Depression in adults with a chronic physical health problem: Evidence Update March 2012

A summary of selected new evidence relevant to NICE clinical guideline 91 'Depression in adults with a chronic physical health problem: treatment and management' (2009)

Evidence Update 12

Evidence Updates provide a regular, often annual, summary of selected new evidence published since the literature search was last conducted for the accredited guidance they update. They reduce the need for individuals, managers and commissioners to search for new evidence and inform guidance developers of new evidence in their field. In particular, Evidence Updates highlight any new evidence that might reinforce or generate future change to the practice described in the most recent, accredited guidance, and provide a commentary on the potential impact. Any new evidence that may impact current guidance will be notified to the appropriate NICE guidance development centres. For contextual information, Evidence Updates should be read in conjunction with the relevant clinical guideline, available from the NHS Evidence topic page (www.evidence.nhs.uk/topic/depression). NHS Evidence is a service provided by NICE to improve use of, and access to, evidence-based information about health and social care.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

National Institute for Health and Clinical Excellence

Level 1A
City Tower
Piccadilly Plaza
Manchester M1 4BT

www.nice.org.uk

Contents

Introduction

This Evidence Update identifies new evidence that might reinforce or generate future change to the practice laid out in the following reference guidance:

 [1]**Depression in adults with a chronic physical health problem. NICE clinical guideline 91 (2009). Available from www.nice.org.uk/guidance/CG91**

Over 6400 pieces of evidence were identified and assessed of which 13 were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An Evidence Update Advisory Group, comprised of subject experts, reviewed the prioritised evidence and provided a commentary.

Other NICE guidance

The following guidance is also of relevance to management of depression in adults with a chronic physical health problem in the UK, however this Evidence Update does not discuss any potential effect the new evidence may have on these recommendations because there is a separate Evidence Update (available from www.evidence.nhs.uk/evidence-update-13) for this guidance:

 [1]Depression in adults. NICE clinical guideline 90 (2009). Available from www.nice.org.uk/guidance/CG90

- Improving supportive and palliative care for patients with cancer. NICE Cancer Service Guidance (2004). Available from www.nice.org.uk/nicemedia/live/10893/28816/28816.pdf

Quality standards

- Depression in adults. NICE quality standard. Available from www.nice.org.uk/guidance/qualitystandards/depressioninadults/home.jsp

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

[1] NICE-accredited guidance is denoted by the Accreditation Mark 

Key messages

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key messages for this Evidence Update. It also indicates the EUAG's opinion on whether new evidence identified by the Evidence Update reinforces or has potential to generate future change to the current guidance listed in the introduction.

The relevant NICE guidance development centres have been made aware of this evidence, which will be considered when guidance is reviewed. For further details of the evidence behind these key messages and the specific guidance that may be affected, please see the full commentaries.

	Effect on guidance	
Key message	**Potential change**	**No change**
Care of all people with depression • Evidence supports the positive impact of information provision, group physical activities and support programmes on depressive symptoms.		✓
Stepped care • Limited evidence in a single therapeutic area showed the benefit of collaborative care, possibly before earlier steps of intervention, but is unlikely to be sufficient to warrant a change in current recommendations.		✓
Step 1: recognition, assessment and initial management in primary care and general hospital settings • Some evidence in patients with a chronic physical health problem (cancer) supports the association between depression and mortality.		✓
Step 2: recognised depression in primary care and general hospital settings – persistent subthreshold depressive symptoms or mild to moderate depression • Evidence provides support for current guidance, including computerised cognitive behaviour therapy (CBT).		✓
Step 3: recognised depression in primary care and general hospital settings – persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial intervention, and moderate and severe depression • Although evidence supports the current recommendations for antidepressant pharmacotherapy or psychotherapeutic interventions (CBT or couples behaviour therapy), it does not indicate a preferred option. • Evidence supports current guidance for antidepressant treatment in patients with depression and chronic physical health problems, although evidence is insufficient to guide the specific choice of medication. • Current guidance that CBT is a preferred psychotherapeutic approach is supported by new evidence. • Evidence supports the value of collaborative care, with a case manager and combined interventions.		✓ ✓ ✓ ✓

1 Commentary on new evidence

These commentaries analyse the key references identified specifically for the Evidence Update, which are identified in bold text. Supporting references are also provided.

Evidence considered as part of this Evidence Update of NICE clinical guideline (CG) 91 comes from large randomised controlled trials (RCT) and reviews of RCTs that either focus on specific conditions (for example, coronary artery disease, diabetes), group together related conditions (for example, neurological conditions) or take a general view considering together many comorbid conditions. There are limitations to each type of evidence: focusing on individual conditions may limit the generalisability of the findings, grouping conditions together to give a general conclusion may not be appropriate if the contributing studies do not adequately represent the clinical picture (such as excluding patients with dementia from a review of neurological conditions).

It should also be noted that the incidence of depression varies markedly depending on the comorbid condition, and in some diseases (for example, Parkinson's disease) may be an integral part of the physical health problem rather than a consequence of general functional impairment. NICE CG91 offers general recommendations, and is complemented by disease-specific guidelines (for example, Parkinson's disease, see NICE CG35) that may consider the management of depression if this is a particular feature of the condition. Some of the evidence included in this update may also be relevant to disease-specific guidelines.

1.1 Care of all people with depression

A review by **de Man-van Ginkel et al. (2010)** focused on interventions delivered by nurses to patients with depression following stroke and included 15 studies (2054 participants) with a range of designs and one systematic review of 17 RCTs (1773 patients). With a wide variety of outcomes reported, a meta-analysis was not possible. In line with NICE CG91 guidance, the positive impact of information provision, group physical activities and support programmes on depressive symptoms was noted. Beneficial effects from life review therapy and motivational interviewing were also noted in the review, although the limited evidence base (one study on each intervention) is unlikely to affect current guidance.

Key reference

de Man-van Ginkel JM, Gooskens F, Schuurmans MJ et al. (2010) A systematic review of therapeutic interventions for poststroke depression and the role of nurses. Journal of Clinical Nursing 19: 3274–90 Abstract: www.onlinelibrary.wiley.com/doi/10.1111/j.1365-2702.2010.03402.x/abstract

1.2 Stepped care

An RCT by **Huffman et al. (2011)** assessed a depression care management programme in patients hospitalised with cardiac disease. Patients with depression (but not psychotic symptoms or other symptoms needing psychiatric referral) were randomly assigned to collaborative care (n = 90) or usual care (n = 85). A case manager, in consultation with a study psychiatrist, worked with patients assigned to collaborative care to coordinate pharmacotherapy and psychological interventions that were deemed appropriate. The cardiac in-patient care team were informed of the depression in patients assigned usual care, and could instigate treatment in line with usual practice; information was not provided on any treatment for depression received by these patients. Patients assigned to collaborative care showed significantly greater response in depressive symptoms than those receiving usual care after 6 weeks (59.7% vs 33.7% response, odds ratio [OR] = 2.91, p = 0.003) and 12 weeks (51.5% vs 34.4% response, OR = 2.02, p = 0.042), but this was not maintained after 6 months (48.7% vs 43.9% response, OR = 1.21, p = 0.57). NICE CG91 recommends a stepped-care model for the provision of interventions to treat and manage adults with

depression and a chronic physical health problem. Although the study provided some evidence for the value of collaborative care in this patient population that may not previously have received step 2 or individual step 3 therapies, the organisation of the NHS may not be conducive to this approach because few cardiac units have a social worker and psychiatrist available to coordinate and deliver the intervention. This evidence from this narrowly-defined patient population is unlikely to change the recommendations of NICE CG91 for stepped care.

Key reference
Huffman JC, Mastromauro CA, Sowden G et al. (2011) Impact of a depression care management program for hospitalized cardiac patients. Circulation: Cardiovascular Quality and Outcomes 4: 198–205
Abstract: www.circoutcomes.ahajournals.org/content/4/2/198.abstract

1.3 Step 1: recognition, assessment and initial management in primary care and general hospital settings

NICE CG91 notes that practitioners should be aware that patients with a chronic physical health problem are at a high risk of depression, particularly if they have functional impairment, underlying the guidance on effective case identification and recognition, and on risk assessment and monitoring. Although not directly providing evidence on how to recognise or assess depression in patients with chronic physical health problems, a meta-analysis by **Pinquart and Duberstein (2010)** of 76 prospective studies involving over 160,000 patients with cancer showed that 91% of the bivariate associations between depression and mortality, and 90.5% of the multivariate analyses that controlled for confounding variables, reported a relative risk of more than 1.0. This finding supports the rationale for NICE CG91 guidance by demonstrating that a diagnosis of depression and elevated level of depressive symptoms are predictive of increased mortality in patients with cancer. The authors suggested that consideration could be given to screening for depression as part of cancer treatment. Although screening was not a focus of this meta-analysis, the conclusion is consistent with the recommendation to screen for psychological distress in the NICE guidance on cancer services 'Improving supportive and palliative care for adults with cancer'.

Key reference
Pinquart M, Duberstein PR (2010) Depression and cancer mortality: a meta-analysis. Psychological Medicine 40: 1797–1810
Full text: www.ncbi.nlm.nih.gov/pmc/articles/PMC2935927/pdf/nihms203992.pdf

1.4 Step 2: recognised depression in primary care and general hospital settings – persistent subthreshold depressive symptoms or mild to moderate depression

Low-intensity psychosocial interventions

A systematic review by **Sherr et al. (2011)** examined the efficacy of various interventions to treat depression in 90 studies of people with HIV, primarily among men in North America (total number of participants not stated). Of nine studies included that examined psychosocial interventions, five showed no benefit. The studies were diverse and only two examined a similar intervention (art therapy), one of which was effective and the other was not (no data provided). Evidence was also mixed from the four studies of exercise, two of which were effective and two were not (no data provided). Consequently, this evidence is insufficient to inform NICE CG91 advice on the use of low-intensity psychosocial interventions.

An RCT by **van Bastelaar et al. (2011)**, conducted in 255 patients with diabetes and depressive symptoms, evaluated the efficacy of web-based cognitive behaviour therapy (CBT) by comparing scores of people undergoing this intervention with those placed on a waiting list for the same intervention. The intervention consisted of eight consecutive lessons, with feedback on homework assignments provided by certified health psychologists.

Depressive symptoms were significantly reduced by the web-based CBT (41% experienced clinical improvement vs 24% in the control group, p < 0.001). Diabetes-specific emotional distress was also significantly reduced by the intervention (p = 0.03), but there was no impact on glycaemic control. The findings are limited by the sample selection method (self-selected patients) and the short duration of follow-up (1 month). Recommendations in NICE CG91 for low-intensity psychosocial interventions include computerised CBT, which this study appears to support.

Key references

Sherr L, Clucas C, Harding R et al. (2011) HIV and depression – a systematic review of interventions. Psychology, Health & Medicine 16: 483–527
Abstract: www.tandfonline.com/doi/abs/10.1080/13548506.2011.579990

van Bastelaar KMP, Pouwer F, Cuijpers P et al. (2011) Web-based depression treatment for type 1 and type 2 diabetic patients: a randomized controlled trial. Diabetes Care 34: 320–5
Abstract: http://care.diabetesjournals.org/content/34/2/320.full

1.5 Step 3: recognised depression in primary care and general hospital settings – persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions, and moderate and severe depression

Treatment options

At step 3, NICE CG91 advises either an antidepressant (normally a selective serotonin reuptake inhibitor [SSRI]) or high-intensity psychological interventions (group or individual CBT or behavioural couples therapy). Recent evidence supports this view; there is no new evidence to indicate any preference between these options, in line with current guidance.

A Cochrane review by **Baumeister et al. (2011)** assessed both pharmacological and psychological interventions for depression in approximately 4000 patients with coronary artery disease. However, comparison of the alternative approaches was not possible from the 16 RCTs included, only one of which included both types of intervention. The effects of drug treatment and psychological interventions were analysed separately and results are presented in the appropriate subsections below.

A meta-analysis by **O'Neil et al. (2011)** to assess the impact of treatment for depression on health-related quality of life (HRQOL) in cardiac patients included five RCTs (n = 2105); two of psychotherapeutic interventions, one of pharmacotherapy and two of collaborative care or combined therapy. The analysis did not distinguish between the different types of intervention. HRQOL was assessed in four of the studies using the Short Form 36, with the other study using the Clinical Global Impressions Scale Score. After 6 months, treatment resulted in statistically significant improvement in mental HRQOL compared with usual care or placebo (standard mean difference [SMD] = −0.29, 95% confidence intervals [CI] −0.38 to −0.20, p <0.0001) and a modest but significant effect on physical HRQOL (SMD = −0.14, 95% CI −0.24 to −0.04, p = 0.009).

A systematic review by **van der Feltz-Cornelis et al. (2010)** examined the effect of interventions to treat depression in patients with diabetes in 15 RCTs (1724 patients; type 1 and 2 diabetes; five studies investigated a psychotherapeutic intervention, three of which also included a diabetes self-management intervention; seven studies assessed antidepressant medication; three studies were of collaborative care in a primary care setting with stepped care starting with choice of psychotherapy or pharmacotherapy). A combined outcome measure was used, with equal weighting for depressive symptom severity and glycaemic control, as well as separate measures. There was a moderate impact on the combined clinical

measure when all studies were analysed together (effect size d = −0.370, 95% CI −0.470 to −0.271), with a greater impact from psychotherapeutic interventions (d = −0.581, 95% CI −0.770 to −0.391, n = 310) than antidepressant drugs (d = −0.467, 95% CI −0.665 to −0.270, n = 281) although this could have been due in part to the impact of diabetes education and self-management on glycaemic control; an effect was also noted in the large population-based studies of collaborative care (d = −0.292, 95% CI −0.429 to −0.155, n = 1133). The review indicated that, in addition to benefits on depressive symptoms, the treatment approaches recommended by NICE CG91 have the additional potential to be effective for glycaemic control.

Key references

Baumeister H, Hutter N, Bengel J (2011) Psychological and pharmacological interventions for depression in patients with coronary artery disease. Cochrane Database of Systematic Reviews issue 9: CD008012
Full text: www.onlinelibrary.wiley.com/doi/10.1002/14651858.CD008012.pub3/pdf

O'Neil A, Sanderson K, Oldenburg B et al. (2011) Impact of depression treatment on mental and physical health-related quality of life of cardiac patients: a meta-analysis. Journal of Cardiopulmonary Rehabilitation and Prevention 31: 146–56
Abstract: www.journals.lww.com/jcrjournal/pages/articleviewer.abstract

van der Feltz-Cornelis CM, Nuyen J, Stoop C et al. (2010) Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a systematic review and meta-analysis. General Hospital Psychiatry 32: 380–95
Abstract: www.ghpjournal.com/article/S0163-8343(10)00061-7/abstract

Antidepressant drugs

A systematic review by **Dowlati et al. (2010)** evaluated the efficacy of antidepressant drugs (mirtazapine, citalopram, fluoxetine, sertraline) in patients with coronary artery disease and major or minor depression. Four RCTs were included (n = 402 patients treated with antidepressants; n = 396 receiving placebo). Compared with placebo, antidepressant treatment in this patient population significantly decreased Hamilton Depression Rating Scale (HDRS) score (weighted mean difference 1.41; 95% CI 0.53 to 2.29; p = 0.002) and Beck Depression Inventory score (weighted mean difference 2.27; 95% CI 0.60 to 3.94; p = 0.008), and increased the proportion of patients responding with 50% or greater reduction in HDRS score (OR = 1.72; 95% CI 1.17 to 2.54). There was no significant difference in the proportion of patients who dropped out from treatment with placebo or active treatment, although information on drop-outs due to adverse events could be obtained from only two of the studies. It should be noted that one of the studies included in this review assessed citalopram. Both citalopram and its enantiomer, escitalopram, are now contraindicated in people with congenital long QT syndrome, known pre-existing QT interval prolongation, or in combination with other medicines that prolong the QT interval. Electrocardiogram measurements should be considered for patients with cardiac disease, and electrolyte disturbances should be corrected before starting treatment with citalopram, (for more information see: www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON137769).

All of the RCTs included in the review discussed above were also included in the Cochrane review by **Baumeister et al. (2011)**, which considered a total of 16 RCTs of pharmacological and psychological treatment for depression in approximately 4000 patients with coronary artery disease (also see 'Treatment options' above). Eight trials (n = 1098 patients) compared pharmacological treatment with placebo; meta-analysis was possible with three studies, indicating a beneficial effect on depression score (SMD = −0.24, 95% CI −0.38 to −0.09) and remission rate (OR = 1.80, 95% CI 1.18 to 2.74). Treatment for depression appeared to have no impact on all-cause mortality (four studies) or cardiac events (three studies). The review also included one study that compared the effects of paroxetine and nortriptyline treatment in 81 patients; no differences in depression outcomes were observed.

Pizzi et al. (2011) reported another systematic review of patients with depression and coronary heart disease that included six studies (observational and RCTs; one study was incorrectly randomised and one was a re-analysis of RCT data; n = 2461). A significantly greater improvement in symptoms of depression among patients treated with SSRIs was noted compared with the control group (placebo or no antidepressants). Furthermore, SSRI use was associated with a significant decrease in re-admission for coronary heart disease (risk ratio [RR] = 0.63, 95% CI 0.46 to 0.86) and mortality rate (RR = 0.56, 95% CI 0.35 to 0.88). However, although analysis of data from only the 734 patients in the properly randomised studies showed a significant positive impact of SSRIs on depressive symptoms, the impact on readmission rates and mortality did not reach significance.

In the systematic review by **Sherr et al. (2011)** (see section 1.4 for details), of 11 studies that assessed pharmacotherapy, the interventions in six studies were effective, two studies showed the interventions were not effective and three studies were inconclusive. A further two of three studies without random allocation to treatment but with a placebo or control group also showed a beneficial effect on depressive symptoms.

A systematic review by **Iovieno et al. (2011)** included 25 RCTs of antidepressant therapy in patients with significant and/or severe or unstable co-morbid axis-III disorders (that is, physical health problems). Antidepressants were more effective at reducing depression symptoms than placebo (RR = 1.42, $p < 0.0001$). A positive effect of antidepressants was also observed in subgroup analysis of the six studies in post-stroke patients (RR = 1.43, $p = 0.04$, n = 377) and five studies in HIV/AIDS (RR = 1.66, $p = 0.005$, n = 425) but not in four studies of patients with cancer (RR = 1.26, $p = 0.19$, n = 254). This review provided some indication of a higher response rate to antidepressant treatment among patients with chronic physical health problems than in the general population.

A total of 51 placebo-controlled RCTs (n = 3603) were included in a Cochrane review by **Rayner et al. (2010)** of antidepressant therapy for depression in physically ill people. The review included 11 studies in stroke, seven in HIV/AIDS, six in Parkinson's disease, four in cancer, three each in chronic obstructive pulmonary disease (COPD), diabetes and myocardial infarction, and two in renal failure; other studies looked at different conditions or were in patients with mixed diagnoses. The primary outcome measure was efficacy 6–8 weeks after randomisation. The response to treatment was shown to be superior with antidepressants compared with placebo (OR = 2.33, 95% CI 1.80 to 3.00, $p < 0.00001$, 25 studies; 1674 patients), although fewer patients receiving placebo dropped out of the studies (OR = 1.32, 95% CI 1.00 to 1.75, $p = 0.05$, 22 studies, 1555 patients).

Subgroup analysis ranked the response rate compared with placebo in the order tricyclic antidepressants (TCA, OR = 3.85, 95% CI 1.88 to 7.87, $p = 0.0002$, seven studies, 337 patients), mianserin/mirtazapine (OR 2.46, 95% CI 1.28 to 4.73, $p = 0.007$, three studies, 166 patients), SSRIs (OR 1.92, 95% CI 1.48 to 2.49, $p < 0.00001$, 16 studies, 1135 patients). Compared with patients receiving placebo, drop-out rates were increased with TCA therapy (OR = 1.69, 95% CI 0.98 to 2.92, $p = 0.06$, six studies, 299 patients) and SSRIs (OR = 1.43, 95% CI 1.04 to 1.96, $p = 0.03$, 15 studies, 1092 patients) but not with mianserin/mirtazapine (OR = 0.88, 95% CI 0.05 to 14.14, $p = 0.93$, two studies).

The authors noted that differences in efficacy and tolerability of different antidepressant drug classes arose from indirect comparisons, resulted in overlapping confidence intervals, and included different proportions of responders. It was also noted that few trials included patients with cognitive impairment, very severe depression or suicidal ideation, or in severely physically unwell patients, who are representative of many in an acute medical setting. More research in these patient groups may be useful.

Subsets of the papers included in the Cochrane review discussed above were analysed separately in publications by the same group. Price et al. (2011) included 20 RCTs conducted

in adults with a neurological disorder, of which half were in patients who had a stroke, six were in Parkinson's disease, two were in multiple sclerosis, one in brain injury and one in epilepsy; studies in patients with dementia, cognitive impairment and headache were excluded, although such conditions are common neurological disorders. After 6–8 weeks, antidepressant therapy in this patient population resulted in significantly increased remission compared with placebo (OR = 2.23, 95% CI 1.54 to 3.23, number needed to treat [NNT] = 7, ten studies, 683 patients).

The subset of RCTs conducted in palliative care (defined to include not only patients in end-of-life care but also those with a life-threatening illness but not at imminent risk of dying) was analysed in Rayner et al. (2011). Of the 25 RCTs included, seven were in HIV/AIDS, four were in cancer, three in COPD, two in end-stage renal failure and one in chronic heart failure; the six studies in Parkinson's disease and two in multiple sclerosis were also assessed in the analysis by Price et al (2011). After 6–8 weeks, antidepressant therapy in this patient population resulted in a significantly increased response compared with placebo (OR = 2.25, 95% CI 1.38 to 3.67, p = 0.001, 12 studies; 685 patients). The authors noted that the effect size could be overestimated because of selective reporting and publication bias, although the consistency of benefit in analyses that excluded trials at high risk of bias and broad definition of depression suggested genuine benefit.

Overall, the evidence from these studies supports the recommendation of NICE CG91 for antidepressant treatment in patients with depression and chronic physical health problems, although evidence continues to be insufficient to guide the specific choice of medication, beyond the general preference for SSRIs. At least in patients with coronary artery disease, use of antidepressants does not appear to result in additional risks and there is limited evidence that cardiac outcomes may be improved by such treatment.

Key references

Dowlati Y, Herrmann N, Swardfager WL et al. (2010) Efficacy and tolerability of antidepressants for treatment of depression in coronary artery disease: a meta-analysis. Canadian Journal of Psychiatry 55: 91–9
Abstract: www.ncbi.nlm.nih.gov/pubmed/20181304

Iovieno N, Tedeschini E, Ameral VE et al. (2011) Antidepressants for major depressive disorder in patients with a co-morbid axis-III disorder: a meta-analysis of patient characteristics and placebo response rates in randomized trials. International Clinical Psychopharmacology 26: 69–74
Abstract: www.journals.lww.com/intclinpsychopharm/pages/articleviewer.abstract

Pizzi C, Rutjes AWS, Costa GM et al. (2011) Meta-analysis of selective serotonin reuptake inhibitors in patients with depression and coronary heart disease. American Journal of Cardiology 107: 972–9
Abstract: www.ajconline.org/article/S0002-9149(10)02541-5/abstract

Rayner L, Price A, Evans A et al. (2010) Antidepressants for depression in physically ill people. Cochrane Database of Systematic Reviews issue 4: CD007503
Full text: www.onlinelibrary.wiley.com/doi/10.1002/14651858.CD007503.pub2/pdf

Supporting references

Price A, Rayner L, Okon-Rocha E et al. (2011) Antidepressants for the treatment of depression in neurological disorders: a systematic review and meta-analysis of randomised controlled trials. Journal of Neurology, Neurosurgery & Psychiatry 82: 914–23
Abstract: www.jnnp.bmj.com/content/82/8/914.abstract

Rayner L, Price A, Evans A et al. (2011) Antidepressants for the treatment of depression in palliative care: systematic review and meta-analysis. Palliative Care 25: 36–51
Abstract: www.pmj.sagepub.com/content/25/1/36.abstract

Psychological interventions

The Cochrane review by **Baumeister et al. (2011)** (also see 'Treatment options' and 'Antidepressant drugs' above) of approximately 4000 patients with coronary artery disease and major or minor depression included seven RCTs that investigated psychological

interventions (for example, CBT, resource-orientated psychotherapy, telephone counselling). Two trials provided sufficient information for meta-analysis compared with placebo, showing a non-significant difference on depression score. Limited evidence from one study showed a beneficial impact of interpersonal psychotherapy compared with clinical management. This evidence is probably insufficient to affect NICE CG91 recommendations.

In the systematic review by **Sherr et al. (2011)** (see section 1.4 for details), of 22 RCTs of psychological interventions, 15 showed a significant benefit, six showed no benefit and one was unclear. Studies that included CBT or a cognitive behavioural component appeared particularly effective, accounting for all 15 studies with beneficial outcomes (with one study of this type of intervention resulting in no benefit). This evidence supports the recommendation in NICE CG91 for the use of CBT-based psychological interventions.

Collaborative care

As part of a stepped-care programme, NICE CG91 recommends collaborative care (a coordinated approach to mental and physical healthcare, with a dedicated coordinator, support from a multi-professional team and use of a range of interventions) for patients with a chronic physical health problem with associated functional impairment and moderate to severe depression that has not responded to other interventions. Evidence from an RCT conducted by **Ell et al. (2010)** in the USA involving 387 patients with diabetes (all of low-income and predominantly Hispanic) suggests that under-served populations may also benefit from collaborative care as part of a stepped-care programme. The intervention group received first-line treatment choice of problem-solving therapy provided by bilingual clinical specialists in diabetes depression or antidepressant medication (usually an SSRI); monthly telephone follow-up identified non-responders or partial responders (after 9–12 weeks) who received both treatments. Patients who remained non-responders were considered for additional therapy and specialist referral. Significantly more patients in the intervention group showed 50% or more reduction in depressive symptoms from baseline than in the usual care group after 6, 12 and 18 months (OR = 2.46–2.57, all $p < 0.001$).

In the systematic review by **Sherr et al. (2011)** (see section 1.4 for details), of the four studies that combined psychological interventions with drug treatment, three showed a beneficial impact compared with single interventions. This evidence supports the NICE CG91 recommendation to use a range of interventions in patients who have not responded adequately to individual interventions.

Key reference
Ell K, Katon W, Xie B et al. (2010) Collaborative care management of major depression among low-income, predominantly Hispanic subjects with diabetes: a randomized controlled trial. Diabetes Care 33: 706–13
Full text: www.care.diabetesjournals.org/content/33/4/706.full.pdf+html

1.6 Step 4: complex and severe depression

No new key evidence was found for this section.

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified that have not previously been listed on the NHS Evidence UK Database of Uncertainties about the Effects of Treatments (DUETs).

Antidepressant drugs

- Selective serotonin reuptake inhibitors (SSRIs) in patients with depression and coronary heart disease
  www.library.nhs.uk/DUETs/viewResource.aspx?resid=411732

Further evidence uncertainties for depression in adults with chronic physical health problems can be found at www.library.nhs.uk/duets/ and in the NICE research recommendations database at www.nice.org.uk/research/index.jsp?action=rr.

DUETs has been established in the UK to publish uncertainties about the effects of treatment that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance and the closely linked guidance on depression in adults:

- Depression in adults with a chronic physical health problem. NICE clinical guideline 91 (2010). Available from www.nice.org.uk/guidance/CG91
- Depression. NICE clinical guideline 90 (2010). Available from www.nice.org.uk/guidance/CG90

Searches

The literature was searched to identify systematic reviews and RCTs with at least 100 participants relevant to the scope. Searches were conducted of the following databases, covering the dates 1 August 2010 (the end of the search period of the most recent Annual Evidence Update) to 12 September 2011:

- CINAHL
- Cochrane Database of Systematic Reviews – Cochrane Library
- Embase
- MEDLINE
- PsycINFO
- AMED (for St John's Wort only)

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. A single broad search strategy was used, reflecting the breadth of the topic, based on the search strategy used in the reference guidance. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews (www.sign.ac.uk/methodology/filters.html).

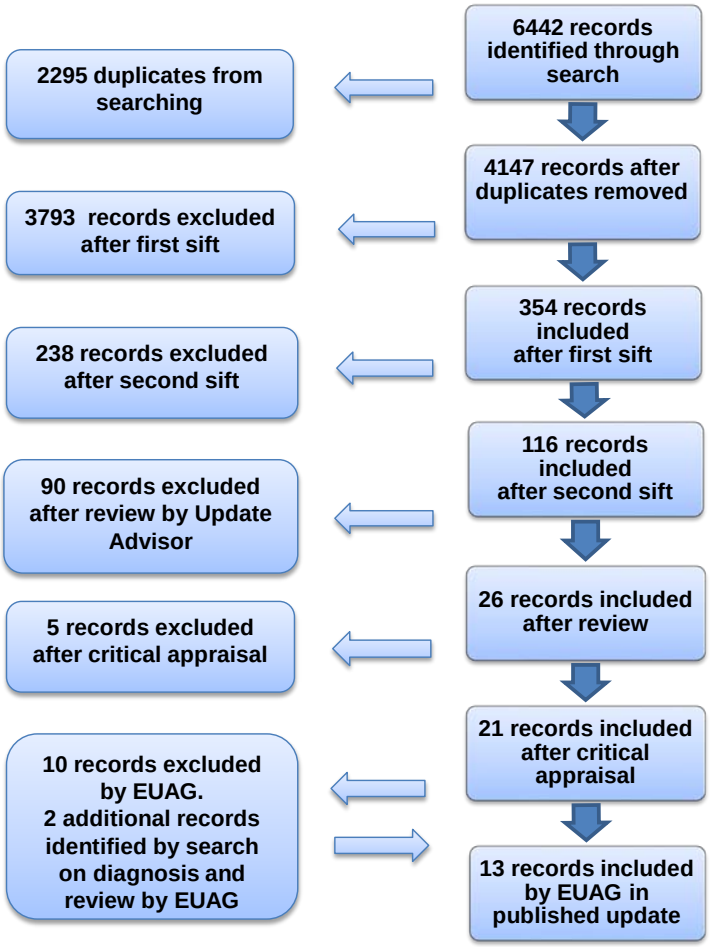
A single search strategy was used for the Evidence Updates of the clinical guidance on both depression in adults (NICE CG90) and depression in adults with a chronic physical health problem (NICE CG91). Epilepsy, dementia, brain injury or trauma were added to the list of conditions sifted and included in this Evidence Update, as suggested by the Update Adviser (the chair of the EUAG). The output relevant to each Evidence Update was separated by sifting.

Two other studies (Baumeister et al. 2011, Van der Feltz-Cornelis et al. 2010) were also identified outside of the literature search. Figure 1 provides details of the evidence selection process. The long list of evidence excluded by the Update Adviser, and the full search strategies, are available on request from contactus@evidence.nhs.uk

Table 1 MEDLINE search strategy (adapted for individual databases)

1	exp Depression/
2	exp Depressive Disorder/
3	or/1-2
4	(depression or depressive).ti.
5	SAD.ti.
6	melancho*.ab,ti.
7	pseudodementia.ab,ti.
8	reactive depression.ab,ti.
9	dysphori*.ab,ti.
10	or/4-9
11	3 or 10

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and NHS Evidence project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of subject experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

Dr Anna Higgitt – Chair

Consultant Psychiatrist, Central and North West London NHS Foundation Trust

Dr Dave Anderson

Consultant Old Age Psychiatrist, Mersey Care NHS Trust, Liverpool

Professor Else Guthrie

Consultant in Psychological Medicine, Manchester Mental Health and Social Care Trust

Dr Mark Haddad

Clinical Research Fellow, Institute of Psychiatry, King's College London

Dr Christian Hosker

Consultant Liaison Psychiatrist, Leeds NHS Partnership Foundation Trust

Dr Nicky Thomas

Consultant Health Psychologist, Guy's and St Thomas' NHS Foundation Trust, London

NHS Evidence project team

Alan Lovell

Evidence Hub Manager

Elly O'Brien

Information Specialist

Diane Storey

Editor