Effectiveness Bulletin

Managing depression in primary care

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Depression is a common problem which ranges from a fluctuation in mood (minor depression or dysthymia) to episodes of major depression involving affective and biological signs.

In any year general practitioners (GPs) diagnose an episode of major depression in around 3% of their patients,¹ which places a major load on resources in primary care. Only around half of patients with major depression are recognised by GPs.²⁻³ Training⁴ or the use of routine screening instruments⁵⁻⁶ can improve the ability of GPs to detect major depression, and there is evidence that early detection and treatment may reduce the likelihood that the condition will persist.⁷

Major depression is an important concept in the recognition and appropriate treatment of patients who present with depressive signs. Episodes of major depression are more common among women than men (ratio of women to men about 2:1),⁸ and are strongly associated with social circumstances.⁹⁻¹² Three main classification systems are currently used in research and clinical practice: *Diagnostic and Statistical Manual of Mental Disorders Third Edition, Revised* (DSM-III-R),¹³ Research Diagnostic Criteria (RDC),¹⁴ and ICD (tenth revision).¹⁵ The DSM-III-R classification is commonly used in trials and is appropriate for clinical practice; its criteria for major depression are summarised in the box.

Depression and suicide

There is a clear link between depression and suicide, but in primary care it is not possible to predict accurately which depressed patients

will attempt to commit suicide.¹⁶⁻¹⁹ There is currently no evidence in the United Kingdom that improved recognition and treatment of depression in primary care will lead to a decreased rate of suicide.

A recent study in the island of Götland (Sweden) provides weak evidence that the short term rate of suicide may be reduced through training and cooperation of GPs.²⁰⁻²¹ Other indicators of quality of care improved and savings in drug and hospital care were over 30 times greater than the cost of the programme. Such a study has not been replicated in the United Kingdom. Elsewhere, a systematic review of the evidence for the effectiveness of early detection of depression in symptomless people in preventing suicide recommended against routine screening for depression because of a lack of conclusive evidence that treatment improved outcome and because routine evaluation of suicide risk by primary care givers has not been evaluated.²²

Evaluating the effectiveness of treatments

The rate of spontaneous improvement among untreated people with major depression is considerable. Patients receiving no treatment (but receiving active non-specific interventions) in the placebo group of the trials showed a mean improvement in their score on the Hamilton depression rating scale at four weeks of 40-45% and 60%.²³⁻²⁵

Particular care is required in analysing and interpreting the results of trials examining the effectiveness of treatments for depression because of high drop out rates. Analysis by intention to treat (that is, by initial randomisation to treatment) is rarely undertaken; analysis by completion of treatment may be biased as dropping out is self selected and non-random.²⁶ There is considerable evidence that results obtained under the strict conditions of a trial may not be generalisable to usual clinical settings. Trials conducted on a more pragmatic basis (using a protocol based on clinical practice) can provide more useful evidence of the effectiveness of treatments.²⁷ Systematic audit procedures could be used to indicate whether the findings in clinical trials can be replicated in routine clinical practice.²⁸

Effectiveness of drug treatments

Two main groups of antidepressant drugs are

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Summary of DSM-III-R criteria for major depression

At least five of the following symptoms present during the same two week period, including at least one of (1) depressed mood or (2) loss of interest or pleasure

- (1) Depressed mood
- (2) Appreciably diminished interest or pleasure in normal activities
- (3) Significant weight loss or gain
- (4) Insomnia or hypersomnia
- (5) Agitated or retarded
- (6) Fatigue or loss of energy
- (7) Feelings of worthlessness or excessive guilt
- (8) Diminished ability to think or concentrate, or indecisiveness
- (9) Recurrent thoughts of death or suicidal thoughts or actions

commonly used in general practice. Tricyclic antidepressants and related compounds, first introduced in 1959, are the most common. The early tricyclic antidepressants have more pronounced side effects and are toxic in overdose whereas newer tricyclic or related preparations are generally less toxic.²⁹ Selective serotonin reuptake inhibitors (SSRIs), a fairly new class of antidepressants, have attracted considerable controversy and are currently being heavily promoted for use as first line treatment in depression. SSRIs are claimed to have two major advantages over tricyclic antidepressants and related compounds; though of equivalent efficacy, they have fewer side effects and they are dramatically less toxic in overdose.³⁰ However, they are around ten times more expensive than the more commonly prescribed tricyclic antidepressants and related compounds (table).

TRICYCLIC ANTIDEPRESSANTS

Evidence from randomised controlled trials in primary care indicates that a range of tricyclic antidepressants are effective in treating major depression in primary care when used in recognised therapeutic doses: the response is reduced with low dose regimens.^{23-25 31-33} Only patients with major depression respond well, as confirmed in an outpatient setting.^{32 34} Severity of depressive episode is the most powerful predictor of positive outcome of treatment among outpatients.^{34 35}

Amitriptyline has been most extensively evaluated in primary care, where it produced a 50%–100% improvement in Hamilton score against placebo at four to six weeks.^{23 24 31 32}

The response to tricyclic antidepressants does not depend on demographic variables (age, sex, and social class), previous history of depression, apparent cause (endogenous/reactive) of depressive episode,³⁶ or the presence or absence of social stress.²³ When anxiety and depression coexist there is good evidence from primary care that drug treatment produces a parallel reduction in anxiety.^{23 25 31-33}

The clinical course of depression after cessation of antidepressants has not been

investigated in primary care, but evidence from randomised controlled trials examining the outpatient treatment of major depression indicates that continued treatment with tricyclic antidepressants for several months after the episode has resolved may significantly reduce relapse and recurrence.^{37 38}

Drop out rates of 22–32% have been reported in the primary care trials. Assessing the degree of compliance with treatment is problematic and a proportion of those allocated to receive antidepressants in the trials probably did not follow the prescribed regimen.³⁹ Side effects are often reported as a reason for patients dropping out of trials, though reports of side effects are common among those taking placebo. Other factors, including perceived lack of efficacy of treatment, unhappiness about taking tablets, and improvement or deterioration of symptoms, are also common self reported reasons for dropping out.

A recent study found that around half of patients who receive treatment with antidepressants in primary care did not have major depression and so were unlikely to benefit from the treatment,⁴⁰ though there is some evidence that tricyclic antidepressants may have a similar effect to benzodiazepines in the management of symptoms of anxiety and sleep disorders.⁴¹ Patients with major depression may also be prescribed antidepressants at doses lower than those shown to be effective,⁴² and many patients who are recognised as having major depression may stop taking their treatment in the first few weeks^{42 43} and are unlikely to gain benefit.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS

SSRIs have different side effects from tricyclic antidepressants and related compounds, they are fairly expensive (table), and their role in treating depression is controversial.^{30 44-47} Zimeldine, the only SSRI evaluated in primary care,⁴⁸ was withdrawn when its widespread use indicated serious side effects in a few patients.

Sixty three double blind randomised controlled trials comparing SSRIs with

Profiles of main groups of antidepressant drugs commonly used in general practice

	Daily maintenance dosage (mg)	Cost range for 30 days' treatment (£)	Major side effects	Dangerous reactions
Older tricyclics				
Amitriptyline (non-proprietary)	50–100	0.72–1.44	General (drowsiness, dry mouth, blurred vision, constipation, urinary retention, sweating), withdrawal: reduction in dosage recommended over four weeks, anticholinergic, antimuscarinic, sedative	High risk in overdose, occasional heart block and arrhythmias
Clomipramine (non-proprietary)	30–50	2.93–3.68		
Dothiepin (non-proprietary)	75–150	4.07–8.14		
Imipramine (non-proprietary)	50–100	0.42–0.84		
Trimipramine	75–150	7.42–14.83		
Newer tricyclics and related compounds				
Lofepramine	140–210	10.68–16.02	General (drowsiness, dry mouth, blurred vision, constipation, urinary retention, sweating), withdrawal: reduction in dosage recommended over four weeks, weak antimuscarinic, weak anticholinergic, weak sedative	Low risk in overdose
Mianserin	30–90	5.24–15.71		
Trazodone	150–300	12.45–24.90		
Serotonin reuptake inhibitors				
Fluoxetine	20	32.05	May impair performance at skilled tasks, less anticholinergic than tricyclics, diarrhoea, nausea, vomiting, insomnia, sexual dysfunction, tremor, sweating	Low risk in overdose
Fluvoxamine	100–200	25.00–50.00		
Paroxetine	20–30	33.90–50.85		
Sertraline	50–100	28.40–42.61		

Source: British National Formulary, March 1992; Monthly Index of Medical Specialties (MIMS), June 1992

tricyclic or related antidepressants were identified,⁴⁹ which covered outpatient, inpatient, and primary care (one trial) settings. These trials suggest that SSRIs have a similar efficacy to the tricyclic antidepressants but their use is associated with increased use of additional drug treatment with sedatives and anxiolytics for insomnia and anxiety. Many trials contained small numbers of subjects and did not fully report their results. All the trials had short follow up periods, and any longer term differences between treatments were not evaluated. There is no good evidence for isolating subgroups of major depression for which SSRIs may be particularly effective.

When tolerability of the SSRIs was compared with the tricyclic antidepressants, by comparing total drop out⁵⁰ from each arm of the trials in which this was reported (58 pooled trials, including a total of 5518 patients), no difference was observed, the drop out rates in both groups being similar (overall odds ratio 0.95 (95% confidence interval 0.82 to 1.11)).⁴⁹

Older tricyclic antidepressants tend to be more cardiotoxic in overdose (measured as deaths/million prescriptions) than newer antidepressants,²⁹ but the older drugs are more widely used and may be prescribed to a different group of patients than the newer preparations. Given the short time periods in which these drugs have been in use and the relatively few prescriptions to date, definite conclusions would be premature.

In 1990 a total of 448 deaths resulted from poisoning involving (though not necessarily caused by) ingestion of tricyclic or related drugs.⁵¹ No deaths involving the ingestion of SSRIs were reported in that year, but one death was solely attributed to fluvoxamine in 1989.⁵² These deaths constituted only 21% of all poisonings and 7% of all suicides and undetermined deaths in 1990.⁵¹ Given the difficulty in predicting who will attempt suicide,¹⁶⁻¹⁹ the widespread use of SSRIs would be required to prevent suicide as the result of overdose from antidepressants. It is also unclear what impact this strategy would have on actual suicide rates, as some patients might seek alternative readily available means.

Effectiveness of non-drug treatments

A range of non-drug treatments for depression is used in primary care, including cognitive therapy, counselling, social worker support, and interpersonal psychotherapy. Non-drug treatments may be more acceptable to individual patients, as almost half of respondents in a recent survey perceived antidepressants to be an ineffective treatment for depression.⁵³

Six trials have examined the effectiveness of non-drug treatments for depression in primary care, though none compared them with a no treatment control.⁵⁴⁻⁵⁹ All primary care trials have some form of "treatment as usual" comparison group, in which patients in the control arm of the trial receive their GP's usual treatment. Cognitive therapy produced a more rapid improvement in depression when

compared with treatment as usual,⁵⁵⁻⁵⁶⁻⁵⁹ although relative differences in outcome disappeared within 16 weeks after completing therapy.⁵⁴⁻⁵⁸ Social work support may benefit women with an acute episode of depression on top of longstanding depression when compared with treatment as usual (the study has not been replicated for men)⁵⁷ and counselling by health visitors may double the recovery of women with postnatal depression compared with treatment as usual.⁵⁴ A trend (which did not reach significance) towards more rapid improvement of patients treated with amitriptyline by a consultant psychiatrist than of those receiving counselling or support by social workers, cognitive therapy, or treatment as usual at four weeks was not sustained at 16 weeks. When anxiety and depression coexisted there was evidence from primary care that cognitive therapy for depression produces a parallel reduction in anxiety.⁵⁹ The drop out rate in these trials among those receiving cognitive therapy ranged from 20-38%,⁵⁵⁻⁵⁶⁻⁵⁸⁻⁵⁹ among those receiving health visitor counselling was 9%,⁵⁴ and among those receiving social work support was 15%.⁵⁷

Non-drug treatments have been compared with drug treatments in large outpatient trials.³⁴⁻³⁵ Drug treatments were shown as the most effective treatment for major depression, but cognitive therapy and interpersonal psychotherapy were also effective, especially in less severe episodes.

The evidence that counselling in primary care is an effective treatment for patients with psychological problems other than major depression is equivocal.⁶⁰⁻⁶⁴ Measuring the effectiveness of these interventions for such conditions is problematic and requires carefully designed research. Around a third of practices employ a whole time therapist for counselling, but variation in professional background and qualifications is considerable.⁶⁵

Cost of treatment

Data from Trent region indicate that the cost to fundholding GPs of referral to a psychiatrist is around £90 (range £40-£140) for a first visit and £40 (range £20-£70) for subsequent visits; the cost of a domiciliary visit by a psychiatrist is around £100 (range £60-£180).⁶⁶ The cost of employing a counsellor in the GP setting varies from £15-£35 per hour, depending on employment status and level of supervision, training, and responsibility (Ball, Derbyshire Family Health Services Authority, personal communication). The cost to GPs of referral for psychotherapy is around £170 for a first visit (range £110-£250) and £80 for follow on visits (range £50-£110), based on data from Trent region.⁶⁶ The table shows the cost of drug treatment.

Advice to decision makers

GPs have the major role in treating depression, and there is a potential for developing strategies for treating and preventing depression.⁶⁷ Purchasing authorities should

ensure that secondary psychiatric services are organised coherently, with strong links with primary care, and that appropriate resources are available. They should take a lead role in facilitating the establishment of clinical guidelines,⁶⁸ which should be devised with the participation of a wide range of professional organisations and consumers, including GPs, fundholding practices, multidisciplinary secondary care mental health teams, district health authorities and purchasing consortia, family health services authorities, voluntary organisations contributing to the care of mentally ill people, and local authority mental health services.

Family health services authorities and district health authorities should consider allocating resources to fund suitably qualified therapists to undertake cognitive therapy for those depressed patients who may not otherwise receive adequate treatment for major depression. Despite the absence of clear evidence for the effectiveness of counselling family health services authorities may also consider funding counsellors or providing and training other professionals to help GPs to care for the large numbers of patients with depression and psychological problems other than those with major depression.

Clinical guidelines for managing depression will be influenced by the available services locally, but they should include the following:

- Criteria for detecting or recognising major depression in primary care, based on DSM-III-R, ICD (tenth revision), or other similar and acceptable diagnostic classifications
- Clear advice about appropriate treatment packages, including explicit criteria for prescribing different drug treatments. The guidelines may include a limited list of drugs, ensuring that expensive preparations are reserved for patients with specific drug needs, such as low cardiotoxicity or safety in overdose, or those who have failed to benefit from more conventional treatments
- Consideration of strategies for improving compliance with treatments – which may entail longer initial appointments to allow treatment options to be discussed and agreed between patients and GPs and possible side effects to be discussed
- Explicit criteria for referral to secondary care services, which should include an option for advice under which the GP might gain help in assessing and planning a patient's management, without necessarily transferring care to the secondary sector. Other possible forms of collaboration between the secondary and primary care sectors may flourish where the organisation of services favours partnership between professional and voluntary groups
- Specification of audit measures to ensure the quality of services. Audit measures should include rate of identification of major depression against a screened population of GP attenders, referrals by GPs to other professionals, prescription of different drugs, identifying the numbers of patients with

major depression who miss follow up appointments and ascertaining the reasons for defaulting in a proportion of them.

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