

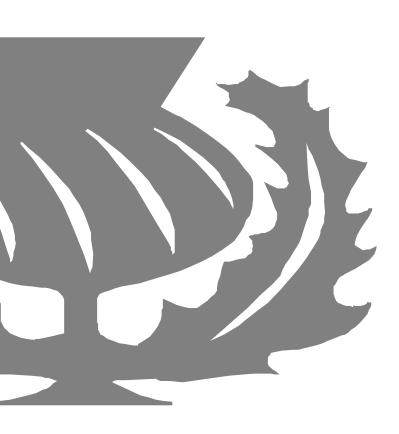




Non-pharmacological management of mild to moderate depression

A national clinical guideline

National Meeting Draft 21st August 2008



KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1 + +	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias		
1 +	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias		
1 -	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias		
2++	High quality systematic reviews of case control or cohort studies		
	High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal		
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal		
2 -	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal		
3	Non-analytic studies, eg case reports, case series		
4	Expert opinion		

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation.

- A At least one meta-analysis, systematic review, or RCT rated as 1⁺⁺, and directly applicable to the target population; or

 A body of evidence consisting principally of studies rated as 1⁺, directly applicable to the target population, and demonstrating overall consistency of results
- A body of evidence including studies rated as 2⁺⁺, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1⁺⁺ or 1⁺
- A body of evidence including studies rated as 2⁺, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2⁺⁺
- D Evidence level 3 or 4; or
 Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINTS

Recommended best practice based on the clinical experience of the guideline development group.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on our web site at www.sign.ac.uk

DRAFT – NOT FOR CIRCULATION

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1 Introduction

1.1 IMPORTANCE OF DEPRESSION

Depression is a significant health problem. It affects men and women of all ages and social backgrounds. Around one in five of the population of Scotland will experience depression at some point in their lives. Prevalence is higher in women than men.¹ It can range in severity from a relatively mild disturbance in a person's ability to enjoy their social and family lives to a severe illness where the person begins to lose touch with elements of reality, may stop eating and drinking and have a strong urge to end their life. The impact of the disorder will also be experienced by family, friends and colleagues.² Depression is one of the ten most frequent reasons for consultation with a general practitioner (GP). In Scotland in 2005/06 there were 503,700 consultations.³ Over 50% of people with depression do not seek treatment.⁴

As well as the personal and social consequences of depression there are also negative economic effects. Depression prevents many people seeking, maintaining or returning to employment and it is associated with sickness absence. In an economic analysis the total loss of output due to depression and chronic anxiety in the UK was estimated at £12 billion per year.⁵

1.2 THE NEED FOR A GUIDELINE

The most common treatment for depression is medication. A total of 3.65 million items of antidepressant medication were prescribed in Scotland during 2006/07 at a cost of £43.7m. It is estimated that 8.8% of the Scottish population aged 15 and over make daily use of antidepressant drugs.⁶

Where depression is not severe, medication may not be the most appropriate treatment option. Efficacy, potential harms and patient choice are important considerations. Medication does not influence any underlying problems or teach new ways of coping with low mood. The current National Institute for Health and Clinical Excellence (NICE) guideline recommends that for the initial treatment of mild depression medication should not be used.⁷

In Scotland, over-reliance on a pharmacological approach to depression has been recognised and is addressed in the National Mental Health Delivery Plan.⁸ Health Efficiency Access and Treatment (HEAT) targets are a core set of ministerial objectives, targets and measures for the NHS. A key target in mental health is to reduce the annual rate of increase of defined daily dose per capita of antidepressants to zero by 2009/10 and put in place the required support framework to achieve a 10% reduction in future years. This HEAT target is supported by a number of commitments that include increasing the availability of evidence based psychological therapies, and the implementation of an integrated care pathway (ICP) for depression.⁹

The ICP for depression includes a standard that requires an offer of matched self help and signposting. In addition, for those who choose a non-pharmacological approach, or for whom medication is not effective, there should be the offer of a brief depression-focused psychological intervention.⁹

The Doing Well by People with Depression (DWPD) programme highlighted the need for patients to be able to choose from a range of responses to and interventions for depression across all service providers. The evaluation recognised the value of self help and social prescribing and recommended that training for healthcare professionals pay sufficient attention to psychological therapies. Local areas were advised that in developing services they should consider a broad range of evidence based clinical interventions.¹⁰

1.3 REMIT OF THE GUIDELINE

Depression is often a multifactorial illness with biological, social and psychological factors all

contributing to the development and maintenance of a depressive episode. Similarly, during a period of depression, people typically report symptoms in all three domains: at a biological level eg sleep disruption, appetite changes; at a psychological level eg impaired concentration and memory, increased negative thinking; at a social level eg loss of self confidence, withdrawal from social contact. Recovery in one of these domains may be reflected in concurrent improvement in the others thus the interventions for depression examined in this guideline are wide ranging covering both biological and psychosocial modes.

Non-pharmacological therapies encompass psychological therapies, exercise and lifestyle interventions and several different alternative and complementary treatments, many of which are not routinely available within the NHS. This guideline provides an assessment of and presents the evidence base for the efficacy of lifestyle and self directed interventions, alternative/complementary therapies and psychological therapies for depression in adults aged 18 years and over.

Depression in children and young people is a significant issue but is beyond the scope of this guideline development project.

1.3.1 AUDIENCE

This guideline will be of interest to those developing mental health services, health care professionals in primary and secondary care and patients with depression. It will also be helpful to voluntary organisations.

1.4 DEFINITIONS

The development group adopted a pragmatic definition of depression. Given the nature of the treatment approaches studied, study populations tended to be patients with mild to moderate depression. Many studies either do not make clear the severity of depression studied and/or use diagnostic systems that do not include severity descriptors. The development group used exclusion criteria to exclude very mild depression and severe depression.

Guideline recommendations cannot be extrapolated to patients with severe depression.

Studies were excluded where there was no formal diagnosis by ICD 9, ICD 10, DSM-III or DSM-IV, or use of a recognised, validated and reliable measurement scale specifically for depressive symptoms.

Studies in patients groups with indicators of very severe depression or with significant psychological comorbidities were excluded as below:

- psychotic depression
- depression in the perinatal period and postnatal depression
- bipolar disorder
- personality disorder
- dysthymia
- primary addiction
- significant cognitive impairment (brain injury or dementia)
- learning disability.

Studies in patients with significant physical comorbidities were also excluded.

A large number of studies of mild to moderate depression had mixed patient groups, typically with anxiety disorders, included in the analysis. These studies were excluded unless there was a clear analysis of the depression sub-group.

1.5 OUTCOMES

The primary outcome of interest for the guideline was reduction in depressive symptoms as measured by a recognised depression score.

Where appropriate, secondary outcomes including illness duration, quality of life, and patient satisfaction were considered.

1.6 COMPARISONS/PLACEBO EFFECT

Concomitant medication is a significant confounding factor in studies of non-pharmacological therapies particularly in relation to treatment as usual and waiting list control comparison groups. This was taken into account when using considered judgement to assess the overall weight of evidence and corresponding grade of recommendation.

The effectiveness of interventions is generally measured against a control group to control for the placebo effect. In depression, a powerful beneficial placebo effect has been estimated at 30-50% in clinical trials. A treatment intervention which improves depressive symptoms by not more than a relevant placebo cannot be recommended.

1.7 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.7.1 PATIENT VERSION NOT AVAILABLE IN THIS DRAFT

A patient version of this guideline is available from the SIGN website, www.sign.ac.uk

1.7.2 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in the section on implementation.

2 Exercise

2.1 INTRODUCTION

Exercise is a subset of physical activity, which is any movement of the body that results in energy expenditure rising above resting level and includes activities of daily living, domestic chores, gardening and walking. (Casperson et al 1985) Exercise is undertaken to improve health or as part of sports or leisure time activities including swimming, jogging, brisk walking, going to the gym, tennis and football. Exercise may be prescribed for people with depression with 1,300 exercise referral schemes available in the UK. Less than 42 per cent of GPs have access to referral schemes and there is considerable variation in what is offered (Dugdill et al 2005). Planning and undertaking exercise allows setting and achieving goals, skill development and building self confidence and it may also provide a mechanism for social support if exercising with others. Lack of confidence or reduced motivation, due to depression, may be seen as a barrier to participation.

2.2 EFFECTIVENESS OF EXERCISE

Evidence from systematic reviews and meta-analyses consistently supports structured exercise (in a range of environments; home, leisure centre, community, countryside or healthcare setting) as an effective treatment in reducing symptoms of depression. Within some reviews and meta-analyses, pooled data include uncontrolled studies and non-randomised studies and there can be a wide range of comparison groups. Some of the earlier meta-analyses included studies without a clinical diagnosis of depression among the study participants. Drawing conclusions from reviews and meta-analyses alone is difficult as the detail of specific findings can be lost in the overall conclusions about effect size and limitations regarding the quality of the methodology of included studies. A well designed meta analyses which only included RCTs reported a low to moderate effect size for exercise compared to no treatment and a similar effect size when compared to cognitive behaviour therapy (CBT) but concluded that effectiveness could not be determined because of limitations in the methodology of the studies. ¹¹ A more recent meta-analysis found a large effect size for the effectiveness of exercise in the treatment of depression highlighting that the more recent studies provided the highest effect size. 12 They concluded that the findings indicate a causal link between exercise and a reduction in depression. Due to the inconsistency in the interpretation of findings in these metaanalyses. 11, 12 the guideline development group undertook a systematic search of the literature, critically appraising only those RCTs where the participants had a clinical diagnosis of depression. Some of the RCTs reviewed for this guideline have been included in previous meta-analyses and systematic reviews.

Exercise (both aerobic eg walking and jogging and anaerobic eg weight training) reduces depressive symptoms in patients with mild to moderate depression and is as effective as antidepressant medications. This applies to interventions delivered in a range of settings and in younger and older adults.^{7, 11-33} Limitations of the evidence base include small sample sizes in some studies and the use of volunteer subjects who may be particularly motivated to adhere to an exercise programme. A range of control groups is used in studies to control for social group effects and therapist effects whilst some studies use placebo pills, waiting list control or treatment as usual. There is large variation in the duration and intensity of exercise interventions and females and older people were over-represented. Drop-out rates were similar to medication trials (20-40%).

A number of parameters determining the effectiveness of exercise in depression have been evaluated, examining the required amount, duration, frequency and intensity required to produce benefit. One study found a requirement for a minimum: frequency of three sessions per week; of 30 – 40 minutes duration each; and a total energy expenditure 17kcal/kg per week. ²² Other studies suggest a required intensity of exercise correlated to energy expenditure of 70-80% of heart rate reserve. ^{17-19, 21, 23, 30}

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The magnitude of the effect of exercise as a treatment for depression is similar to that of antidepressant medications, with around 45% of patients responding to the treatment. 18,22 The benefits of exercise have generally been shown to be independent of social group effect. ^{22,} 1 +^{25, 26, 34, 35} Although one study showed exercise and social control leading to similar reductions in BDI score, exercise in this study was below the recommended intensity. ³³ 1-In one study comparing supervised aerobic exercise (running) with cognitive therapy, exercise was as effective as psychotherapy in reducing depressive symptoms in patients with mild to 1moderately severe depression. 20 The benefits of a completed programme of exercise can be long lasting (up to one year plus). ¹⁷, 1+ Exercise is generally safe, has few side effects and is likely to have other health benefits 1 +including prevention of overweight and obesity and cardiovascular disease. 13, 14 4

- Structured exercise is recommended as a treatment option for patients with mild to moderate depression.
- Healthcare practitioners treating patients with depression should be aware of the benefits of exercise and the local availability of opportunities for access to and support for structured exercise programmes.
- Policy makers and healthcare practitioners responsible for service development should be aware of the evidence of effectiveness of exercise in mild to moderate depression.

In patients with depression which is resistant to antidepressant medication, there is evidence from two studies that the addition of an exercise programme (in conjunction with the antidepressant treatment) was effective in reducing depression, whereas continuation of the antidepressant medication without exercise was not.^{25, 28} This is insufficient evidence on which to base a recommendation.

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DRAFT - NOT FOR CIRCULATION GUIDELINE TITLE

Nutritional supplements 3

3.1 **FOLATE**

No evidence was identified on folate alone as a treatment for depression.

A well conducted systematic review identified two studies (n = 127, n = 24) which assessed the use of folate as a supplement to psychotropic medication and found that adding folate reduced Hamilton Depression Rating Scale (HDRS) scores on average by a further 2.65 points (95% CI 0.38 to 4.93). Fewer patients treated with folate experienced a reduction in their HDRS score of less than 50% at ten weeks (relative risk (RR) 0.47, 95% CI 0.24 to 0.92). The number needed to treat (NNT) with folate for one additional person to experience a 50% reduction on this scale was 5 (95% CI 4 to 33).⁵¹ The two studies used different preparations/doses of folate and the smaller study recruited only patients with low folate (red blood cell folate < 200 microgrammes per litre).

Evidence is insufficient to clarify whether folate supplementation may benefit only those low in folate or all patients taking antidepressants.

3.2 **GINKO BILOBA**

Poor quality RCTs of ginko biloba / ginko extract in two distinct clinical groups; one in postmenopausal women, and one in patients with winter depression found ginko to be no more effective than placebo on mood and development of depressive symptoms respectively. ^{44, 45} There was no good quality evidence identified on which to base a recommendation.

3.3 **HYPERICUM EXTRACT (ST JOHN'S WORT)**

St John's Wort is a perennial herb of the genus Hypericum. Hypericum extract is available in the UK without prescription.

Clinical trials have been conducted on specific extracts from the flowers and leaves and the composition of the extracts depends on the raw material used and the extraction methods and solvents. There is no standard preparation or dose. 36-38 Although most of the clinical trials have been carried out using 300 mg preparations of Hypericum extract taken three times daily, doses range from 600 mg to 1800 mg daily. 36

A good quality Cochrane systematic review identified 37 trials involving 4,925 patients, 26 trials involving comparisons with placebo and 14 with synthetic antidepressants. Although generally rated as being of good methodological quality, several of the older trials were criticised because of their inclusion of patients with few and/or mild symptoms who did not meet criteria for major depression and/or used low doses of comparator drugs, thereby possibly overestimating the efficacy of hypericum. Newer trials (post 1995) had larger sample sizes, longer duration, and more often used placebo run-in design. In trials not restricted to patients with major depression, the combined response rate ratio for hypericum extracts compared with placebo from six larger trials was 1.71 (95% confidence interval (Cl), 1.40-2.09) and from five smaller trials was 6.13 (95% Cl, 3.63 to 10.38). In trials restricted to patients with major depression, from six larger trials was 1.15(95% Cl 1.02-1.29) and from six smaller trials was 2.06 (95% Cl, 1.65 to 2.59). ³⁶

The 26 placebo-controlled trials reviewed and the results of subsequent well conducted RCTs found that extracts of hypericum are superior to placebo in alleviating acute symptoms of mild to moderate depression.^{36, 39, 40}

In the review of 14 trials comparing extracts of hypericum with synthetic antidepressants (both TCAs and SSRIs) there was no consistent difference in efficacy in the acute treatment of mild to moderate depression. ³⁶This was confirmed in more recent RCTs ^{38, 39, 41}

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There was some evidence that extracts of *hypericum* may be as effective as synthetic antidepressant in protecting against relapse when used as prophylaxis. 42, 43

In moderate to severe major depression one study found extract of *hypericum* to be at least as effective as paroxetine. ⁴²

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No studies were identified comparing *hypericum* extracts with psychological interventions.

In general, extracts of *hypericum* have a lower side effect profile and are better tolerated than synthetic antidepressants. Extracts of *hypericum* may interact with other antidepressants, oral contraceptives, and anticoagulants (Clement et al 2006 Holistic Nursing Practice 197-203) and may decrease the plasma level of a range of prescribed drugs such as anticoagulants, oral contraceptives, and antiviral agents. There is evidence that the combination of *hypericum* extract with SSRIs can lead to serotonin overload or serotonin syndrome, particularly in older people. (Ernst et al Annals of Internal Medicine 2002, 136 42-53)



Extract of hypericum (St John's Wort) is recommended as a treatment option for patients with mild to moderate depression.



Extract of *hypericum* (St John's Wort) may be helpful in treatment of mild to moderate depression where patient preference or adverse reactions prevent use of synthetic antidepressants.



Patients wishing to use extract of *hypericum* (St John's Wort) should be advised to consult a qualified herbalist or pharmacist for advice and be made aware of the risk of interactions with common medications such as the contraceptive pill and warfarin.

3.4 INOSITOL

A good quality systematic review identified two small trials of inositol in patients with depression. Neither study found a significant beneficial effect of 12 mg daily inositol supplementation of an SSRI.⁵² There is insufficient evidence on which to base a recommendation.

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3.5 POLYUNSATURATED FATTY ACIDS

Five systematic reviews of the use of PUFAs in the treatement of patients with depression were identified. Most trials included in the reviews examined the use of PUFAs as supplements to antidepressant treatment. 46-50 Studies were mainly small and heterogeneous and there was evidence of publication bias. Most trials used eicosapentaenoic acid (EPA) but some used docosahexaenoic acid (DHA) or a mixture of PUFAs.

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The evidence base for PUFA use in depression is difficult to summarise and although there is some evidence to support modest benefit of PUFAs as a supplement to antidepressant treatment larger trials are needed.

3.6 S-ADENOSYL-L- METHIONINE

One well conducted systematic review of 28 small and heterogeneous studies found a modest clinically significant benefit of s-adenosyl-L-methionine (SAMe) over placebo in treatment of depression.⁵³ SAMe was associated with an improvement of approximately six points in the score of the HDRS. There were no significant differences in outcome when SAMe was compared with tricyclic antidepressants.

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Limitations of studies included heterogeneity in patient groups and the short duration of intervention and follow up. A range of doses were used and differing routes of administration (oral intramuscular and intravenous) employed. There was also a likelihood of publication bias. No recommendation can be made.

4 Complementary and alternative therapies

4.1 ACUPUNCTURE

Three good quality systematic reviews of poor quality RCTs of acupuncture in patients with depression were identified. 54-56 Limitations of the studies included insufficient sample sizes, heterogeneity of subjects, unclear enrolment criteria, inadequate details of randomisation, imprecise outcome measures, limited duration of treatment, absence of follow up and no power analyses. There is insufficient evidence on which to base a recommendation for the use of acupuncture either as sole treatment for depression or as an adjunct to antidepressant medication.

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4.2 ANIMAL THERAPY

There is evidence from one systematic review that the introduction of animal assisted activities may have beneficial effects on the severity of depressive symptoms in older people resident in nursing homes and residents of psychiatric institutions. The degree to which the benefits found are a result of animal contact or human contact with the animal facilitator is unclear and requires further investigation.{Souter, 2007 #103}

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Only one study was identified in non-institutionalised individuals. This study on animal facilitated therapy with dolphins reported benefit but was considered of limited relevance to the Scottish population. {Antonioli, 2005 #247}

There is insufficient evidence on which to base a recommendation.

4.3 HOMEOPATHY

One good quality systematic review identified only two RCTs, one of poor quality and one which only enrolled six patients. There is insufficient evidence on which to base a recommendation.

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4.4 LIGHT THERAPY

A high quality Cochrane review of light therapy for non-seasonal depression identified 20 RCTs comparing bright light with inactive placebo treatments for non-seasonal depression. The review found some evidence that bright light may confer modest benefits on severity of depression symptoms in the very early stages of treatment of people with depressive disorder in hospital and long term care settings. Studies included in the review were generally small (average n=31) and used short duration of intervention mainly as an adjunct to antidepressant medication, sleep deprivation or both. Many of the studies in the review were of poor methodological quality providing insufficient evidence on which to base a recommendation.

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4.5 YOGA

A systematic review of five RCTs conduced in India examined the effectiveness of different forms of yoga in patients with depression ranging in severity from mild to severe.⁵⁷ All trials reported positive benefits of yoga interventions on the severity of self reported or assessor-rated symptoms of depression. Basic details of trial methodology were poorly reported and a meta-analysis was not attempted due to the diversity of outcome measures, absence of assessor blinding in all but one of the studies, and inadequate information on participant characteristics. There were not details on method of randomisation, compliance and attrition rates. Methodological problems of the included trials mean that no recommendation can be made.

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4.6 OTHER THERAPIES

No good quality evidence was identified on the use of aromatherapy, massage therapy, reflexology, Reiki or Tai Chi as treatments for patients with depression.

5 Lifestyle modification

5.1 REDUCING ALCOHOL CONSUMPTION

No good quality evidence was identified on the effect of reducing alcohol consumption on depressive symptoms. In an analysis of secondary outcomes, one RCT suggested that, in older patients with alcohol dependence and depression, heavier drinking was associated with reduced response to antidepressant medication.⁶⁰

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5.2 REDUCING CAFFEINE INTAKE

No good quality evidence was identified on the effects of reducing caffeine intake on depressive symptoms.

5.3 INCREASING PHYSICAL ACTIVITY

The benefits of exercise/structured physical activity on depressive symptoms are outlined in section two.

5.4 ABSENCE FROM/RETURN TO WORK

No applicable evidence was identified on the effect of absence from or return to work in patients with depression. No recommendation can be made.

6 Self help

6.1 SELF HELP SUPPORT GROUPS

No studies were identified comparing self help groups as a sole intervention with waiting list control or treatment interventions. The NICE guideline on depression suggests as good practice that patients should be informed of self help groups and support groups and be encouraged to participate in such programmes where appropriate.⁷ There is no standard definition of support groups in the literature.

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6.2 WRITTEN SELF HELP

Guided self help covers a range of interventions including interactive packages and paper or web-based written self help materials which patients work through with therapist support.

A systematic review of self help interventions in depression found that greatest effectiveness is associated with supportive therapist monitoring ie guided self help, where there is input from a therapist to guide progress.⁶³ NICE reviewed nine RCTs and reported that guided self help based on either CBT or behaviour principles produces a clinically significant reduction in depressive symptoms when compared with no intervention.⁷ A facilitated self help intervention was more effective than usual GP care in people aged 60 or older with depression.⁶⁴

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The majority of studies on guided self help in depression are modelled around the principles of CBT.



Self help guided by therapist input is recommended as a treatment option for patients with mild to moderate depression.

6.3 COMPUTERISED SELF HELP

A health technology assessment (HTA) identified ten studies on computerised CBT (CCBT) and reported consistent evidence of reduction in depressive symptoms. A range of interventions were examined in a broad range of patient groups making synthesis of results and identification of the most useful package of materials difficult. The 'Beating the Blues' package was identified as effective. ⁶⁵ An RCT comparing an online interactive CBT course (Moodgym) with a written course of psychoeducation found that both were effective at reducing depression symptoms compared with a control (attention placebo). ⁶⁶

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Evidence for CBT as a therapy approach is outlined in section 7.5



Self help in the form of computerised CBT is recommended as a treatment option for patients with mild to moderate depression.

6.4 BIBLIOTHERAPY

The guideline development group defined bibliotherapy as the use of prose, poetry, biography and other creative writing as a therapy. No good quality evidence was identified.

Examination of healthy reading schemes, books on prescription or psychoeducation (use of reading about depression) was not undertaken.

7 Psychological therapies

7.1 INTRODUCTION

Psychological therapies include a range of treatments that are usually based on a time-limited interpersonal relationship between the therapist and patient/client. The aim of psychological therapies is to alleviate the symptoms of depression using a variety of techniques which put different emphasis on the past, present or future.

Examination of the optimal input/number of therapy sessions is ongoing.

7.2 BEHAVIOURAL ACTIVATION

A meta-analysis of 16 studies found activity scheduling to be effective in reducing depressive symptoms compared to treatment as usual and waiting list control, and as effective as cognitive therapy. ⁷⁴ This is consistent with the conclusions of a study incorporating behaviour therapy as part of a larger meta-analysis specifically in patients aged over 50 with depression. ⁶⁸ The need for behaviour activation to take place within a skilled therapeutic context was emphasised in the reviews.

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Behavioural activation is recommended as a treatment option for patients with mild to moderate depression.

7.3 COGNITIVE ANALYTIC THERAPY

No good quality evidence was identified on the use of cognitive analytic therapy as an intervention for patients with mild to moderate depression.

7.4 COGNITIVE BEHAVIOURAL ANALYSIS SYSTEM OF PSYCHOTHERAPY (CBASP)

CBASP is the first system of psychotherapy developed specifically to treat chronic depression. The guideline development group is considering reviewing the evidence on CBASP as an addition to this guideline post national meeting and would welcome feedback on the need for this to be examined.

7.5 COGNITIVE BEHAVIOUR THERAPY

There is robust and consistent systematic review evidence that CBT is more effective than either treatment as usual or waiting list control in the treatment of depression in adults and older adults and is at least as effective as antidepressant medication. For those studies where follow up was examined, the evidence suggests that CBT is at least as effective as antidepressant medication over six months to two year follow up. CBT is not more effective in the treatment of depression than other systematic psychological therapies.⁶⁷⁻⁷¹ ⁷²

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CBT is recommended as a treatment option for patients with mild to moderate depression.

One systematic review of CBT in adults with major depressive disorder who had not responded to at least one course of antidepressant medication identified two studies providing adequate data for interpretation. Although there was benefit of CBT (15-30 sessions) in treatment resistant depression, the evidence base is insufficient to support a recommendation in this patient group.⁷³

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Computerised CBT is discussed in section 6.3.

7.6 COUNSELLING

An RCT compared GP treatment as usual (GPTAU) with GPTAU plus counselling (average six sessions, range one to 16 sessions) in patients with BDI scores of 14 or over. Prescribed psychotropic medication was taken by 29% of the GPTAU plus counselling group and by 22% of the GPTAU. At six and 12 months follow up there were no significant differences between the study groups in BDI scores. Fewer participants in the counselling group achieved 'caseness' compared to the controls at six and 12 months but this difference was not sustained at 36 months.^{77 78,79}

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Another RCT had patient preference arms and compared randomised antidepressant treatment with randomised counselling, preference antidepressant and preference counselling. Recommended number of counselling sessions was six. GPs were guided to prescribe one of three antidepressants. There was no clear superiority of any treatment approach at eight weeks. At 12 months follow up generic counselling was as effective as antidepressants but antidepressants may result in more rapid recovery and are likely to be chosen by those who are more severely depressed.

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Counselling may be considered as a treatment option for patients with mild to moderate depression.

7.7 EMOTIONAL FREEDOM TECHNIQUE

No good quality evidence was identified on the use of emotional freedom technique as a treatment in patients with depression.

7.8 EYE MOVEMENT DESENSITISATION AND REPROCESSING

No good quality evidence was identified on the use of eye movement desensitation and reprocessing as a treatment in patients with depression.

7.9 FAMILY THERAPY

Studies of the effect of family therapy on depressive symptoms have been conducted in very specific patient populations and the results are not easily generalised. The clinical effectiveness of family therapy is dependent on having partner/family members willing to participate in and engage with therapy.

For patients with recurrent major depressive disorder who relapse, family therapy plus maintenance dosage antidepressant is superior to dose increase plus clinical management in reducing further relapse over a 12 month follow-up period.⁸⁴

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Twelve sessions of cognitive behavioural family intervention are as effective as 12 sessions of behavioural family intervention in alleviating depressive symptoms in mothers who have a child with conduct disorder.⁸⁵

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There is insufficient evidence on which to base a recommendation.

7.10 HYPNOSIS

One RCT with a range of methodological problems found that CBT supplemented by hypnosis produced a significantly larger reduction in depressive symptoms than CBT alone. This effect was sustained at six and 12 month follow-up. It is unclear if the interventions were equivalent in terms of duration of therapy offered to patients.⁵⁸

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There is insufficient evidence on which to base a recommendation.

7.11 INTERPERSONAL THERAPY FURTHER CRITICAL APPRAISAL ONGOING

A good quality systematic review of nine studies reported consistent evidence that IPT, delivered according to the standard manual over 12-20 sessions, is equivalent in effectiveness to antidepressant medication (prescribed at therapeutic doses) and to CBT in patients with mild to moderate depression.⁸⁰ A more recent RCT comparing IPT with CBT concluded that both therapies are equally effective for depression but CBT may be preferred in severe depression.⁸¹

1+

A systematic review examining achievement of complete remission in major depression found that IPT, CBT and medication were equally effective. 82

1+

IPT is a manualised therapy which does not require patient literacy.



IPT is recommended as a treatment option for patients with mild to moderate depression.

7.12 MARITAL THERAPY

A systematic review identified eight studies evaluating the effect of marital therapy on depression. A variety of treatment models were subsumed within the marital therapy approach, including CBT, emotion-focused, interpersonal and systemic therapy. Similarly, a variety of control comparisons were used, including CBT, interpersonal, drug therapy, combined individual and drug therapy and waiting list. Duration of treatment ranged from 10-20 weeks and follow up ranged from post-test to two years. Studies were characterised by small sample size, lack of intention to treat analysis and high numbers lost to follow up. The review concluded there was no evidence to suggest that martial therapy is more or less effective than individual therapies or drug therapy in the treatment of depression, even when associated with marital distress. In comparison to no/minimal treatment the outcome for depression was better in the marital therapy group, although this is based on only two small studies. The poor methodological quality of the included studies mean there is insufficient evidence on which to base any recommendation for treatment.

1+

7.13 MINDFULNESS

In one systematic review, mindfulness based cognitive therapy conducted in a group setting (8 x 2-2.5 hr sessions) reduced relapse in chronic depression (three or more depressive episodes) by over 50% over a one year follow-up period. 75

1 + +

A

Mindfulness based cognitive therapy is recommended as a treatment option to reduce relapse in patients with depression who have had three or more episodes.

7.14 NEUROLINGUISTIC PROGRAMMING

No good quality evidence was identified on the use of neurolinguistic programming as a treatment in patients with depression.

7.15 PROBLEM SOLVING THERAPY

A well conducted meta-analysis of problem solving therapies (PST) in depression found that the intervention can be effective but there were inconsistent results and significant heterogeneity across RCT studies. ⁷⁶ In patients aged over 50 PST was found to be as effective as other well conducted therapies.

1 + +



Problem solving therapy may be considered as a treatment option for patients aged over 50 with depression.

7.16 PSYCHODYNAMIC PSYCHOTHERAPY

A number of variants of psychodynamic psychotherapy are employed in studies and this lack of standardisation makes comparisons difficult.

One good quality systematic review identified six studies comparing short term psychodynamic psychotherapy with CBT for outpatients with major depression and found the two therapies to be equally effective in the treatment of depression.⁷⁰

1+

An RCT comparing short psychodynamic supportive psychotherapy (SPSP, 16 sessions over six months), alone and in combination with medication showed that SPSP was as effective as combined therapy. This study found that SPSP was more acceptable to patients than combined treatment with a high number refusing medication.⁸³

1+



Psychodynamic psychotherapy may be considered as a treatment option for patients with mild to moderate depression.

7.16.1 MUSIC THERAPY

A Cochrane review of five small, diverse and poor quality studies concluded that music therapy on its own or as an adjunct to psychological therapies, appears to be associated with improvements in mood that go beyond standardised care alone. Music therapy was well tolerated and studies had low dropout rates. ⁵⁹

1 + +

There is insufficient evidence on which to base a recommendation.

7.15.2 ART THERAPY

No good quality evidence was identified on the use of art therapy.

7.17 REMINISCENCE THERAPY

Four studies of reminiscence therapy in older adults (aged 55-87) with depression were identified.⁸⁷⁻⁹⁰ Reminiscence therapy was compared with problem solving training, goal focused psychotherapy and no treatment control. Results were equivocal and poor methodological quality of the studies and the lack of standardisation of intervention means that there is insufficient evidence on which to assess effectiveness.

1-

7.18 THOUGHT FIELD THERAPY

No good quality evidence was identified on the use of thought field therapy as a treatment in patients with depression.

8 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing treatment of depression with patients and carers and might also be useful in guiding the production of information materials.

8.1 FREQUENTLY ASKED QUESTIONS

Why me?

Depression is common; an estimated 1 in 5 of the population of Scotland will experience depression at some point in their lives. The cause or causes of depression are not clear, but are likely to include genetics, upbringing, environmental stressors and physical health. Depression can involve problems with behaviour, thinking, functioning and physical health.

What can I do?

There are a large number of therapies aimed at treating depression. Treatment is individual – what works for one person might not work at all for you. To an extent, treatment is something of a voyage of discovery, both in finding what suits, and in the effect that treatment has. You should also remember that depression, and its treatment is dynamic – how you feel, and what you think, will change over time. Consequently, some treatments will work better at one point than at others.

There is no "magic bullet". A combination of treatments is likely to be the most effective. Talk to your health professionals, your carers, family and friends about what you want, and listen to advice. If you feel able to, and have an interest, find out more about your condition. Make a treatment plan and try and stick to it, however hard it is for you, but do not shy away from making your feelings known and do what you think is best for you. Most of all, talk about how you feel, and, if necessary, be prepared to argue your case.

Remember that the professionals to whom you talk (GP, consultant, nurse, therapist) are there to help you and that you WILL get better.

Is one therapy better than another?

It is hard or even impossible to say which therapy might be the best for any one person. SOME therapies work better for SOME people at SOME times.

How do I know which therapy is best for me?

You should feel free to choose a form of therapy that fits with your ideas about your problem and yourself, and feel confident that it will work. What helps one person with depression might not help another. This is true of antidepressant medicines as well as psychological therapies and other solutions.

Do not give up if the first thing you try does not work for you. You might feel like giving up, but remember that depression itself can leave you thinking that treatment is hopeless, whereas, in actual fact, depression is treatable.

You should also understand that it can take time to feel better. Typically, around 50% of people undergoing treatment for depression will see an improvement in the symptoms within six months. However, this very much depends on the individual. It might well take longer to see an

improvement, but, with suitable treatment, things WILL get better.

Are treatments safe?

In general terms, all treatments have the potential to cause harm. People seeking to use alternative/complementary therapies should make sure the practitioner is a member of a recognised association. You should never be afraid to ask about possible harmful side effects and evidence of efficacy.

Often, people feel that a particular therapy isn't working for them, without being able to explain why. This can be because the therapy deals with matters that are uncomfortable to you, or, often, it is down to how comfortable you feel in the therapy environment, or how you get on with the therapist. While there is little point in continuing with a therapy that you do not enjoy, it should be remembered that treating depression can raise issues in your mind that can be unpleasant to deal with, but this may show that the treatment is having a positive effect.

Treatment for depression can be hard work, but it is important to try and stay the course.

Sometimes, you might feel distressed as a result of treatment. You should act on this straight away, by talking to your carers and health professionals. There are National helplines available, which are listed below. Writing down your thoughts and feelings can be helpful.

What are psychological therapies?

There are lots of different psychological therapies which can include cognitive, behaviour, interpersonal, arts or psychodynamic therapy and counselling. These types of talking treatments are carried out by people who are trained in that field. NHS access to these will depend on what services are available in your area and you may have a substantial wait. There are also private practitioners who may be able to provide these therapies.

All psychological therapies should involve a relationship with a professional who is caring, accepting and a good listener. Many counsellors see their relationship with the client as healing in itself, and your sense of comfort in talking to a counsellor is likely to be a critical issue. Some add specific treatments to help their client with particular issues.

How do I find a therapist?

Most counsellors are in private practice, although they often offer a scale of fees depending on circumstances. Many companies and organisations provide a counselling service as a work benefit to employees. It is recommended that people choose a counsellor who has been accredited, or is working towards accreditation, by one of the national bodies (see below)

The following organisations have lists of registered therapists on their websites:

- British Association for Counselling and Psychotherapy
- British Association for Behavioural and Cognitive Psychotherapies
- Counselling and Psychotherapy in Scotland
- British Psychological Society
- Scottish Institute of Human Relations
- British Psychoanalytic Council.

What are alternative and complementary therapies?

Alternative or complementary therapies are techniques used to treat a disorder or disease that are not formally embraced by mainstream medicine. Such therapies are unlikely to be freely available within the NHS and are often provided by private practitioners.

Do they work?

With the exception of St John's Wort, the guideline does not recommend any of the alternative therapies for the treatment of depression. In large part, this is not necessarily because the therapy is demonstrated to be ineffective, but because the evidence base in the medical research on these therapies is very weak – that is to say, the research done so far has not been comprehensive enough to reach a conclusion.

Depression, however, is a very individual experience. Some people might find that an alternative therapy helps them cope better with some of the symptoms of depression, or that it appears to alleviate some symptoms.

8.2 SOURCES OF FURTHER INFORMATION OR SUPPORT

Your GP should be your first point of contact regarding health matters.

Community Mental Health Teams (CMHT) are usually based either at a hospital or your local community mental health centre. Some teams provide 24 hour services so that you can contact them in a crisis. If you are already in contact with a CMHT, you may find it useful to keep their number by your phone in case you need it. Otherwise you should be able to contact your CMHT via your local social services or social work team.

Help Lines

Samaritans 0845 790 9090

Breathing Space 0800 838587

NHS 24 0845 242424

CarersLine 0808 808 7777

SANEline 0845 767 8000

Depression Alliance Scotland 0845 123 2320

The following organisations provide information and undertake work in particular areas of mental health.

Age Concern Scotland

Causewayside House 160 Causewayside Edinburgh EH9 1PR

Tel: 0845 833 0200

Email: enquiries@acscot.org.uk

Website: www.ageconcernscotland.org.uk

Bipolar Fellowship Scotland

Studio 1016 Mile End Mill Abbey Mill Business Centre Seedhill Road Paisley PA1 1TJ Tel 0141 560 2050

Email <u>info@bipolarscotland.org.uk</u>
Website: <u>www.bipolarscotland.org.uk</u>

Carers Scotland

91 Mitchell Street Glasgow G1 3LN

Tel: 0141 221 9141

Email: <u>info@carerscotland.org</u>
Website: <u>www.carer</u>scotland.org

Depression Alliance Scotland

11 Alva Street Edinburgh EH2 4PH

Tel: 0131 226 1846 Website: www.dascot.org

Depression UK

Self Help Nottingham Ormiston House 32-36 Pelham Street Nottingham NG1 2EG

Tel: 0870 774 4320 (Information line) Website: www.depressionuk.org

Health Rights Information Scotland

Scottish Consumer Council Royal Exchange House 100 Queen Street Glasgow G1 3DN

Tel: 0141 226 5261

Email: hris@scotconsumer.org.uk

Website: www.hris.org.uk

Website: www.hris.org.uk

Mental Health Foundation Scotland

Merchants House 30 George Square Glasgow G2 1EG.

Tel: 0141 572 0125 Email scotland@mhf.org.uk

Website: www.mentalhealth.org.uk/about-us/scotland/

Penumbra

Norton Park 57 Albion Road Edinburgh EH7 5QY

Tel: 0131 475 2380

Email: enquiries@penumbra.org.uk Website: www.penumbra.org.uk

Project Ability

18 Albion Street Glasgow G1 1LH

Tel: 0141 552 2822

Email: info@project-ability.co.uk
Website: www.project-ability.co.uk

The Richmond Fellowship Scotland

3 Buchanan Gate Buchanan Gate Business Park Cumbernauld Road Stepps North Lanarkshire G33 6FB

Tel: 0845 013 6300 Email: <u>info@trfs.org.uk</u> Website: <u>www.trfs.org.uk</u>

Royal British Legion Scotland

New Haig House Logie Green Road Edinburgh EH7 4HR

Tel: 0131 557 2782 Email: <u>lao@rblscotland.org</u> Website: www.rblscotland.org

SAMH

(Scottish Association for Mental Health) Cumbrae House 15 Carlton Court Glasgow G5 9JP Tel: 0141 568 7000

Email: enquire@samh.org.uk Website: www.samh.org.uk

SANE

1st Floor Cityside House 40 Adler Street London E1 1EE

Tel: 020 7375 1002 Email: <u>info@sane.org.uk</u> Website: <u>www.sane.org.uk</u>

'see me'

9-13 Maritime Street Edinburgh EH6 6SB Tel:0131 624 8945

Email: <u>info@seemescotland.org</u>
Website: www.seemescotland.org.uk

WellScotland

National Programme Team Scottish Government (3ER) St Andrews House Regent Road Edinburgh EH1 3DG

Email: well@scotland.gsi.gov.uk Website: www.wellscotland.info

VOX (Scotland)

(Voices of Experience) c/o Mental Health Foundation (Scotland) 5th Floor Merchants House 30 George Square Glasgow G2 1EG

Tel: 0141 572 1663

Email: voxscotland@yahoo.co.uk
Website: www.voxscotland.org.uk

The following organisations are relevant to the questions asked in the preparation of this guideline and can provide further information about their work.

Aromatherapy Council
Association of Master Herbalists
Association of natural Medicine
British Acupuncture Council

British Complementary Medicine Association

British Reflexology Association

Fitness Scotland

General Council for Massage Therapy International Institute of Reflexology National Institute of Medical Herbalists Register of Exercise Professionals

Self Help UK

Society of Homeopaths

Tai Chi Union

The British Wheel of Yoga

www.aromatherapycouncil.co.uk/

www.associationofmasterherbalists.co.uk

www.associationnaturalmedicine.co.uk

www.acupuncture.org.uk/

www.bcma.co.uk www.britreflex.co.uk

www.fitness-scotland.com

www.gcmt.org.uk

www.reflexology-uk.net/site

www.nimh.org.uk

www.exerciseregister.org

www.self-help.org.uk/

www.homeopathy-soh.org

www.taichiunion.com/

www.bwy.org.uk/

9 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

9.1 RESOURCE IMPLICATIONS OF KEY RECOMMENDATIONS

Key recommendation		section	Likely resource implication
R	Recommendation	2.1	To be developed by group/PM using Sara's proforma
R	Recommendation		
R	Recommendation		

9.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

8.2.1 LIFESTYLE ISSUES

- R Recommendation.
- R Recommendation.

8.2.2 TREATMENT

- R Recommendation.
- R Recommendation.

8.2.3 FOLLOW UP

- R Recommendation.
- R Recommendation.

10 The evidence base

10.1 SYSTEMATIC LITERATURE REVIEW

To be added

10.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline. The following areas for further research have been identified:

- folate use as an adjunct to antidepressant use in relation to folate status
- inosotol supplementation
- large-scale, well-controlled trials are needed to find out the favorable target subjects, therapeutic dose of EPA, and the composition of omega-3 PUFAs in treating depression
- trials of acupuncture, massage, reiki, aromatherapy and homeopathy vs antidepressant therapies
- use of power therapies (eye movement desensitisation and reprocessing (EMDR), Neuro-Linguistic Programming (NLP) thought field therapy, emotional freedom technique)
- robust studies on music and art therapies
- comparison of yoga with structured exercise programmes
- effectiveness of reduction of alcohol intake on depressive symptoms
- relative acceptability of medication and other models of treatment.

10.3 REVIEW AND UPDATING

This guideline was issued in 2008 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk.

DRAFT - NOT FOR CIRCULATION GUIDELINE TITLE

Development of the guideline 11

11.1 **INTRODUCTION**

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. The views and interests of NHS Quality Improvement Scotland as the funding body have not influenced any aspect of guideline development, including the final recommendations. Further details about SIGN and the guideline development methodology are contained in "SIGN 50: A Guideline Developer's Handbook", available at www.sign.ac.uk

THE GUIDELINE DEVELOPMENT GROUP 11.2

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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN

Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

11.2.1 Patient Involvement

11.3 CONSULTATION AND PEER REVIEW

11.3.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on and was attended by xx representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

11.3.2 SPECIALIST REVIEWERS INVITED TO COMMENT ON THIS DRAFT

or

11.3.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

SIGN is very grateful to all of these experts for their contribution to the guideline.

Title and full name
Tob title, Work place, City

11.3.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows.

Professor Gordon Lowe Chair of SIGN; Co-Editor

Dr Safia Qureshi SIGN Programme Director; Co-Editor

Dr Sara Twaddle Director of SIGN; Co-Editor

11.4 ACKNOWLEDGEMENTS

SIGN is grateful to the following former members of the guideline development group and others who have contributed to the development of this guideline

Ms Anne Finlay

Team Leader, Edinburgh Council

Dr Rebeca Martinez Dr Steven Morgan Mr Barry Smith Dr Michael Smith Dr Chris Williams

Abbreviations

BDI Beck depression inventory

CBT Cognitive behaviour therapy

CCBT Computerised cognitive behaviour therapy

CI Confidence intervalDHA Docosahexaenoic acidDSM Diagnostic standard maual

DWPD Doing well by people with depression

EMDR Eye movement desensitisation and reprocessing

EPA Eicosapentaenoic acid

CBASP Cognitive behavioural analysis system of psychotherapy

GP General practitioner

GPTAU General practitioner treatment as usual HDRS Hamilton Depression Rating Scale

hr Hour

HEAT Health efficiency access and treatment

HTA Health technology assessment

ICD International classification of disease

ICP Integrate care pathway

NICE National Institute for Health and Clinical Excellence

NLP Neuro-linguistic processing
 NNT Number needed to treat
 PST Problem solving therapy
 PUFA Polyunsaturated fatty acid
 RCT Randomised controlled trial

RR Relative risk

SAMe S-adenosyl-L-methionine

SSRI Selective serotonin reuptake inhibitor

SPSP Short psychodynamic supportive psychotherapy

TCA Tricyclic antidepressant

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