented; side effects not considered in estimation of costs or QALYs
3. UK study; NHS perspective; QALYs generated based EQ-5D ratings (UK tariff)

Update 2017

R.3.41 Physical interventions

Table 29: Clinical / economic question: ECT as part of different sequencing strategies

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Greenhalgh *et al.*, 2005 UK	Potentially serious limitations[2]	Partially applicable[3]	Population: adults with depression requiring hospitalisation Strategies: 1. SNRI, SSRI, Li 2. ECT, SSRI, Li; ECT maintenance in ECT 3. ECT, SSRI, Li; Lithium & TCA maintenance in ECT 4. SNRI, ECT, Li; Lithium & TCA maintenance in ECT 5. ECT, SSRI, Li 6. SNRI, SSRI, ECT; Lithium & TCA maintenance in ECT 7. SNRI, ECT, Li; ECT maintenance in ECT 8. SNRI, SSRI, ECT; ECT maintenance in ECT Outcome: QALY	Strategies 2-8 vs 1: £5,901 -£601 -£1,206 -£564 £3,789 £1,777 £4,698	Strategies 2-8 vs 1: -0.032 -0.066 -0.020 0.049 -0.001 -0.004 0.004	Strategies 1, 2, 3, 6, 7, and 8 dominated ICER of 5 vs. 4: £9,300/QALY	Results modestly sensitive to use of alternative utility values; results robust to small changes in costs and suicide rates

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis based on economic modelling, efficacy data from systematic literature review of RCTs and published meta-analyses, and further assumptions; resource use data based on published literature and expert opinion; national unit costs used; sensitivity analysis conducted including PSA (95% CI reported); impact of side effects considered only in terms of discontinuation
3. UK study; NHS perspective; QALYs estimated based on preferences for vignettes using the McSad health state classification system valued by service users with previous depression in Canada using standard gamble techniques

Update 2017

R.3.51 Psychological, pharmacological, physical and combined interventions

2 **Table 30: Clinical / economic question: various interventions**

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost / 1000 people (£)[1]**	**Incremental effect / 1000 people**	**NMB (£) per person[1]**	**Uncertainty1**
Guideline economic analysis UK	Minor limitations[2]	Directly applicabl[3]	Outcome: QALY	Versus pill placebo: Sertraline 13,593 Mirtazapine 34,754 BA 707,004 CBT indiv 991,804 CBT group -99,791 PDPT 991,943 Counselling 1,023,704 cCBT 69,476 Exercise -44,045 CBT ind + sertr 1,052,806	Versus pill placebo: Sertraline 57.4 Mirtazapine 49.0 BA 108.4 CBT individual 53.4 CBT group 93.8 PDPT 98.0 Counselling 93.2 cCBT -1.6 Exercise 52.8 CBT ind + sertr 157.3	CBT ind + sert 27,658 CBT group 27,541 BA 27,025 Sertraline 26,698 Exercise 26,664 PDPT 26,533 Mirtaz 26,510 Counselling 26,405 CBT indiv 25,642 Pill placebo 25,564 cCBT 25,464	Probability of cost effectiveness at WTP £20,000/QALY: CBT individual + sertraline 0.31; CBT group 0.24; BA 0.13; sertraline 0.05; Exercise 0.13; PDPT 0.03; mirtaz 0.06; counselling 0.05; CBT individual 0.00; pill placebo 0.00; cCBT 0.00 Results of individual psych interventions sensitive to utility values and unit cost of therapist
Notes: 1. Costs uplifted to 2016 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015). 2. Decision-analytic hybrid model, time horizon 12 weeks + 2 years; relative effects based on guideline systematic review and NMA; baseline effects derived from review of naturalistic studies; resource use based on published data supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs and CEAF presented 3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)							

Update 2017

R.4 Interventions for adults with depression who responded inadequately or were intolerant to previous treatment

R.4.1 Psychological interventions

Table 31: Clinical / economic question: cognitive therapy or cognitive behavioural therapy in addition to TAU versus TAU alone

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Scott et al., 2003 UK	Minor limitation[2]	Partially applicable[3]	Intervention: cognitive therapy TAU: antidepressant therapy plus medical management Outcome measure: percentage of relapses avoided	£1,265	18%	£7,030	ICER £7,581 using mean imputation; £8,167 using non-parametric multiple imputation; £11,462 using only the 65% of subjects in the complete case analysis Probability of cognitive therapy being cost-effective 0.60 and 0.80 at WTP of £9,746 and £13,807 per relapse prevented, respectively; probability sensitive to method of missing data imputation
Hollinghurst et al., 2014; Wiles et al., 2016 UK	Minor limitation[4]	Directly applicable[5]	Intervention: cognitive behavioural therapy TAU: GP care, including antidepressant treatment or referral as required Outcome measure: QALY	Endpoint: £928 Mean over 3-5 years: £287	Endpoint: 0.053 Mean over 3-5 years: 0.052	Endpoint: £16,271 Follow-up: £5,482	Results robust to changes in psychologist unit cost & exclusion of hospitalisation costs Using SF-6D-based QALYs: £32,328/QALY Using completers' data: £20,036/QALY Probability of CBT being cost-effective: Endpoint: 0.74 / 0.91; follow-up: 0.92 / 0.95 at WTP of £20,000/£30,000/QALY, respectively

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 17 months; analysis conducted alongside RCT (N=158; full data for 65% of participants); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented.
3. UK study; NHS & PSS perspective; outcome measure % of relapses, no QALY used as an outcome
4. Time horizon 12 months plus 3-5 year follow-up; analysis conducted alongside RCT (N=469; NHS and PSS cost and QALY data available for n=368 at

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
12 months; follow-up data available for n= 248); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented 5. UK study; NHS & PSS perspective; QALYs estimated based on EQ-5D ratings (UK tariff)							

R.4.21 Pharmacological interventions

Table 32: Clinical / economic question: various antidepressants (escitalopram, duloxetine, venlafaxine, mirtazapine)

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Benedict *et al.*, 2010 UK	Potentially serious limitations[2]	Directly applicable[3]	Interventions: duloxetine, venlafaxine, mirtazapine Outcome: QALY	Duloxetine versus: Venlafaxine: -£62 Mirtazapine: -£25	Duloxetine versus: Venlafaxine: 0.05 Mirtazapine: 0.08	Duloxetine dominant	Probability of duloxetine being cost-effective at WTP £20,000/QALY: approximately 0.80
Nordström *et al.*, 2010 Sweden	Potentially serious limitations[4]	Partially applicable[5]	Interventions: escitalopram, duloxetine, venlafaxine Outcome: QALY	Escitalopram versus: Duloxetine: -£15 Venlafaxine: -£55	Escitalopram versus: Duloxetine: 0.025 Venlafaxine: 0.024	Escitalopram dominant	Probability of escitalopram being cost-effective at WTP £20,000/QALY 0.981 and 0.985 compared with duloxetine and venlafaxine, respectively
Notes: 1. Costs converted and uplifted to 2015 UK pounds using purchasing power parity (PPP) exchange rates and the UK HCHS index (Curtis & Burns, 2015). 2. Time horizon 48 weeks; analysis based on decision-analytic modelling; efficacy data derived from meta-analyses of clinical trials with randomisation possibly broken; disutility and costs due to side effects not considered; resource use estimates based on expert opinion; national unit costs used; funded by industry 3. UK study; Scottish NHS perspective; QALYs based on EQ-5D (UK tariff) 4. Time horizon 6 months; analysis based on decision-analytic modelling; efficacy data derived from pooled analysis of trial data, including only participants who had already received antidepressant therapy prior to randomisation; data for duloxetine and venlafaxine pooled together; resource use estimates based on a cohort study conducted in 56 primary care centres in Sweden over 6 months; national unit costs used; CEACs presented for escitalopram versus each of the other drugs considered and not for all 3 options; funded by industry 5. Swedish study; societal perspective but analysis based on healthcare costs presented separately; QALYs based on EQ-5D (UK tariff)							

Update 2017

Table 33: Clinical / economic question: lithium versus antipsychotics as adjuncts to SSRI treatment

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)**	**Uncertainty**
Edwards *et al.*, 2103 UK	Potentially serious limitations[2]	Directly applicable[3]	Outcome: QALY	-£959	0.028	Lithium as an adjunct to SSRI dominant	Probability of lithium being dominant 1 Results sensitive to efficacy of augmentation strategies and discontinuation rates; robust under different assumptions regarding resource use, as well as under changes in remission and relapse risk at follow-up

Notes:

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis based on decision-analytic modelling; efficacy data taken from a systematic review and indirect comparison using 6 RCTs comparing olanzapine + fluoxetine vs. fluoxetine alone in people with treatment-resistant depression and 1 RCT comparing lithium + fluoxetine vs. fluoxetine alone in people who had failed at least one antidepressant (so not from a population with treatment-resistant depression); a common class effect was assumed for the SSRIs and the AAPs; resource use estimates based on expert opinion; national unit costs used; PSA conducted.
3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)

R.5 Interventions for relapse prevention

R.5.1 Psychological interventions

Table 34: Clinical / economic question: mindfulness-based cognitive therapy versus maintenance antidepressant treatment

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Kuyken *et al.*, 2008 UK	Minor limitations[2]	Partially applicable[3]	Outcome: % of people avoiding relapse	£380	13%	£335/relapse prevented (adjusted)	Not statistically significant differences in costs or outcomes
Kuyken *et al.*, 2008 UK	Minor limitations[4]	Directly applicable[5]	Outcomes: % of people avoiding relapse and QALYs	£129	3% -0.04	£5,141/relapse prevented (adjusted)	Not statistically significant differences in costs or outcomes Probability of MBCT being

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
						Dominated	cost-effective less than 0.50 at any WTP per QALY gained

Notes:

1. Costs converted and uplifted to 2015 UK pounds using purchasing power parity (PPP) exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 15 months, analysis conducted alongside RCT (N=125; completers n=115); national unit prices used. statistical analyses conducted, including bootstrapping; CEACs presented for societal perspective
3. UK study; NHS & PSS perspective (societal perspective reported separately); outcome measure was percentage of relapses avoided; no QALYs estimated
4. Time horizon 2 years, analysis conducted alongside RCT (N=424, completers=366); national unit prices used. Statistical analyses conducted, including bootstrapping; CEACs presented
5. UK study; NHS & PSS perspective (societal perspective reported separately); outcome measure was percentage of relapses avoided and QALYs based on EQ-5D ratings (UK tariff)

Update 2017

R.5.21 Pharmacological interventions

Table 35: Clinical / economic question: maintenance SSRIs versus clinical management (SSRIs tapering) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	£111	0.0004	£293,305	Probability of SSRIs being cost-effective at WTP £20,000/QALY: 0.30 Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SSRIs improves as number of previous episodes increases and severity of future relapses increases

Notes:

1. Costs reported in 2016 UK pounds.

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented 3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff							

Table 36: Clinical / economic question: maintenance SNRIs versus clinical management (SNRIs tapering) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	£159	-0.008	Dominated	Probability of SNRIs being cost-effective at WTP £20,000/QALY: 0.07 Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SNRIs improves as number of previous episodes increases and severity of future relapses increases
Notes: 1. Costs reported in 2016 UK pounds. 2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented 3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff							

Update 2017

Table 37: Clinical / economic question: maintenance TCAs versus clinical management (TCAs tapering) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	£176	-0.010	Dominated	Probability of TCAs being cost-effective at WTP £20,000/QALY: 0.09 Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SNRIs improves as number of previous episodes increases and severity of future relapses increases

Notes:

1. Costs reported in 2016 UK pounds.

2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented

3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff

Table 38: Clinical / economic question: maintenance mirtazapine versus clinical management (mirtazapine tapering) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	£151	-0.011	Dominated	Probability of mirtazapine being cost-effective at WTP £20,000/QALY: 0.95 Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SNRIs improves as number of previous episodes

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[1]**	**Incremental effect**	**ICER (£/effect)[1]**	**Uncertainty[1]**
							increases and severity of future relapses increases

Notes:

1. Costs reported in 2016 UK pounds.

2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented

3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff

R.5.31 Psychological, pharmacological and combined interventions

Table 39: Clinical / economic question: MBCT combined with maintenance antidepressant treatment versus MBCT combined with clinical management (antidepressant tapering) versus maintenance antidepressant treatment versus clinical management (antidepressant tapering) versus group CT combined with maintenance antidepressant treatment in people at high risk of relapse who remitted following acute pharmacological treatment and who experienced more severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (AD taper)1**	**Incremental effect vs clinical management (AD taper)**	**NMB (£)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY Interventions in [] considered in SA only	MBCT & AD £188 MBCT & AD taper £65 AD £51 [group CT & AD £164]	MBCT & AD: 0.058 MBCT & AD taper: 0.064 AD: 0.038 [Group CT & AD: 0.052]	MBCT & AD taper £129,554 MBCT & AD £129,309 [groupCT & AD £129,220] AD £129,050 AD taper £128,344	Probability of being cost-effective: AD base-case analysis: MBCT & AD taper 0.83; MBCT & AD 0.16; AD 0.01; AD taper 0.00 AD sensitivity analysis: MBCT & AD taper 0.76; MBCT & AD 0.09; Group CT & AD low cost 0.15; AD 0.00; AD taper 0.00 Results robust to an increase

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (AD taper)1**	**Incremental effect vs clinical management (AD taper)**	**NMB (£)[1]**	**Uncertainty[1]**
							in number of previous episodes, changes in utility values, use of a zero cost for clinical management and a 50% change in relapse cost. Assuming that the preventive effect of MBCT lasts only one year results in MBCT & AD becoming the most cost-effective intervention
Notes: 1. Costs reported in 2016 UK pounds. 2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented 3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff							

Update 2017

Table 40: Clinical / economic question: CT versus fluoxetine versus clinical management (pill placebo) versus no treatment (wait list) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (pill placebo)[1]**	**Incremental effect vs clinical management (pill placebo)**	**NMB (£)[1]**	**Uncertainty[1]**
Guideline economic analysis	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	CT £674 Fluoxetine £225 No treat -£9	CT: 0.014 Fluoxetine: -0.016 No treat: -0.014	Pill placebo £131,837 No treat £131,584 CT £131,405	Probability of being cost-effective: pill placebo 0.58; no treat 0.37; CT 0.04; fluoxetine 0.01

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (pill placebo)[1]**	**Incremental effect vs clinical management (pill placebo)**	**NMB (£)[1]**	**Uncertainty[1]**
UK						Fluo £131,275	Results robust to an increase in number of previous episodes, assuming zero cost of clinical management, and a 50% increase in cost of relapse. CT becomes most cost effective option if number of sessions is reduced to 4; 2nd most cost-effective option if number of sessions is reduced to 4 but preventive effect lasts only 1 year or future relapse episodes are more severe; least cost-effective if less severe depression has a higher utility value or cost of relapse is reduced by 50% or preventive effect of CT lasts only one year
Notes: 1. Costs reported in 2016 UK pounds. 2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented 3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff							

Update 2017

Table 41: Clinical / economic question: CT versus fluoxetine versus clinical management (pill placebo) versus no treatment (wait list) versus MBCT versus group CT in people at high risk of relapse who remitted following acute pharmacological treatment and who experienced more severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (pill placebo)[1]**	**Incremental effect vs clinical management (pill placebo)**	**NMB (£)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY Interventions in [] considered in SA only	CT £674 Fluoxetine £225 No treat -£8 [MBCT £101] Group CT £94]	CT: 0.032 Fluoxetine: -0.013 No treat: -0.032 [MBCT 0.012] [Group CT 0.001]	[MBCT £128,523] Pill placebo £128,389 CT £128,357 [group CT £128,315] Fluo £127,897 No treat £127,759	Probability of being cost-effective: Base-case analysis: Pill placebo 0.39; CT 0.28; fluoxetine 0.06; no treat 0.27; Sensitivity analysis: CT 0.14; fluoxetine 0.04; no treat 0.00; MBCT 0.35; group CT 0.25; pill placebo 0.22 Results robust to the assumption of zero clinical management cost and to 50% change in the cost of relapse; results moderately sensitive to utility values. CT is most cost-effective if number of previous episodes increases to 5 or number of sessions is reduced to 4, even if preventive effect lasts only 1 year; least cost-effective if future relapses are less severe

Notes:

1. Costs reported in 2016 UK pounds.

2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (pill placebo)[1]**	**Incremental effect vs clinical management (pill placebo)**	**NMB (£)[1]**	**Uncertainty[1]**
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff							

Table 42: Clinical / economic question: combined psychological (CBT) and pharmacological (fluoxetine) maintenance treatment versus pharmacological treatment alone versus psychological treatment combined with clinical management (antidepressant tapering) versus clinical management (antidepressant tapering) at high risk of relapse who remitted following acute pharmacological treatment and who experienced more severe depression if they relapsed

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (pill placebo)[1]**	**Incremental effect vs clinical management (pill placebo)**	**NMB (£)[1]**	**Uncertainty[1]**
Guideline economic analysis UK	Minor limitations[2]	Directly applicable[3]	Outcome: QALY	Combo £826 AD £23 Psych & AD taper £765	Combo: 0.059 AD: 0.048 Psych & AD taper: 0.036	AD £129,281 Combo £128,694 Psych & AD taper £128,344 AD taper £128,308	Probability of being cost-effective: AD 0.95; Combo 0.04; AD taper 0.00; Psych & AD taper 0.00 Results overall robust to changes in number of previous episodes, changes in utility values, assuming that the cost of clinical management is zero, 50% change in the cost of relapse, reducing number of psychol therapy sessions to 4 Combo becomes most cost-effective option when the number of sessions of its psych component is reduced from 10 to 4 and the number of previous episodes is at least 7
Notes:							

Update 2017

Economic evidence profile							
Study and country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£) vs clinical management (pill placebo)[1]**	**Incremental effect vs clinical management (pill placebo)**	**NMB (£)[1]**	**Uncertainty[1]**
1. Costs reported in 2016 UK pounds. 2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented 3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff							

1

Update 2017

1