

Appraisal of Screening for Depression

A report for the
UK National Screening Committee

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This report has been compiled by

- Dr Gail Pittam, Senior Public Health Researcher
- Dr Martin Allaby, Consultant in Public Health Medicine

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Solutions for Public Health
4150 Chancellor Court
Oxford Business Park South
Oxford
OX4 2GX

Tel: +44 (0)1865 334700
www.sph.nhs.uk

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Introduction

1. This report reviews screening for depression against the UK National Screening Committee (NSC) criteria for appraising the viability, effectiveness and appropriateness of a screening programme (NSC 2003). It is based on a literature search conducted by the NSC on 31st March 2014 (Coles 2014). Full details of the search strategy are set out in Appendix A.
2. Screening for depression in adults was previously reviewed against the UK NSC criteria in 2006 and 2010. The current NSC policy is that “routine screening of the population or subsets of the population for depression is not recommended” (NSC 2014).
3. The 2010 NSC review focused on a combination of three elements:
 - Questionnaire based tests had moderate to good sensitivity but poor positive predictive values in the general population
 - Screening would detect cases at the milder end of the spectrum but it was uncertain whether treatment would prevent progression to more severe depression
 - Clinical management of depression was not optimized in the UK in terms of prescribing on the part of professionals and compliance on the part of the patient. The components of an effective collaborative care approach had been identified in a phase II clinical trial (CADET) but a phase III study would be needed to evaluate this more thoroughly.
4. The literature search for this current review therefore focused on
 - The test
 - Screening for and treatment of milder forms of depression
 - Identifying further trials and publications from the CADET trial.
5. This review does not include antenatal and postnatal depression (covered in the psychiatric illness and antenatal depression NSC policies) or groups identified as being at high risk of depression, for example people with pre-existing long term medical or mental health conditions, drug users, people who have experienced domestic abuse or violence and people who are institutionalised (e.g. prisoners, people living in care homes etc).
6. The National Institute for Health and Care Excellence has published clinical guidelines on the treatment and management of depression in adults (NICE 2010) and on the identification and management of depression in children and young people (NICE 2005). The clinical guideline for adults recommends case identification and recognition, whereby healthcare professionals should be alert to possible depression, particularly in people with a past history of depression or a chronic physical health problem with functional impairment (NICE 2010). The clinical guideline for children recommends that healthcare professionals working with children and young people in primary care, schools and the community should be trained to detect symptoms of depression and to assess children and young people who may be at risk of depression (NICE 2005).
7. In 2009 the United States Preventative Services Task Force (USPSTF) recommended screening adults for depression when staff-assisted depression care supports¹ are in place to assure accurate diagnosis, effective treatment and follow-up (USPSTF 2009). The USPSTF also recommended screening for major depressive disorder in adolescents (aged 12 to 18 years) when systems are in place to ensure accurate diagnosis,

¹ Staff-assisted depression care support refers to clinical staff that assist the primary care clinician by providing some direct depression care, such as care support or co-ordination, case management, or mental health treatment (USPSTF 2009c).

psychotherapy (cognitive-behavioural or interpersonal) and follow-up (USPSTF 2009b). The USPSTF are in the process of updating both of these topics.

8. In 2013 the Canadian Task Force on Preventative Health Care recommended that adults at average risk of depression, and adults in subgroups of the population who may be at increased risk of depression should not be routinely screened for depression (CTFPC 2013).

The Condition

The condition should be an important health problem

9. Depression is the most common mental disorder in community settings and is a major cause of disability across the world (NICE 2010). In 2007 the estimated number of people in England with depression was 1.24 million with an associated cost to services of £1.7 billion and a cost in lost employment of £5.8 billion, The number of people in England with depression is projected to rise to 1.45 million by 2026 with associated service costs of £3 billion and lost employment costs of £9.2 billion (McCrone et al 2008).
10. Depression includes a wide range of mental health problems that are characterized by the absence of a positive affect (e.g. a loss of interest and enjoyment in ordinary things and experiences), low mood and a range of emotional, cognitive, physical and behavioural symptoms (NICE 2010). The impact of depression on social and occupational functioning, physical health and mortality is substantial, with emotional, motivational and cognitive effects impacting on a person's ability to work effectively. Wider social effects can include greater dependence upon welfare and benefits, loss of self-esteem and self-confidence and social impairments including reduced ability to communicate and sustain relationships during the illness (NICE 2010). Having depression is associated with a four-times higher risk of suicide compared with the general population, rising to a nearly 20 times higher risk in the most severely ill (NICE 2010) Stigma associated with mental health problems generally may result in some people with depression being reluctant to seek help (NICE 2010).
11. The estimated point prevalence for a depressive episode among 16 to 74 year olds in the UK is 2.6%, with a higher prevalence for females (2.8%) than males (2.3%). If the broader category of mixed depression and anxiety is used the point prevalence rises to 11.4% (13.6% for females and 9.1% for males) (NICE 2010). Estimates for the incidence of depression within the adult population range from 3% to 6% per year, with mild depression accounting for 70% of cases, moderate depression 20% and severe depression 10% (NICE 2011).
12. The 12-month prevalence for depression is approximately 3% for post-pubertal adolescents (NICE 2005).
13. A UK study calculated the prevalence of depression in older people aged ≥ 65 years in England and Wales to be 8.7% (95%CI 7.3% to 10.2%) (McDougall et al 2007).
14. A meta-analysis by Mitchell et al (2011) looked at the clinical ability of GPs to detect defined mental disorders unassisted i.e. without systemic help from severity scales, diagnostic instruments, education programmes or collaborative care. The reference standard method was either a self-reported severity scale or an interview. The authors identified nine mild depression studies and found on meta-analysis that GPs correctly identified 33.8% (95%CI 27.3% to 40.7%) of people with mild depression and correctly identified 80.6% (95%CI 66.4% to 91.6%) of people without depression.

15. In an earlier meta-analysis Mitchell et al (2009) identified 41 studies that assessed the ability of GPs to make an unassisted diagnosis of depression (of any severity²) against the reference standard of interview-based diagnosis using a psychiatric expert diagnosis or validated structured or semi-structured interviews applied by a research interviewer. On meta-analysis the detection rate (sensitivity) was 47.3% (95%CI 41.7% to 53.0%), with contemporaneous ratings found to be more accurate than case-note methods (52.6%, 95%CI 46.5% to 58.6% vs. 33.6%, 95% CI 22.4% to 45.7%). For 19 studies that reported data for 'rule-in' and 'rule-out' accuracy the meta-analysis specificity was 81.3% (74.5% to 87.3%).
16. In summary, depression is a common disorder that can have a substantial impact on a person's health and social and occupational functioning. Meta-analysis results suggest that many cases of mild depression and any-severity depression are not detected by GPs during routine clinical care. This criterion is met.

The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage

17. Depression is generally considered to occur on a continuum of severity, with the identification of major depression based on severity, persistence, the presence of other symptoms and the degree of functional and social impairment (NICE 2010).
18. The prodromal (early symptomatic) period for depression varies considerably with some people experiencing a range of symptoms in the months prior to the full illness such as anxiety, phobias, milder depressive symptoms and panic attacks. Other people may develop severe major depressive episode more quickly, for example following a stressful life event. In some cases somatic symptoms may be present and investigated first before mood changes become more apparent (NICE 2010).
19. The natural history of depression is variable. A first episode of major depression can occur at any time from early childhood to old age, though many people have their first depression in childhood or adolescence. The average age for the first episode of major depression is in the mid-20s (NICE 2010). At least 50% of people go on to have at least one more episode of depression after the first major episode, with the risk of relapse increasing to 70% and 90% respectively after the second and third episodes (NICE 2010). People with early onset depression (before the age of 20 years) and depression occurring in old age are more vulnerable to relapse (NICE 2010).
20. Incomplete recovery from depression is thought to be common. For example, studies have shown that 50% of patients still had a diagnosis of depression one year later and at least 10% had persistent or chronic depression (NICE 2010). However, depression can also resolve within a few months. A Dutch prospective cohort study included 7,076 adults (aged 18 to 64 years) and sought to assess the duration of major depressive episodes in the general population (Spijker et al 2002). Depression was assessed using the Composite International Diagnostic Interview and duration of major depressive episode over two years was assessed with a Life Chart Interview. Recovery was defined as no or minimal depressive symptoms in a three-month period. From this population 250 cases of major depressive episodes (first episode or new recurrent episode) were identified. Fifty per cent recovered within three months (95%CI 44 to 56), 63% recovered within six months (95%CI 57 to 69) and 76% recovered within 12 months (95%CI 70 to 82).

² The authors stated that if a study assessed detection rates of different types of depression they used the data for major depression alone.

However, almost 20% had not recovered at 24 months. The severity of the index episode and the presence of co-morbid dysthymia (chronic depression) predicted longer episode duration. In one third of cases the person did not receive any professional care. In those who did not receive professional care the median duration of major depressive episodes was 3.0 months (95%CI 2.1 to 3.9), in respondents who received primary care support the median duration of major depressive episodes was 4.5 months (95%CI 3.4 to 5.6) and in respondents who received mental health system care the median duration of major depressive episodes was 6.0 months (95%CI 3.9 to 8.1) (Spijker et al 2002).

21. A US cohort study set in New York conducted structured psychiatric interviews with 755 young people during adolescence and again during adulthood. Diagnostic interviews were conducted between 1983 and 2004 and all young people were first interviewed by mean age 16 years and at follow-up at mean ages 22 and/or 33 years. The individuals identified as having a minor depressive disorder at a mean age of 14 or 16 years were significantly more likely to have a major depressive disorder at mean age of 22 or 33 (adjusted odds ratio³ 3.99, 95%CI 2.20 to 7.24) (Johnson et al 2009).
22. In another US study 348 low-income adult primary care patients who had screened positive for a psychiatric disorder and had not received mental health care in the year before screening, were reassessed with the Structured Clinical Interview for DSM-IV after a mean of 3.7±0.5 years (Weissman et al 2010). The psychiatric disorders screened for included major depression and bipolar, anxiety and substance use disorders. Of the 39 patients who screened positive for major depression at baseline, 62% (95%CI 45.5% to 77.6%) met criteria for current major depression at follow-up.
23. A small longitudinal study of 179 patients attending one English general practice (Kessler 2002 - cited in NICE 2010, p20) aimed to determine whether depression or anxiety not diagnosed during one general practice consultation is diagnosed during follow up or is self-limiting and not of clinical importance. This study found that the majority of undetected people either recovered or were diagnosed during the follow-up period, however 14% of people with depression still had a clinically severe condition and had not received a diagnosis after three years.
24. The 2010 NSC review identified a Dutch eight year prospective study in progress that aims to describe the long-term course of depressive and anxiety disorders (Penninx et al 2008, cited in Allaby 2010). The final results are due to be published after 2015, however, results after two years from 1,209 patients with depression and/or anxiety living in primary and specialized care settings were published in 2011 (Penninx et al 2011). This found that for people with depression (n=267) the median episode duration was six months and 24.5% had chronic⁴ depression. For people with co-morbid depression and anxiety (n=455) the median duration was >24 months and 56.8% had chronic depression and anxiety.
25. In summary, approximately 50% of cases of depression persist for at least one year and the risk of relapse after a first episode of major depression is also high at over 50%. However, depression can also resolve without treatment in a few months, and this may be most likely in people who do not consult a doctor about their depressive illness. Early results from a cohort study suggest co-morbid depression and anxiety may be associated with a higher rate of chronic disease of longer duration than depression alone. Future results from this cohort study might provide further information about which patients are

³ Age, gender and the presence of a corresponding disorder by mean age 16 were controlled statistically

⁴ Chronic depression and/or anxiety was defined as people with enduring depression and/or anxiety symptoms of at least mild severity during the entire follow-up period without remission (Penninx et al 2011).

likely to recover without substantial intervention and which may need more intensive interventions.

All the cost-effective primary prevention interventions should have been implemented as far as practicable

26. A 2011 Cochrane review (Merry et al 2011) assessed 53 randomised controlled trials of psychological or educational prevention programmes for young people aged five to 19 years who did not currently meet diagnostic criteria for depression and/or were below the clinical range on standardised, validated and reliable rating scales of depression. A total of 14,406 participants were included in these studies. In the studies reporting outcomes on depressive diagnosis, the risk of having a depressive disorder was reduced compared to no intervention: immediately post-intervention (15 studies, n=3,115; risk difference (RD) -0.09, 95%CI -0.14 to -0.05); at three to nine months (14 studies, n=1,842; RD -0.11, 95%CI -0.16 to -0.06); and at 12 months (10 studies, n=1,750, RD -0.06, 95%CI -0.11 to -0.01). At 24 months there was no evidence for continued efficacy (8 studies, n=2,084, RD 0.01, 95% -0.04 to 0.03). Only two studies assessed efficacy to 36 months (Merry et al 2011). The authors concluded that, despite some heterogeneity in the studies, psychological depression prevention programmes were effective in preventing depression with a small number of studies showing a decrease in episodes of depressive illness over a year (Merry et al 2011).
27. A meta-analysis of depression prevention programmes for children and adolescents, (Stice et al 2009) found that greater benefits were observed in targeted studies with high risk participants compared to universal programmes. Other characteristics associated with larger effect sizes identified included studies with a higher percentage of female participants and programmes delivered by professional interventionists (compared to teachers, for example) (Stice et al 2009).
28. In summary, there is some evidence to suggest that implementing more primary prevention interventions could be beneficial, although longer term benefits beyond one year have not yet been established. The NICE clinical guideline on depression in children and young people does not address the primary prevention of depression and it is not clear how widespread such primary prevention interventions are in the UK. There is therefore a degree of uncertainty about whether this criterion is met in the UK.

If the carriers of a mutation are identified as a result of screening the natural history of people with this status should be understood, including the psychological implications.

29. This is not relevant to screening for depression.

The Test

There should be a simple, safe, precise and validated screening test. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed

30. In the 2010 NSC review the nine-item self-administered Patient Health Questionnaire (PHQ-9)⁵ was identified as probably being the most widely and positively evaluated of the questionnaires for detecting depression (Allaby 2010). In the first UK validation of PHQ-9 the questionnaire performed well when compared against the gold standard of a diagnosis of major depressive disorder made by a trained interviewer using the Structured Clinical Interview for DSM-IV (SCID) with a sensitivity of 92% (95%CI 78% to 98%) and a specificity of 78% (95%CI 66% to 88%). However, it was noted that the sample size was small and the corresponding confidence intervals correspondingly wide (Allaby 2010).
31. The literature search conducted for this current review suggests that the Patient Health Questionnaire is still the most widely studied tool with the most common versions being the PHQ-9 and PHQ-2⁶.

For adults

32. Arroll et al (2010) validated the PHQ-2 and PHQ-9 in primary care settings, with 2,642 adults (aged ≥16 years) attending family practices in New Zealand. The Composite International Diagnostic Interview (CIDI) depression was used as the reference standard. The sensitivity and specificity values for diagnosing major depression are given below. Confidence intervals were not reported:
- PHQ-2 (cut-off score 2): sensitivity 86%, specificity 78%
 - PHQ-2 (cut-off score 3): sensitivity 61%, specificity 92%
 - PHQ-9 (cut-off score 10): sensitivity 74%, specificity 91%
33. A 2012 meta-analysis exploring the optimal cut-off score for the PHQ-9 concluded that the PHQ-9 has acceptable diagnostic properties at cut-off scores ranging from 8 to 11, with no significant differences in sensitivity or specificity at a cut-off score of 10 compared to other scores within the 8 to 11 range (Manea et al 2012). When only studies using the PHQ-9 in primary care or community settings were considered, the pooled estimate for sensitivity was 89% (95%CI 66% to 97%) and for specificity was 88% (95%CI 80% to 93%) for a cut-off score of 10. There was a high degree of heterogeneity between the studies ($I^2 = 84.7%$) (Manea et al 2012).
34. Nuevo et al (2009) examined the usefulness of the Beck Depression Inventory (BDI)⁷ as a screening method for depression among the general population of Finland. The BDI was completed by 1,939 randomly selected people who lived in or around a Finnish city. Of these, the 294 who achieved a score of 13 or more on the BDI and a random sample of 5% of the rest of the participating subjects were invited for further assessment using a structured diagnostic interview⁸. In total 311 people completed the further assessment

⁵ The PHQ-9 has 9 questions with a score ranging from 0 to 3 for each question (maximum score of 27). A threshold score of 10 or higher is considered to indicate mild major depression, 15 or higher indicates moderate major depression and 20 or higher indicates severe major depression (Arroll et al 2010)

⁶ The PHQ-2 uses the first two questions of the PHQ-9

⁷ The BDI is a 21-item self-reported instrument

⁸ The Schedules for Clinical Assessment in Neuropsychiatry (SCAN) – a clinical structured interview which generates diagnoses of depressive disorders based on ICD-10 criteria (Nuevo 2009)

(244 who scored ≥ 13 on the BDI and 67 from the sample of 5% who were invited). Following the analysis the authors concluded that the optimal cut-off score was 17, which resulted in a sensitivity of 70.1% and a specificity of 73.7% (95% confidence intervals not reported). The authors noted that other studies have suggested different optimal cut-off scores ranging from 12/13 to 16/17.

For young people

35. Richardson et al (2010a) assessed the validity of the PHQ-9 for adolescents. In this study 4,000 young people aged 13 to 17 years were randomly selected from people who had attended a US health care facility in the previous 12 months and were given an initial survey to self-complete which included the PHQ-2. From this sample a subset of 444 people completed a telephone interview which included the PHQ-9 and the Diagnostic Interview Schedule for Children (DISC-IV). This subset included 242 people with a PHQ-2 score of three or more and 202 people who scored two or less on the PHQ-2 and were frequency matched for age and gender. The authors concluded that the optimal cut-off score for the PHQ-9 was 11, which achieved a sensitivity of 89.5% and a specificity of 77.5% (95% confidence intervals not reported).
36. In the same study, Richardson et al (2010b) also assessed the validity of the PHQ-2 in the subset of 444 young people who completed a phone interview. A cut-off score of three was considered optimal by the authors, which resulted in a sensitivity of 73.7% and a specificity of 75.2%.

For older people

37. Mitchell et al (2010) conducted a meta-analysis assessing the validity of the Geriatric Depression Scale (GDS) against a semi-structured psychiatric interview in older people (aged over 55 years) in primary care. The meta-analysis included 17 studies, seven of which assessed the GDS₃₀⁹ and ten the GDS₁₅¹⁰. The meta-analysis results found a sensitivity of 81.3% (95%CI 77.2% to 85.2%) and a specificity of 78.4% (95%CI 71.2% to 84.4%) for the GDS₁₅. The GDS₃₀ had a sensitivity of 77.4% (95%CI 66.3% to 86.8%) and a specificity of 65.4% (95%CI 44.2% to 83.8%)¹¹. The cut-off levels used in the individual studies within the meta-analysis varied, from three to seven (median 5.5) for the GDS₁₅ and from seven to 11 (median 10) for the GDS₃₀.
38. Table 1 summarises the main performance metrics (sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV)) associated with the PHQ-9 and the GDS for the different populations.

Table 1: Performance metrics associated with the PHQ-9 and GDS

Population	Scale	Prevalence	Sensitivity	Specificity	PPV	NPV
Adults (16-74)	PHQ-9 ^a	2.6%	89.0%	88.0%	16.5%	99.7%
Young People	PHQ-9 ^b	3.0%	89.5%	77.5%	11.0%	99.6%
Older People (≥ 65 years)	PHQ-9 ^a	8.7%	89.0%	88.0%	41.4%	98.8%
	GDS ₁₅ ^c	8.7%	81.3%	78.4%	26.4%	97.8%

a: Manea et al 2012; b: Richardson et al 2010a; c: Mitchell et al 2010

⁹ The GDS₃₀ includes 30 questions and was purposely designed with few somatic symptoms which might otherwise cause problems for diagnoses in older people (Mitchell et al 2010)

¹⁰ The GDS₁₅ is a short form of the GDS₃₀ and includes 15 questions

¹¹ The study authors noted the superior performance of the GDS₁₅ over the GDS₃₀ but were uncertain why the shorter version of the questionnaire was more accurate in some studies.

39. In summary, there are screening tests that have been tested in primary care populations and could be used to screen for depression in adults, young people and older people. However, the positive predictive values associated with these tests are low, suggesting that screening for depression using these tests would generate a substantial number of false positives. This criterion is not met.

The test should be acceptable to the population

40. The previous 2010 NSC review identified one large and three small studies giving some information on the acceptability of screening tests for depression. A study from Germany offered screening for depression to 3,194 randomly selected households and achieved a 67% participation rate; a US study found that 89% of 189 eligible patients offered the PHQ-9 in the waiting room of one primary care clinic were successfully screened; a Swedish study found that 87% of 155 women in a Swedish drop-in primary care clinic accepted an offer of depression screening and 50 of 59 screen-positive women accepted a repeat visit (Allaby 2010).
41. The current literature search identified a New Zealand study of 8,260 adult primary care patients who were approached to take part in a randomized controlled trial study on screening for depression. Of these, only 358 (4.3%) refused to take part and 145 did not complete either the screening questionnaire (PHQ-2 or PHQ-9) or the CIDI interview (Arroll et al 2010).
42. It has been suggested that the PHQ-9 can be completed in less than one minute and scored in less than one minute (Furukawa 2010). It has been suggested that the 21-item Beck Depression Inventory can be completed in five to ten minutes (Furukawa 2010).
43. In summary studies from non-UK countries show that participation rates are generally fairly high suggesting that depression screening tests are likely to be acceptable. However we did not identify any studies assessing the acceptability of screening tests in a UK population. This criterion has therefore not been established for a UK population.

There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals

44. NICE clinical guideline 90 (NICE 2010) covers the identification, treatment and management of depression for adults but does not specify how individuals with a positive screening test result should be managed.
45. NICE clinical guideline 28 (NICE 2005) covers the identification, treatment and management of depression for children and young people.
46. There is guidance in place for identification, treatment and management of depression, however specific policies relating to people identified through screening would need to be developed.

If the test is for mutations the criteria used to select the subset of mutations to be covered by screening, if all possible mutations are not being tested, should be clearly set out

47. This is not relevant to screening for depression.

The Treatment

There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment

48. The 2006 NSC review concluded that the effectiveness of drugs and psychological interventions for depression is established and forms the basis of evidence based guidelines, but did acknowledge that most guidelines focus on moderate to severe depression (Gilbody et al 2006). Both the 2006 and 2010 NSC review concluded that patients with undetected depression have milder forms of depression. The 2010 NSC review also noted that screening for depression might be justified if major depressive disorder could be prevented through early diagnosis and treatment (Allaby 2010).
49. In this current review we have focused on evidence addressing the question of whether intervention in screen detected depression, or the treatment of milder depression, prevents progression to more severe depression. We have not revisited the literature on the outcomes of treatment for depression using pharmacological or psychological interventions.

The prevention of depression

50. A meta-analysis on the Coping with Depression (CWD) course¹² (Cuijpers et al 2009) included six randomised controlled trials (RCTs) (n=724) which assessed the ability of the CWD course to prevent major depression in adults (4 studies) or adolescents (2 studies) who had subthreshold depression established by a diagnostic interview. Participants were followed up for at least one year in all six studies. The mean incidence rate ratio¹³ (IRR) across all six studies was 0.62 (95% CI 0.43 to 0.91, p=0.01; I²=0), which indicates that participants receiving the CWD had a 38% less chance of developing a depressive disorder than people in control conditions. This meta-analysis is an update and revision of a paper cited in the 2010 NSC review (Cuijpers et al 2007), which found that the CWD course had an encouraging, but non-significant, effect in preventing major depressive disorder. The 2009 paper included 2 additional RCTs (Munoz et al 1995, Munoz et al 2007), and used a different statistical method to measure the incidence of depression following the intervention. In their 2007 paper Cuijpers et al calculated the incidence of depression at a fixed point (12 months) following the CWD intervention, and concluded that the effect was not significant. In their 2009 paper Cuijpers et al calculated the incidence of depression using a person-years-at-risk approach, because the follow-up period of the 6 included studies varied considerably (maximum 2 years). Both the two additional trials and the change in statistical method contribute to Cuijpers' shift in conclusion regarding the effect of the CWD course on prevention of major depressive disorder, from being non-significant (p=0.07) in 2007, to significant (p=0.01) in 2009.
51. An RCT assessed the effectiveness of a stepped-care prevention programme in 170 individuals aged ≥75 years with subthreshold levels of depression or anxiety from 33 primary care clinics in the Netherlands (van't Veer-Tazelaar et al 2009). Participants were recruited from members of the study population of a larger prevention project who had

¹² A cognitive behavioural intervention for depression

¹³ The incidence rate of developing a depressive disorder in experimental subjects relative to the incidence rate in control subjects

scored ≥ 16 on the self-report Center for Epidemiologic Studies Depression Scale¹⁴. Participants were randomised to receive usual care (n=84) or a stepped-care programme (n=86) consisting of watchful waiting, cognitive behaviour therapy-based bibliotherapy, cognitive behaviour therapy-problem-solving treatment and referral to primary care for medication if required. The main outcome measure was cumulative incidence of DSM-IV major depressive disorder after 12 months as measured using the Mini International Neuropsychiatric Interview (MINI)¹⁵ administered by trained interviewers at baseline, six months and 12 months. The authors do not specify whether or not the trained interviewers were blinded to which treatment group the participants were in. An intention-to-treat analysis was performed.

52. In the intervention group 11.6% developed a major depressive disorder (n=10) after 12 months compared to 23.8% of the usual care group (n=20), equating to an odds ratio of 0.42 (95%CI 0.18 to 0.96) (van't Veer-Tazelaar et al 2009). At further follow-up after 24 months, 39.3% (n=33) of the usual care group had developed major depression or anxiety compared to 19.8% (n=17) for the stepped-care group, equating to an odds ratio of 0.38 (95%CI 0.19 to 0.76) (van't Veer-Tazelaar et al 2011). The authors concluded that the stepped-care intervention was more effective than usual care in reducing the risk of major depression and anxiety.
53. Lee et al (2012) conducted a systematic review of five RCTs (n=1,083) assessing psychotherapy interventions for community-dwelling older adults (aged ≥ 50 years) with subthreshold depression compared to usual care or waiting-list or placebo controls. Only studies measuring depressive symptoms with reliable and valid tools were eligible for inclusion. Meta-analysis was not performed, but the authors found that four of the five RCTs reported a significant reduction in depression symptoms of about 50%, with moderate effect sizes and follow-up of up to 12 months. However, the interventions used varied and included cognitive behavioural therapy, problem solving therapy and life review, and the level of training and qualifications of the people administering the training also varied. The authors did not provide information on whether the people assessing outcomes in the included trials were blinded to which treatment group the participants were in.

Collaborative care

54. The previous NSC reviews noted that there is evidence that collaborative care¹⁶ in patients with depression helps optimize management and outcomes of depression.

Collaborative care - adults

55. A Cochrane review (Archer et al 2012) assessed the effectiveness of collaborative care for the treatment of depression or anxiety, with a primary outcome of change in depression as measured by observer or patient self-report. Participants had a primary diagnosis of depression (including acute, chronic, persistent, remitted, subthreshold and postnatal) or anxiety (including generalised anxiety, panic, post-traumatic stress disorder, phobias, social anxiety, health anxiety and obsessive compulsive disorder). Participants could also have a co-morbid long-term condition. Sub-group analysis for different forms of depression or anxiety was not performed. The intervention had to be predominantly

¹⁴ The Center for Epidemiologic Studies Depression Scale consists of 20 items and has a total score ranging from 0 to 60. A minimum score of 16 indicates clinically significant levels of depressive symptoms (Van't Veer Tazelaar et al 2009).

¹⁵ The MINI is a brief structured diagnostic interview developed by psychiatrists and physicians in the US and Europe for DSM-IV and ICD-10 psychiatric disorders (van't Veer-Tazelaar et al 2009)

¹⁶ Collaborative care involves a number of health professionals working with a patient. A case manager has regular contact with the patient and organises care, often supported by a medical doctor and a mental health specialist (Archer 2012).

delivered in primary care or community settings. Seventy-nine RCTs were included (n=24,308), ten of which were from the UK. The authors noted that 68% of the comparisons had adequate blinding of the people completing the outcome assessment, however in 24% of comparisons information on the blinding of outcome assessors was either missing or insufficient resulting in an unclear risk of bias. In 8% of cases, the methods used were considered to be at high risk of bias. It was not possible to blind the participants or people delivering interventions in any study. Meta-analysis demonstrated greater improvement in depression outcomes for adults with depression who received the collaborative care model compared to usual care up to 24 months. For 48 comparisons reporting short-term outcomes (≤ 6 months; n=11,250) the risk ratio (RR) favouring collaborative care was 1.32 (95%CI 1.22 to 1.43, $I^2 = 71\%$). For 29 comparisons reporting medium-term outcomes (7 to 12 months; n=8,001) the RR was 1.31 (95%CI 1.17 to 1.48, $I^2 = 83\%$). For six comparisons reporting long-term outcomes (13 to 24 months; n=2,983) the RR was 1.29 (95%CI 1.18 to 1.41, $I^2 = 0\%$). For five comparisons that looked beyond 25 months there was no significant difference between collaborative and usual care (RR 1.12, 95%CI 0.98 to 1.27, $I^2=0\%$). Similar results were found for adults with anxiety.

56. Richards et al (2013) conducted a cluster RCT (CADET) in 51 UK primary care practices comparing the effectiveness of collaborative care with usual care in the management of 581 adult patients with moderate to severe depression. Participants were identified from electronic case records of primary care general practices and were eligible if they met ICD-10 criteria for a depressive episode when interviewed by research personnel. Collaborative care involved six to 12 contacts with participants over 14 weeks, was delivered by care managers and included depression education, drug management, behavioural activation, relapse prevention and primary care liaison. The research workers who assessed eligibility and collected outcome measures (using patients' self-report questionnaires) were blinded to which group the participants were allocated to. At four months the mean depression score was 1.33 points better on the PHQ-9 for people receiving collaborative care (95%CI 0.35 to 2.31, $p=0.009$) after adjustment for baseline depression. At 12 months the mean depression score was 1.36 points better on the PHQ-9 for people receiving collaborative care (95%CI 0.07 to 2.64, $p=0.04$). Whilst these results are statistically significant the wide confidence intervals should be noted as the effect of the intervention may not be clinically important. More participants receiving collaborative care met criteria for recovery at four months (odds ratio 1.67, 95%CI 1.22 to 2.29) and 12 months (odds ratio 1.88, 95%CI 1.28 to 2.75). The odds ratios indicate a moderate association between collaborative care and recovery. The authors concluded that collaborative care had persistent positive effects for up to 12 months after the start of the intervention.

Collaborative care - adolescents

57. Archer et al (2012) also assessed collaborative care versus usual care for adolescents. Two comparisons (n=460) reporting short-term outcomes (≤ 6 months) found that collaborative care was more effective than usual care (RR 0.73, 95%CI 0.56 to 0.96, $I^2=0\%$). However, two comparisons of medium term outcomes (7-12 months) and one comparison of long-term outcomes (13 to 24 months) did not find any significant differences between collaborative and usual care. In one of these studies the assessor was blinded to the participants treatment group resulting in a low risk of bias, however in the other study the assessor was not blinded resulting in a high risk of bias.
58. Richardson et al (2009) looked at the feasibility and acceptability of collaborative care for the treatment of 40 adolescents (aged 12 to 18 years) with major and minor depression in a pilot study with three US primary care clinics. The collaborative care included case management by a depression care manager (DCM) (supervised by child mental health specialists), self-management and enhanced antidepressant medication care or Problem Solving Treatment – Primary Care. Participants had an average of nine contacts with the

DCM over the six month follow-up period. In this uncontrolled study the mean (standard deviation) PHQ-9 score reduced from 14.0 (4.5) at baseline to 5.7 (4.1) at six-month follow-up ($p < 0.001$). Significant improvements were also seen on other scales assessing mood and impairment. The authors concluded that collaborative care is feasible for adolescents and had encouraging results, though the absence of controls makes it impossible to assess how much, if any, of the improvement in PHQ-9 scores was attributable to the collaborative care.

59. In summary, we identified some studies assessing whether the treatment of milder depression prevents progression to more severe depression. The results suggest that intervention for subthreshold depression can reduce the likelihood of major depression compared to usual care in the short to medium-term. However, sample sizes of the individual studies were small and confidence intervals around effect sizes were wide. Only one study looked at outcomes beyond 12 months and we did not identify any studies with follow-up beyond two years. It is not clear whether the people assessing outcomes in the RCTs were blinded to which treatment group the participants were in, which means the risk of bias is also unclear. In order for this criterion to be met studies are required that assess longer-term outcomes for the treatment of depression that is detected on screening and was previously unrecognised.
60. There is also some evidence from RCTs that collaborative care results in better outcomes than usual care for adults up to 24 months, although the evidence for adolescents was limited with no evidence to support significance beyond six months. It was not possible to blind participants to their treatment group in these studies but many, although not all, of the studies did blind the people assessing outcomes to the participants' group. Where blinding was not used there is the potential for outcome assessment bias. Other limitations include small sample sizes, moderate effect sizes and wide confidence intervals which reduce confidence in the clinical significance of the results. It should also be noted that none of these studies sought to assess collaborative care in a screening population and it is uncertain whether these results would be generalisable to a screening context.

There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered

61. The National Institute for Health and Care Excellence published a clinical guideline on the treatment and management of depression in adults in 2010 (NICE 2010) and a clinical guideline on the identification and management of depression in children and young people in 2005 (NICE 2005). However, these do not specifically relate to people identified through screening.
62. There is guidance in place for the identification, treatment and management of depression, however specific policies relating to people identified through screening would need to be developed.

Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme

63. Collaborative care is recommended within the stepped care model described in the NICE clinical guideline, but only if the depression is in the context of a chronic physical health problem with associated functional impairment (NICE 2010).

64. It is not known how widely collaborative care is implemented in the UK for the population of interest to this review of screening for depression, therefore there is uncertainty about whether this criterion is met.

The Screening Programme

There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity

65. Previous systematic reviews have attempted to identify RCTs of depression screening with varying results. A 2008 review on screening and case-finding instruments for depression (Gilbody et al 2008) included five RCTs; a 2009 systematic review done in conjunction with the US depression screening guideline (O'Connor et al 2009) included nine RCTs; and a 2012 systematic review done in conjunction with the Canadian guideline on depression screening (Joffres et al 2012) did not include any RCTs (Thombs & Ziegelstein 2014).
66. Thombs & Ziegelstein (2014) assessed the RCTs cited in these reviews against three key criteria: i) determining eligibility and randomising patients before screening, ii) excluding patients already known to have depression or already being treated for depression and iii) providing similar depression care options to patients in both trial arms, whether they are identified as depressed by screening or via other methods, such as self-report or unaided clinician diagnosis. Overall, none of the trials cited in the 2008 review or the US 2009 review were judged to have met all three criteria for a test of depression screening (Thombs & Ziegelstein 2014).
67. Thombs & Ziegelstein (2014) also searched for ongoing trials intended to evaluate the effects of depression screening but did not identify any studies that fulfil the criteria for tests of depression screening.
68. The systematic review conducted for the 2013 Canadian recommendation did not find any studies evaluating the benefits of screening the average-risk population for depression in primary care settings (CTFPHC 2013).
69. No additional RCTs assessing the ability of screening for depression to reducing mortality or morbidity were identified in the literature search for this review.
70. This criterion is not met.

There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public

71. A prospective cohort study in the Netherlands attempted to test and provide collaborative depression care for high risk primary care patients, such as patients with a previous mental health problem, unexplained somatic complaints or a high level of use of primary care services. Of the 1,687 patients sent a screening questionnaire, 780 returned the questionnaire, 226 tested positive and 17 (1% of those invited) initiated treatment for depression (Bass et al 2009). However, it should be noted that the high-risk population for this study may not be generalisable to a screening population.
72. A US pharmacist-conducted screening programme for depression screened 3,726 people (aged ≥ 18 years) for depression (Rosser et al 2013). All participants received the PHQ-2

and the 67 (1.8%) who screened positive received the PHQ-9. Only one patient who screened positive on the PHQ-2 refused to complete the PHQ-9. Seventeen people who screened positive on the PHQ-9 (score of ≥ 10) were referred to their physician for follow-up. At an average of 10 weeks follow-up, ten of the 17 people had seen their physician and received treatment, two were lost to follow-up and five did not receive treatment.

73. In summary, we did not identify any evidence addressing whether the complete screening programme would be acceptable to the general population in the UK. Evidence from other countries suggests that the likely uptake of a screening offer and subsequent treatment should be assessed in the UK before screening is put in place.

The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment)

74. We did not identify any studies directly addressing the harms of screening.
75. Possible harms associated with screening identified in the previous 2006 NSC review included issues relating to stigma associated with mental health problems, the risk of labelling someone with transient disease as having an illness, possible discrimination by insurance companies and diverting resources from patients with greater need (Gilbody et al 2006). The potentially high number of false positive screening results also brings the risk of over-treatment.
76. A qualitative study in the Netherlands interviewed 23 people aged ≥ 75 years who had screened positive for depression, five of whom had accepted the offer of treatment through a Coping with Depression course (van der Weele et al 2012). Reasons for not accepting treatment included negative expectations about participating in the treatment or negative thoughts about themselves, such as being too old to learn new things. People who declined the course also mostly considered depression to be a much more severe state than they were experiencing themselves.

77. This criterion is not met.

The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (i.e. value for money).

78. Mihalopoulos et al (2012) assessed the population-level cost-effectiveness of screening Australian children and adolescents aged 11 to 17 in school, followed by a psychological intervention for those showing elevated signs of depression. The authors concluded that the screening and intervention represented good value for money, however this modelling may not be generalisable to a UK context.
79. The literature search for this review identified one study assessing the cost effectiveness of screening, however we did not identify any studies assessing cost-effectiveness in a UK context. This criterion is not met.

The remaining NSC criteria, covering managing and monitoring a screening programme, staffing, facilities for testing and treatment and evidence-based information for screening participants have not been considered as it would be premature to assess screening for depression against these criteria at present.

Implications for policy

Although depression is the most common mental disorder in community settings and can have a substantial impact on people's lives, there are important areas within the NSC criteria for appraising the viability, effectiveness and appropriateness of a screening programme that are still not met.

- As with the previous 2010 review we identified questionnaire-based tests with moderate to good sensitivity, but their positive predictive values are still poor in the general population, meaning that screening would result in a substantial number of false positive screening results.
- Although there is some encouraging evidence that psychological intervention for people with subthreshold depression may prevent the onset of major depression in the following two years, the upper limit of the confidence interval for this effect (incident rate ratio = 0.91, equivalent to a 9% reduction in the incidence of major depression) indicates that wider introduction of preventive psychological intervention might have quite limited impact.
- It is still uncertain whether intervention for subthreshold depression would reduce the likelihood of major depression in the longer-term (beyond two years).
- There is evidence from RCTs that collaborative care results in better outcomes than usual care, however this has not been evaluated in a screen detected population and it is uncertain how widely the approach has been implemented in the UK.
- Key criteria for RCTs assessing screening for depression have been identified. No RCTs have been done that meet these.

Implications for research

There are a number of areas where further research would be beneficial:

- An RCT assessing the ability of screening for depression to reduce mortality and morbidity that meets all of the following three criteria:
 - determining eligibility and randomising patients before screening
 - excluding patients already known to have depression or already being treated for depression
 - providing similar depression care options to patients in both trial arms, whether they are identified as depressed by screening or via other methods, such as self-report or unaided clinician diagnosis.
- Studies assessing the longer term outcomes (beyond two-years) for the treatment of screen-detected or subthreshold depression using assessors who are blinded to the participants group. Ideally this follow-up period would be incorporated into the design of the RCT of screening for depression.
- Further information on which patients who screen positive for depression are likely to recover without substantial intervention and which may need more intensive intervention.
- Studies on the likely acceptability of screening for depression in a UK population.

Appendix A

Literature search on screening for depression Paula Coles, Information Scientist, March/ April 2014

BACKGROUND:

The previous review and consultation on screening for depression by the UK NSC was completed in 2010 (<http://www.screening.nhs.uk/depression>)

SOURCES SEARCHED: Medline, Embase, PsychINFO, Cochrane Library.

DATES OF SEARCH: January 2009 – April 2014 (all searches carried out on 31st March 2014)

SEARCH STRATEGY:

1. Depression/ (74058)
2. exp Depressive Disorder/ (79294)
3. dysthymic disorder.tw. (588)
4. (depressive adj (disorder\$ or illness\$)).tw. (23294)
5. depress\$.ti. (99322)
6. ((subclinical or subsyndromal or subthreshold or subdiagnostic) adj2 depressi\$).tw. (704)
7. 1 or 2 or 3 or 4 or 5 or 6 (179590)
8. Psychiatric Status Rating Scales/ (58421)
9. Health Status Indicators/ (19665)
10. Mass Screening/ (80640)
11. (screen\$3 or test or tests or testing or detect\$3).tw. (3050427)
12. 8 or 9 or 10 or 11 (3128273)
13. (management adj (program\$ or programme\$)).tw. (8229)
14. collaborative care.tw. (1054)
15. clinical management.tw. (19278)
16. exp Antidepressive Agents/ (119711)
17. Depressive disorder/th (9638)
18. Exercise Therapy/ (25255)
19. exp Behavior Therapy/ (51181)
20. "Outcome Assessment (Health Care)"/ (47842)
21. Treatment Outcome/ (612175)
22. outcome measure\$.tw. (142675)
23. health outcome\$.tw. (20964)
24. quality of life.tw. (145577)
25. Morbidity/ (23087)
26. Prognosis/ (352426)
27. (adverse adj (events or effects)).tw. (146166)
28. (overtreatment or over treatment).tw. (3006)
29. ((inappropriat\$ or unness\$ or unneed\$) adj3 (treat\$ or therap\$ or regimen\$)).tw. (4049)
30. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (151321)
31. randomized controlled trial.pt. (368089)
32. controlled clinical trial.pt. (87922)
33. (random\$ adj5 (alloca\$ or assign\$ or control\$)).tw. (239392)
34. (clinical adj5 trial\$).tw. (221434)
35. ((observ\$ or longitudinal or compar\$) adj5 (report\$ or stud\$ or trial\$)).tw. (621118)
36. systematic review.tw. (45414)
37. meta-analys?s.tw. (59346)
38. (guideline\$ or recommendation\$).ti. (71068)
39. 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 (1352495)
40. 7 and 12 and 30 and 39 (6102)
41. 7 and 12 and 38 (183)
42. 40 or 41 (6186)
43. limit 42 to yr="2009 -Current" (2290)
44. Beck depression inventory.tw. (7286)
45. (general health questionnaire or GHQ-60 or GHQ-30 or GHQ-28 or GHQ-20 or GHQ-12).tw. (3827)
46. Primary care evaluation of mental disorders.tw. (194)

47. (Zung self assessment depression scale or Zung self-rating depression scale).tw. (546)
48. (Hamilton depression rating scale or HDRS).tw. (3097)
49. (Patient health questionnaire or PHQ-9 or PHQ-2).tw. (1619)
50. AB Clinician depression screen.tw. (1)
51. depression anxiety stress scales.tw. (116)
52. brief symptom inventory.tw. (1007)
53. brief assessment schedule depression cards.tw. (11)
54. (Clinically Useful Depression Outcome Scale or CUDOS).tw. (17)
55. (Clinical Outcomes in Routine Evaluation Outcome Measure or CORE OM).tw. (63)
56. (Mini International Neuropsychiatric Interview or MINI).tw. (32025)
57. (Major Depression Inventory or MDI).tw. (2450)
58. (Symptom Checklist for Depression or SCL-DEP6).tw. (65)
59. (Anxiety and Depression Detector).tw. (1)
60. PRIME-MD.tw. (267)
61. (Geriatric Depression Scale or GDS).tw. (3072)
62. (Symptom Checklist or SCL-8).tw. (3213)
63. ((Hospital Anxiety and Depression Scale) or HADS).tw. (4713)
64. (Clinically Useful Depression Outcome Scale or CUDOS).tw. (17)
65. 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 (60207)
66. Depression/ (74058)
67. exp Depressive Disorder/ (79294)
68. depress\$.ti. (99322)
69. 66 or 67 or 68 (175308)
70. Mass Screening/ (80640)
71. screen\$.ti. (114886)
72. 70 or 71 (154920)
73. 65 and 69 and 72 (947)
74. limit 73 to yr="2009 -Current" (415)
75. 43 or 74 (2679)

Similar searches also carried out in Embase, PsycINFO and Cochrane Library.

Medline	2,679
Embase	2,807
PsycINFO	810
Cochrane Library	1,061
Total	7,357

Duplicates were removed leaving 5,145 unique references.

Inclusions:

- The general population (children and adolescents, adults and older people)
- Use of depression screening questionnaire in the general population, not previously diagnosed with depression
- Screening for depression (of any severity) in the general population
- Treatment of subclinical, subsyndromal, mild, moderate etc depression
- Systematic reviews of depression treatment or management in depression of unspecified severity

Exclusions:

- Antenatal and postnatal depression (covered in the psychiatric illness in pregnancy and antenatal depression policies)
- Groups identified as being at “high risk” for depression, including:
 - Those with pre-existing long-term medical or mental health conditions
 - Drug users
 - Those who have experienced domestic abuse or violence

- Those people who are institutionalised e.g. prisoners, those living in care or nursing homes etc.

360 references were deemed to be relevant.

An additional simple search was carried out to ensure that all subsequent published CADET trial studies were retrieved.

1. CADET.tw (196)
2. Collaborative care for depression.tw (86)
3. 1 or 2 (280)
4. Limit 3 to yr="2009-Current" (101)

One additional reference was found using this strategy in Medline.

These 361 references were classified into the following categories

Systematic reviews, meta- and pooled-analyses The condition (4) The test (7) Treatment for subclinical depression (10) Prevention (6) Screening (12)	39
Systematic reviews on treatment for major (or otherwise unspecified severity) depression Pharmacological therapy (63) Psychological therapy (38) Combined therapy (8) Exercise (4) Collaborative care (2)	115
Guidelines and recommendations	13
The condition Characteristics (19) Epidemiology (14)	33
The test In children and adolescents (10) In the general population (30) In older people (18)	58
Treatment for subclinical depression In children and adolescents (5) In the general population (39) In older people (3) Cost-effectiveness (1)	48
Prevention In children and adolescents (11) In the general population (3) In older people (3)	17
Screening In the general population (9) In older people (3)	12
Screening plus intervention In children and adolescents (4) In the general population (12) In older people (10)	26
Total	361

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