

Effectiveness of complementary and self-help treatments for depression

Anthony F Jorm, Helen Christensen, Kathleen M Griffiths and Bryan Rodgers

EVERY YEAR, 5.8% of Australian adults experience a depressive disorder,¹ and such disorders are the biggest source of non-fatal disease burden in Australia, accounting for 8% of disability.² Depressive symptoms that fall short of a diagnosis of a depressive disorder are also very common and are an additional contributor to disability.³

A number of treatments for depressive disorders are supported as effective by evidence-based systematic reviews, and these have been incorporated in clinical practice guidelines. However, it is estimated that only 50% of Australians who are depressed receive an evidence-based professional intervention.⁴ One possible reason for this is that many Australians state a preference for self-help and complementary therapies for depression.^{5,6} For example, in a national sample, 57% regarded vitamins, minerals, tonics or herbal medicines as likely to be helpful for treating depression, compared with 29% who regarded antidepressants as likely to be helpful.⁵ People in the community have also been found to use self-help interventions more commonly than professional treatments when they have anxiety and depressive symptoms. In one survey, the most commonly used self-help interventions over a six-month period were taking alcohol to relax (55% of respondents), taking pain relievers (55%) or becoming involved in physical activity (50%), compared with 35% who consulted a general practitioner, 20% who took antidepressants, and 4% who received psychotherapy.⁶ Australians also commonly use complementary therapies. It has been estimated that almost half of Australian adults used complementary medicines in the past year and a fifth consulted complementary practitioners.⁷ Although we do not know how much of this use is attributable to mental health problems, results from surveys in the United States indicate that people who are depressed have a higher use of complementary treatments.^{8,9}

Given their frequent use, complementary and self-help treatments warrant the same degree of evaluation as conventional treatments. The community needs information about which treatments are likely to be effective, which are not, and which have not been adequately evaluated. General practitioners can play an important role in providing guidance.

Centre for Mental Health Research, The Australian National University, Canberra, ACT.

Anthony F Jorm, PhD, DSc, Professor and Director; Helen Christensen, MPsychol, PhD, Deputy Director; Kathleen M Griffiths, BSc, PhD, Fellow; Bryan Rodgers, MA, PhD, Senior Fellow.

Correspondence: Professor A F Jorm, Centre for Mental Health Research, The Australian National University, Canberra, ACT 0200. anthony.jorm@anu.edu.au

ABSTRACT

Objectives: To review the evidence for the effectiveness of complementary and self-help treatments for depression.

Data sources: Systematic literature search using PubMed, PsycLit, the Cochrane Library and previous review papers.

Data synthesis: Thirty-seven treatments were identified and grouped under the categories of medicines, physical treatments, lifestyle, and dietary changes. We give a description of each treatment, the rationale behind the treatment, a review of studies on effectiveness, and the level of evidence for the effectiveness studies.

Results: The treatments with the best evidence of effectiveness are St John's wort, exercise, bibliotherapy involving cognitive behaviour therapy and light therapy (for winter depression). There is some limited evidence to support the effectiveness of acupuncture, light therapy (for non-seasonal depression), massage therapy, negative air ionisation (for winter depression), relaxation therapy, S-adenosylmethionine, folate and yoga breathing exercises.

Conclusion: Although none of the treatments reviewed is as well supported by evidence as standard treatments such as antidepressants and cognitive behaviour therapy, many warrant further research.

MJA 2002; 176: S84-S96

The purpose of this review is to provide an overview of the evidence on complementary and self-help treatments. We define:

- a complementary treatment as one that involves practices and beliefs that are not generally upheld by the dominant health system in Western countries; and
- a self-help treatment as one that can be used by a person without necessarily consulting a healthcare professional.

Although some self-help treatments are complementary, others are not (eg, bibliotherapy, exercise). Our review focuses on depressive disorders and depressive symptoms, but excludes bipolar disorder.

Methods

Treatments were identified by searching the 21 most popular websites on depression,¹⁰ amazon.com's list of the top 25 books on stress management, and treatments mentioned in pamphlets gathered from pharmacists and health food shops. Once the treatments had been identified, PubMed, PsycLit and the Cochrane Library were searched using the following terms: Name-of-Treatment AND (Depressi* OR Dysthym* OR Affective OR Mood). Searches were carried out of literature up to August 2001. Three recent review articles and

1: National Health and Medical Research Centre (NHMRC) levels of evidence¹⁵

Level	Description
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a parallel control group
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case-series, either post-test, or pretest/post-test
V*	No evidence or minimal evidence such as testimonials

*We have added Level V to the NHMRC scheme to allow for even weaker types of evidence

2: Treatments for which there is no evidence evaluating effects on depression

Treatment	Description and rationale
Medicines	
Ginseng	The roots of ginseng plants, or preparations of them, are used to improve energy levels and vigour. Ginseng is held to help the body cope with stress through its effects on the adrenal gland.
Lemon balm	This member of the mint family has been used traditionally for a number of medicinal purposes, including sedative and antidepressant effects.
Painkillers	Although there is no sound rationale for expecting painkillers to be helpful, many people report taking them when they feel depressed. Codeine (a narcotic), in higher doses, does have some mood-enhancing properties, and there has been speculation that aspirin could have beneficial mood-modulating effects.
Vervain	The aerial parts of this flowering plant are a traditional herbal remedy and have been used for treating depression.
Lifestyle	
Colour therapy	It has been proposed that colours in the environment can affect the mood of someone who is depressed.
Prayer	Prayer is a traditional way of relieving illness and is often used by the public for mental health problems.
Dietary changes	
Chocolate	Chocolate has several properties that could affect mood. It has a high carbohydrate content (hypothesised to increase serotonin production), contains several psychoactive substances (phenylethylamine, caffeine and theobromine, anandamide analogues), and has pleasant sensory characteristics (hypothesised to stimulate the release of endorphins).

a book on complementary therapies for mental disorders were also consulted.¹¹⁻¹⁴ Articles were included only if they reported studies of individuals selected to have a depressive disorder or a high level of depressive symptoms. Occasionally, articles on depressive symptoms in non-clinical samples not selected for depression or depressive symptoms are mentioned in the reviews below if they form an important part of the literature. However, they were not used in rating the effectiveness of treatments. Articles on bipolar disorder were excluded.

The evidence was evaluated using the levels of evidence shown in Box 1.¹⁵ It should be noted that these levels relate to the quality of the evidence, not the effectiveness of the intervention. A treatment could have been evaluated by rigorous methodologies and found to be ineffective, or, conversely, evaluated by weaker methodologies but found to be highly effective.

Results

For convenience, treatments have been grouped under the categories of medicines, physical treatments, lifestyle, and dietary changes. For some treatments, no evidence regarding effects on depression was available. These treatments are briefly summarised in Box 2.

Medicines**Ginkgo biloba**

Description: Extracts of the leaves of the maidenhair tree, *Ginkgo biloba*, are available in tablet form from health food shops.

Rationale: *Ginkgo biloba* has mainly been used for treating impaired cerebral circulation. The symptoms of this condition overlap with some symptoms of depression, suggesting the possible usefulness of ginkgo in depression.¹⁶

Quality of evidence: Level II.

Review of effectiveness: We found no trials on the treatment of depression with ginkgo. However, one randomised controlled trial has examined ginkgo as a treatment for the prevention of Seasonal Affective Disorder/Winter Type (winter depression).¹⁶ No effects were found.

Conclusion: There is currently no evidence supporting *Ginkgo biloba* as effective for depression.

Glutamine

Description: Glutamine is an amino acid. Glutamine supplements are available from health food shops.

Rationale: Glutamine is a precursor of the neurotransmitter glutamate. There is evidence that the processing of glutamine into glutamate might be affected in depression.¹⁷ Glutamine is promoted in health food shops as a "brain food" which gives more energy and improves mood.

Quality of evidence: Level IV.

Review of effectiveness: Only uncontrolled case studies have been reported to support glutamine as a treatment for depression.¹⁸

Conclusion: There is currently no good evidence to support glutamine as a treatment for depression.

Homoeopathy

Description: Homoeopathy is a system of alternative medicine involving administration of substances that are diluted until very little or none of the substance remains.

Rationale: Homoeopaths see the patient's symptoms as a sign of how the body is helping itself. To assist healing, they administer very diluted substances that produce the same symptoms and further stimulate the body's healing powers.

Quality of evidence: Level III-1.

Review of effectiveness: One placebo-controlled study has been carried out.¹⁹ Although this found homoeopathy to be effective for depression, the study's methodology was poor.

Conclusion: There is currently no adequate evidence as to whether homoeopathy is effective for depression.

Natural progesterone

Description: Natural progesterone is usually supplied in a cream, but is also available as a suppository. It differs from the synthetic progestogens or progestins. Natural progesterone has received widespread public attention as a result of its promotion in the popular book *What your doctor may not tell you about menopause*.²⁰ It can be purchased over the Internet.

Rationale: Progesterone might influence serotonergic function in the brain. It has therefore been postulated that supplementation might be a useful treatment for postnatal, premenstrual, perimenopausal and postmenopausal depression (when progesterone levels are low).

Quality of evidence: Level V.

Review of effectiveness: There have been two recent systematic reviews of the effectiveness of progesterone in treating postnatal depression. The first, a Cochrane review, failed to find any studies of acceptable methodological quality.²¹ The only study of the effectiveness of natural progesterone in postnatal depression²² was excluded on the grounds of insufficient quality. The excluded study found no effect of natural progesterone on postnatal depression. The second systematic review also concluded that there is little evidence to suggest that the hormone was effective, and that the available evidence is of low quality.²³ There are no studies of the effectiveness of natural progesterone for perimenopausal, menopausal or premenstrual depression. However, a systematic review of double-blind prospective studies found that natural progesterone does not improve mood in women diagnosed with premenstrual syndrome in general.²⁴

Conclusion: There is currently no evidence that progesterone is effective for the treatment of depression.



Phenylalanine

Description: Phenylalanine is an essential amino acid. Phenylalanine supplements are available from health food shops.

Rationale: Phenylalanine is a precursor of catecholamine neurotransmitters.

Quality of evidence: Level II.

Review of effectiveness: A controlled trial found that phenylalanine worked as well as imipramine.²⁵ However, there was no placebo control, so neither treatment may have been effective. Another study found that phenylalanine was more effective than placebo in women with premenstrual depressed mood.²⁶ However, the generalisability to other types of depression is unknown.

Conclusion: While there are some promising studies, the evidence is not substantial enough to recommend phenylalanine as an antidepressant.

S-Adenosylmethionine

Description: S-Adenosylmethionine (SAME) is an amino acid derivative that occurs naturally in all cells. It is available in tablet form and has recently been approved for use in Australia.

Rationale: SAME plays a role in many biological reactions by transferring its methyl group to DNA, proteins, phospholipids and biogenic amines.²⁷ This could result in SAME indirectly influencing neurotransmitter metabolism and receptor function.

Quality of evidence: Level I.

Review of effectiveness: A meta-analysis of six randomised controlled trials found that 70% of subjects showed some response to SAME, compared with 30% for placebo. Furthermore, pooling of data from seven trials comparing SAME with tricyclics found no difference.²⁸ Although these results are encouraging, the studies all had small sample sizes and were short

term, and there have been no comparisons with the newer antidepressants.

An advantage of SAME is that it seldom has side effects. However, the Therapeutic Goods Administration has warned that individuals who are using prescription antidepressants for bipolar depression should not use SAME unless under the supervision of a healthcare practitioner.²⁹

Conclusion: SAME is a promising treatment, but needs to be evaluated in larger, longer-term trials and compared with the newer antidepressants.

St John's wort

Description: St John's wort (*Hypericum perforatum*) is a herb available in tablets, capsules and liquid form from supermarkets and health food shops.

Rationale: St John's wort is a traditional herbal remedy in Europe. Its mode of action is not fully understood, but it appears to inhibit the synaptic reuptake of serotonin, norepinephrine and dopamine.³⁰

Quality of evidence: Level I.

Review of effectiveness: A meta-analysis of 27 randomised controlled trials concluded that this treatment is superior to placebo and not different from tricyclic antidepressants in the treatment of mild to moderate depression.³¹ A meta-analysis of six studies that met stringent methodological criteria concluded that St John's wort is 50% more likely to produce an antidepressant effect than placebo and is equivalent to standard antidepressants.³² The side effects and drop-out rate are lower with St John's wort than with tricyclic antidepressants. Fewer trials have compared St John's wort with the newer antidepressants, but results to date indicate that it is as effective as selective serotonin reuptake inhibitors.³³⁻³⁵ Although most of the evidence on St John's wort is positive, the largest trial so far found no difference between St John's wort and placebo.³⁶ This study was too recent to be included in the meta-analyses cited above.

Although St John's wort is generally reported to have fewer side effects than antidepressants, the Therapeutic Goods Administration has warned that it can interact with a number of prescription medicines, leading to a loss of therapeutic effect of these medicines. Medicines affected include HIV protease inhibitors, HIV non-nucleoside reverse transcriptase inhibitors, cyclosporin, tacrolimus, warfarin, digoxin, theophylline, anticonvulsants, oral contraceptives, SSRIs and related drugs, and triptans. An information sheet is available for healthcare professionals.³⁷

Conclusion: The use of St John's wort for mild to moderate depression is supported by most of the available evidence.

Selenium

Description: Selenium is an essential trace element. Selenium supplements are available from health food shops.

Rationale: It has been suggested that a subclinical deficiency in selenium might affect mood. Some countries have a low level of selenium in the soil, leading to reduced dietary intake. Australia is not one of these countries; New Zealand is.

Quality of evidence: Level V.

Review of effectiveness: A double-blind study has found that selenium supplements improve mood in normal subjects, suggesting the possibility of a subclinical deficiency.³⁸ However, there are no reported studies of the effectiveness of selenium supplementation as a treatment for depression.

Conclusion: There is currently no evidence to support selenium as a treatment for depression.

Tyrosine

Description: Tyrosine is an amino acid produced from phenylalanine. Tyrosine supplements are available from health food shops.

Rationale: Tyrosine is a precursor of catecholamine neurotransmitters.

Quality of evidence: Level II.

Review of effectiveness: One controlled trial has been carried out.³⁹ This trial compared tyrosine with imipramine and placebo and found no evidence that tyrosine had an antidepressant effect.

Conclusion: On the limited evidence available, tyrosine is not supported as a treatment for depression.

Vitamins

Description: Vitamins are organic chemicals that are required in small amounts for the proper functioning of the body. They are available from pharmacists, health food shops and supermarkets. They are administered in tablet, capsule or powder form, or by intramuscular or intravenous injection. Vitamins are also present in foods.

Rationale: It has been suggested that folate and vitamin B₁₂ might facilitate monoamine neurotransmitter synthesis by promoting synthesis of tetrahydrobiopterin, a cofactor involved in converting amino acids to serotonin, dopamine and norepinephrine.⁴⁰ Folate and vitamin B₁₂ might also facilitate the production of S-adenosylmethionine, leading to an increase in serotonin levels.⁴⁰ There is less detailed discussion of the proposed mechanisms by which other B vitamins might work. Several B vitamins are involved in amino acid metabolism, and vitamin B₆ is involved in the synthesis of serotonin from tryptophan. It is thought some vitamins (eg, the antioxidants) might improve mood by decreasing oxygen free radicals in the brain.⁴¹ Vitamin D might affect mood through activation effects on the brain.⁴² Vitamin D levels decrease during winter, leading to the suggestion that a deficiency in vitamin D might play a role in winter depression.⁴³

Quality of evidence: Folate: Level I (antidepressant augmentation).

Review of effectiveness: Folate. There have been four published, double-blind, randomised-controlled studies of the effectiveness of folate.⁴⁴⁻⁴⁷ Three of these trials (two using intent-to-treat analyses^{44,45}) found that methylfolate/folic acid combined with an antidepressant was more effective than an antidepressant alone,⁴⁴⁻⁴⁶ although in one study the effect was confined to women.⁴⁴ In another, the effect was observed for clinical outcome scores but not depression scores and included only patients with low folate levels.⁴⁵ The fourth study (intent-to-treat design) reported that methylfolate is at least as effective as trazadone for patients with a combined diagnosis of Alzheimer's disease and depression, with both groups showing an improvement in depression scores, and 45% of the folate group and 29% of the trazadone group showing a partial or complete response to treatment.⁴⁷ Positive effects of folate have also been reported for depressed alcoholics and depressed (but otherwise healthy) older people, although in less well controlled studies. In an open pre-post trial (one week placebo wash-out) of methylfolate with older patients with depressive disorder there was an 81% response rate among completers and a marked decrease in depression scores.⁴⁸ Similarly, a

study using a double-blind, pre-post design with one-week placebo washout reported an improvement in depression among alcoholics with depressive disorder.⁴⁹

Other B vitamins. There have been three randomised trials of the effectiveness of B vitamins other than folate for depression⁵⁰⁻⁵² and two less well controlled trials. The results of these studies are summarised below.

■ *Vitamin B₁.* There are no reported controlled trials of the effect of thiamine alone for depressed patients. However, according to one recent review, there is evidence from several double-blind, placebo-controlled studies that thiamine improves mood among people who are not selected for depression.⁵³

■ *Vitamin B₆.* A randomised controlled trial comparing the effect of vitamin B₆ with placebo on the mood of women who reported significant premenstrual mood changes found no effect of B₆ on self-reported mood change.⁵² By contrast, a meta-analysis of 10 studies involving patients with premenstrual syndrome did conclude that vitamin B₆ improves mood (odds ratio, 2.12).⁵⁴ However, the review was not restricted to patients complaining of mood problems, nor was it confined to randomised controlled trials. Two other trials of the effectiveness of B₆ for depression did not use a randomised controlled trial design. One used parallel groups and reported that adding B₆ to an antidepressant did not confer any additional benefit compared with antidepressants alone.⁵⁵ Arguably, this two-week trial was too short to permit meaningful conclusions to be drawn. The other study used a placebo-controlled cross-over design and found B₆ to be more effective than placebo in women who were B₆ deficient and suffering from depression due to the contraceptive pill.⁵⁶

■ *Vitamin B₁₂.* No significant difference between placebo and vitamin B₁₂ was found in a small, short (two-week) randomised controlled trial of the vitamin in people with winter depression.⁵¹

■ *Combined B₁, B₂ and B₆.* It has been suggested that B vitamins are most effective when taken together. There has been one small, short, randomised controlled trial comparing a combination of B vitamins (B₁, B₆ and B₁₂) and tricyclic antidepressants with placebo and tricyclic antidepressants.⁵⁰ Although the results were described as containing "promising" trends, the effects on mood were not significant.

Vitamin C. Although it has been suggested that vitamin C may be effective for depression,⁵⁷ there are no reports of group trials on the effectiveness of ascorbic acid in treating depression.



Vitamin D. In a small, short, single-blind, randomised-controlled trial involving patients with winter depression, depression was alleviated in patients receiving vitamin D but not in those receiving light therapy.⁴³

Vitamin E. There are no reported randomised controlled trials of the effectiveness of vitamin E for depression. In a very small, uncontrolled trial, vitamin E was administered to nine subjects with prolonged major depressive disorder who had responded partially to antidepressants.⁴¹ All but one patient had tried at least two antidepressants and there had been no change in the patients' clinical states in the six months preceding the trial. Following the addition of vitamin E, there was a significant improvement in depressive symptoms in the group, and six of the nine patients showed more than 80% improvement in their depression scores.

Conclusion: There is promising evidence relating to the effectiveness of folate for depression, but more research is required to confirm the findings and to identify people for whom it may be indicated (eg, males vs females; younger vs older; alcoholics vs all; augmentation vs primary treatment). There is insufficient good-quality evidence to determine whether other vitamins are effective for depression.

Physical treatments

Acupuncture

Description: Acupuncture is a traditional Chinese treatment in which needles are inserted at specific points in the body and either manipulated or electrically stimulated (electroacupuncture).

Rationale: The traditional Chinese theory is that health depends on the balance of yin and yang forces that circulate along channels in the body. Acupuncture corrects imbalances in these forces. Western scientific research with animals has indicated that acupuncture can stimulate the synthesis and release of norepinephrine and serotonin.⁵⁸

Quality of evidence: Level II.

Review of effectiveness: A small, randomised controlled trial compared acupuncture for symptoms of depression, acupuncture for other symptoms (placebo group) and a wait-list control group.⁵⁹ The specific acupuncture group improved more than the placebo group, but only marginally more than the wait-list group. A larger trial examined the benefits of adding acupuncture to antidepressant medication. Both specific acupuncture and placebo acupuncture added a therapeutic benefit, but did not differ from each

other.⁶⁰ Three controlled trials carried out in China have shown that electroacupuncture is as effective as tricyclic antidepressants.^{58,61} While two of these studies were double-blind, it is not clear if the third was. The double-blind studies included patients with both unipolar and bipolar depression, complicating the interpretation of the results.

Conclusion: Acupuncture appears promising as a treatment for depression, but requires further research.

Air ionisation

Description: Electrical devices are available to increase the concentration of negative ions in the air. These devices have been used as a treatment for winter depression, but not for other types of depression.

Rationale: Brain serotonin levels decrease in autumn and winter, which may lead to a propensity to depression. It has been proposed that negative air ions lead to an increase in serotonin levels.

Quality of evidence: Level II for winter depression; Level V for other types of depression.

Review of effectiveness: Two randomised controlled trials have compared high-density air ionisation (1×10^4 ions/cm³) with low-density air ionisation (2.7×10^6 ions/cm³) for winter depression.^{62,63} Patients were exposed to an air ioniser at home for 30 minutes each morning over 2 to 3 weeks. These studies found that high-density air ionisation was more effective than low-density ionisation. No studies have been carried out on the effectiveness of air ionisation for other types of depression.

Conclusion: There is promising evidence for high-density air ionisation as a treatment for winter depression.

Light therapy

Description: Patients are exposed to a bank of bright lights for about an hour a day. They can read or do other activities during the period of exposure, provided the light is within their visual field. An early morning walk also gives sufficient light exposure, even on overcast winter days.⁶⁴

Rationale: Exposure to bright light is used as a treatment for winter depression. Light therapy has also been proposed for non-seasonal depression. The reduced availability of sunlight in winter is hypothesised to cause a phase delay in the circadian rhythm, which in some people leads to depression. Exposure to light in the morning produces a phase advance and relieves the depression.

Quality of evidence: Level I for winter depression; Level II for non-seasonal depression.

Review of effectiveness: A series of well-controlled trials has shown that light therapy is effective for winter depression, particularly if given in the early morning.⁶⁵⁻⁶⁷ A meta-analysis of trials showed that the brighter the light, the better the response.⁶⁸ A review of trials of light therapy with non-seasonal depression also showed positive effects, although the evidence is more limited.⁶⁹

Conclusion: Light therapy appears to be effective for people with winter depression and might be helpful for non-seasonal depression.

Massage

Description: Massage therapy involves "the manipulation of soft tissue by trained therapists for therapeutic purposes".⁷⁰

Rationale: Massage therapy has ancient origins. Researchers have proposed two mechanisms for an effect in depression:

- massage shifts electroencephalogram activation from a right frontal pattern (associated with sad affect) to a left frontal or symmetrical pattern (associated with happy affect);
- massage increases vagal activity and stimulates facial expressions and vocalisations which contribute to less depressed affect.⁷⁰

Quality of evidence: Level II.

Review of effectiveness: Two randomised controlled trials have been carried out. In one, depressed children and adolescents either received massage over five days or viewed relaxing videotapes.⁷¹ The massage group improved more on depressed mood and anxiety. In the second study, depressed adolescent mothers were randomly assigned to massage therapy or relaxation therapy over a five-week period.⁷² Only the massage group showed a reduction in depression. Neither study assessed whether massage therapy had longer-term effects.

Conclusion. From the limited evidence available, massage therapy appears to have short term benefits. Its longer-term effects have not been evaluated.

Lifestyle

Aromatherapy

Description: Essential oils of plants can be heated to diffuse in a room or used as components of massage oils. The essential oils proposed for use in depression include bergamot, geranium, German chamomile, lavender and rosemary.⁷³

Rationale: Aromatherapy is a traditional treatment with no scientific rationale.

Quality of evidence: Level IV.

Review of effectiveness: Case reports of aromatherapy in depression, but no controlled trials, have been reported.⁷⁴

Conclusion: There is currently no evidence to support aromatherapy as a treatment for depression. However, aromatherapy is often used in combination with massage, which does have some evidence to support its effectiveness.

Bibliotherapy

Description: A person receives a standardised treatment in book form and works through it independently. Most bibliotherapy uses cognitive behaviour therapy.

Rationale: Cognitive behaviour therapy is usually administered by a professional therapist. It involves the therapist teaching the

patient strategies for controlling negative emotions and practising these in daily life. Meta-analyses of randomised controlled trials show that it is effective for treating anxiety and depression. Cognitive behavioural bibliotherapy tries to impart these same strategies using a standard manual.

Quality of evidence: Level I.

Review of effectiveness: A meta-analysis of six studies evaluating a range of books found that bibliotherapy is superior to no treatment for depression.⁷⁵ On measures of depressive symptoms, treated individuals averaged 0.82 standard deviation units above wait-list controls (individuals placed on a treatment waiting list). Bibliotherapy was as effective as individual or group therapy in the four studies that examined this comparison. Most studies used small samples. Participants were recruited usually by media announcements, and therapists maintained minimal contact. Two more recent studies^{76,77} support the findings of the meta-analysis. In the first, people from the community with depressive symptoms and who met criteria for major depressive disorder were compared with a wait-list control group. There were significant improvements in depressive symptoms and dysfunctional thoughts. A follow-up study reported that the effects were maintained over a three-year period. The second study⁷⁷ examined the efficacy of bibliotherapy in 30 adolescents using a cross-over design. The intervention was found to significantly reduce symptoms and lead to clinically significant levels of change. Bibliotherapy does not lead to a greater dropout rate compared with other interventions.⁷⁸

Conclusion: This treatment looks promising, but there is a need for further studies comparing it with standard professional treatments.

Bibliotherapy has not been tested on people with severe depression (these participants have been actively excluded) or people seeking help in a clinical setting. A high reading level is required for a number of the self-help books. Specific books with evidence to support them are *Control your depression*⁷⁹ and *Feeling good: the new mood therapy*.⁸⁰

Dance and movement

Description: Dance and movement therapy is a professional treatment provided by dance therapists in which patients are encouraged to express themselves in movement. Dance and movement can also be used as a self-treatment.

Rationale: Expression of feelings in movement is thought to be beneficial for mood. However, no specific mechanism has



been proposed. Dance and movement involve physical exercise, which may in itself be beneficial, as well as group interaction and listening to music.

Quality of evidence: Level III-3.

Review of effectiveness: One trial has examined the effectiveness of this treatment with depressed people.⁸¹ It randomly assigned depressed patients to receive treatment on some days and not on others. Mood was compared on treatment versus no-treatment days for each of 12 patients. Some patients were found to have better mood on treatment days. However, long-term effects on depression were not studied.

Conclusion: The effects of dance and movement on depression have yet to be adequately evaluated.

Exercise

Description: Exercise can improve endurance or improve strength, flexibility or coordination.

Rationale: Psychologically based explanations suggest that exercise might interrupt dysfunctional thoughts, serve to distract negative thoughts, or, if the exercise programs are supervised or conducted in groups, increase social interaction. Exercise may increase levels of the monoamine neurotransmitters that mediate stress and depressive reactions. Strenuous exercise may release endorphins, which have “morphine-like” qualities. Fitness levels are lower in depressed individuals. Therefore, it has been argued that increased aerobic fitness may directly lift mood.

Quality of evidence: Level I.

Review of effectiveness: Three meta-analyses of the effects of exercise on mood are available. The first two do not address specifically whether exercise is effective in clinically depressed individuals, nor do they

provide clear outcomes separately for randomised controlled trials in depressed subjects.^{82,83} A more recent review specifically examined the effectiveness of exercise in depression.⁸⁴ This review identified 11 studies which compared exercise with “no treatment”. Two of these reports were conference abstracts and two were doctoral dissertation studies. The mean difference in effect size for the studies was -1.1 standard deviation units (95% CI, -1.5 to -0.6). However, three of these studies⁸⁵⁻⁸⁷ evaluated exercise as an adjunct to standard treatment or permitted the continuation of antidepressant medication/psychotherapy. As a result, the effects of exercise may have been underestimated. Our search of published reports where antidepressant or adjunctive treatment was not permitted identified seven studies using randomised controlled trials to evaluate exercise that used clinically

depressed groups.⁸⁷⁻⁹³ Six of these were included in the earlier review, but one study⁹² is additional. Two studies included in the earlier review were excluded from our analysis because they included adjunctive treatments.^{85,86} Five of the seven randomised controlled trials⁸⁸⁻⁹² compared exercise with a no-treatment control, and all found exercise (jogging, running, walking, progressive resistance training, bicycling) to be superior. Exercise was more effective than relaxation⁸⁸ in one study, but not in another.⁸⁷ In other studies, exercise was more effective than light therapy (for non-seasonal depression),⁹² and as effective as social contact⁹⁰ and antidepressants.⁹³ Follow-up findings from the latter study indicate that individuals who benefited from exercise at four months had significantly lower relapse rates than individuals who took antidepressant medication.⁹⁴ One study that directly compared two types of exercise found no difference between weightlifting and running.⁸⁹

Conclusion: The authors of the earlier review⁸⁴ concluded that the effects of exercise might be overestimated, as many individuals who were not motivated to exercise may have been screened out, people with depression were recruited from the community rather than from clinics, and outcomes were expressed in terms of change in symptoms rather than shifts in diagnosis. They concluded "it is not possible to determine from the available evidence the effectiveness of exercise in the management of depression". In our view, this is a conservative interpretation. Further randomised controlled trials, particularly in younger people and using intent-to-treat analyses, are needed, as three of the seven articles we reviewed used older people.^{90,91,93} However, given the large effect sizes reported in these trials, the recent evidence that the effects of exercise persist at follow-up^{94,95} and the consistency of positive findings in studies excluding potentially effective treatments as "control treatments" we conclude that the use of exercise for depression is supported by the available evidence.

LeShan distance healing

Description: A healer meditates on the ill individual. The healer does not have to meet the ill person.

Rationale: Lawrence LeShan, a psychologist, has developed a theory that healing occurs naturally when the healer is in an altered state of consciousness, often achieved through meditation.

Quality of evidence: Level II.

Review of effectiveness: There is one randomised, double-blind trial examining LeShan distance healing as an adjunct to psychiatric treatment for major depression.⁹⁶ No significant effect was found, but the study lacked the statistical power to detect a small effect.

Conclusion: The limited available evidence does not support the effectiveness of LeShan distance healing.

Meditation

Description: There are many types of meditation, but all involve focusing attention on something, such as a word, a

phrase, an image, an idea or the act of breathing. For some people, meditation is a spiritual activity and they use appropriate thoughts as the focus of their meditation. However, meditation can be used as a relaxation method without any spiritual goal.

Rationale: Meditation is usually advocated for "stress" or anxiety rather than depression. However, because anxiety is often comorbid with depression, it could have a therapeutic role.

Quality of evidence: Level II.

Review of effectiveness: There is one randomised controlled trial on meditation as a treatment for depression.⁸⁷ This trial compared meditation with physical exercise and group therapy and found little difference between these treatments. However, there was no comparison with no treatment or placebo.

Conclusion: The effects of meditation on depression have yet to be fully evaluated.

Music

Description: Music has effects on the emotions and so has been tried as a therapy for depression.

Rationale: Music is hypothesised to have effects on frontal and limbic system functioning, although the mechanisms are unknown.^{97,98}

Quality of evidence: Level II.

Review of effectiveness: Randomised controlled trials of the acute effect of music on mood in depressed patients have found no effects.^{97,98} However, a controlled trial of music therapy which incorporated elements of cognitive behaviour therapy (a known effective treatment) did find a beneficial effect on depressive symptoms. There is also a Chinese study reporting a more rapid response in depressed patients exposed to music combined with antidepressants compared with patients receiving antidepressants alone, but the details of the method are not available in English.⁹⁹

Conclusion: There is no evidence that listening to music *per se* helps relieve depression.

Pets

Description: Pet ownership is promoted in the media as good for health. Regular exposure to pets is used as a therapy for people living in long-term care.

Rationale: Social support is thought to be beneficial for depressed people. Animals have the potential to have a similar effect to human social support.

Quality of evidence: Level III-2.

Review of effectiveness: Few randomised controlled trials have been carried out with depressed people and all have had methodological weaknesses. One trial with psychogeriatric inpatients found no therapeutic benefit, but it gave exercise (a possibly active treatment) to the control group and did not specifically analyse the results for the depressed subgroup.¹⁰⁰ Another negative study involved hospitalised psychiatric patients, but evaluated anxiety symptoms rather than depression as the outcome.¹⁰¹ A third trial with depressed students did find benefits, but did not use random assignment and the control group had lower depres-

sion initially.¹⁰² All studies have looked only at the short-term benefits of pet therapy rather than at the long-term benefits of pet ownership. There have been cross-sectional studies of the association between pet ownership and depressive symptoms in the general population, but these studies cannot determine cause and effect.

Conclusion: There is no adequate evidence that contact with pets alleviates depression.

Pleasant activities

Description: The depressed person identifies activities they find pleasant and does them more frequently.

Rationale: Depressed people have been observed to engage in a lower rate of pleasant activities. Therefore, engaging in a higher rate might improve their mood.

Quality of evidence: Level II.

Review of effectiveness: Encouraging a depressed person to engage in pleasant activities is a common component of cognitive behaviour therapy, which is one of the best treatments for depression. However, there has been little research into this component on its own. One randomised controlled trial found that scheduling pleasant activities helped relieve depression as much as cognitive behaviour therapy and interpersonal skills training. Furthermore, immediate treatment with pleasant activities produced a quicker response than delayed treatment.¹⁰³ However, a series of case studies using an interrupted time series design found that increases in pleasant activities did not affect mood.¹⁰⁴

Conclusion: While engaging in pleasant activities is an important component of cognitive behaviour therapy for depression, there is little evidence for its effectiveness when used alone.

Relaxation therapy

Description: Relaxation therapy refers to a number of techniques designed to teach a person to relax voluntarily. Most techniques evaluated with depression involve progressive muscle relaxation.

Rationale: Relaxation therapy is primarily designed to reduce anxiety, but has been used with depression because of the high comorbidity of anxiety and depression.

Quality of evidence: Level II.

Review of effectiveness: Seven small, controlled trials have been carried out on relaxation therapy with depression. These have found relaxation therapy to be better than no treatment,^{88,105-107} as good as tricyclic antidepressants^{108,109} and cognitive behaviour therapy,^{105,106,109} or less effective than exercise.⁸⁸ Relaxation therapy combined with antidepressant medication has been found to be more effective than medication alone.¹¹⁰



Conclusion: Relaxation therapy looks a promising treatment, but requires research in larger studies with longer-term follow-up.

Yoga

Description. Yoga includes exercises for attaining bodily and mental control and well-being.

Rationale. Yoga is often used for relief of stress and anxiety. Given the comorbidity of anxiety and depression, it may have a role in treatment of depression.

Quality of evidence. Level II.

Review of effectiveness. Two randomised controlled trials have been carried out on the use of yogic breathing exercises in depression. One compared yogic breathing with no treatment in students who had a high level of depressive symptoms.¹¹¹ After training, the students were instructed to practise for 30 minutes each morning for 30 days. The treated group was found to improve significantly more than the control group. In the second study, hospitalised patients with melancholic depression were randomly assigned to receive training in yogic breathing, electroconvulsive therapy (ECT) or imipramine.¹¹² All groups were found to improve, with the greatest improvement

after ECT. Yogic breathing did not differ from imipramine. This study did not have a placebo or no treatment control group.

Conclusion: The limited amount of research on yogic breathing looks promising. This treatment requires further evaluation.

Dietary changes

Alcohol avoidance

Description: Drinking alcohol is common in many countries and features in celebrations and other social occasions.

Rationale: Heavy drinkers, and especially those with alcohol-misuse or dependence disorders, have an increased risk of suffering from depression. There are two main ways in which reducing alcohol intake might help:

- heavy alcohol consumption might lead directly to depression, and so avoiding alcohol would reverse this effect; and
- avoiding alcohol could help by reducing problems caused by drinking (eg, financial, occupational, relationship and health problems).

Quality of evidence: Level V.

Review of effectiveness: There have been no controlled trials of reducing alcohol intake in heavy drinkers with depression. However, studies of patients admitted to alcohol

treatment programs show very high rates of depression initially and a very rapid decline in depressive symptoms following cessation of alcohol.^{113,114} The rate of recovery is much greater than seen in patients with depression unrelated to alcohol use.

Conclusion: Avoiding or reducing alcohol consumption might be an effective way of reducing depression in people with alcohol-misuse disorders. There is no evidence that it is effective for people who do not have drinking problems.

Alcohol for relaxation

Description: Drinking alcohol is common in many countries and features in celebrations and other social occasions.

Rationale: It has been suggested that alcohol has stress-buffering properties.^{115,116} Some recent surveys have shown that moderate drinkers have lower levels of depressive symptoms than non-drinkers, but the reasons for this are not known.¹¹⁷⁻¹¹⁹

Quality of evidence: Level V.

Review of effectiveness: There have been no controlled trials of using alcohol for treating depression. Experimental studies with normal populations have shown that alcohol has mood-enhancing effects, but many factors are involved, including the quantity consumed, individuals' past experience of drinking, and the circumstances in which drinking takes place.^{120,121}

Conclusion: There is insufficient evidence to determine whether moderate alcohol consumption is effective in alleviating depression.

Caffeine avoidance

Description: Caffeine is a stimulant found particularly in coffee, tea and cola drinks.

Rationale: It has been proposed that some individuals have a sensitivity to caffeine which leads to depression.¹²² These people tend to have a particular constellation of symptoms (see Sugar avoidance). There is also some evidence that caffeine can increase anxiety in individuals who experience panic attacks.¹²³ Because anxiety disorders often co-occur with depression, caffeine avoidance may confer an indirect benefit by relieving anxiety.

Quality of evidence: Level II.

Review of effectiveness: One small, randomised controlled trial has been carried out on patients whose depression was thought to be due to dietary factors.¹²² Patients were randomly assigned either to avoid sugar and caffeine or (as a control) to avoid red meat and artificial sweeteners. Patients assigned to avoid sugar and caffeine showed significantly greater improvement in depressive symptoms. Ten patients were assigned to sugar and caffeine avoidance, and subsequent testing indicated that three were sensitive to caffeine. There is no evidence on whether caffeine avoidance helps most people with depression.

Conclusion: Avoiding caffeine might benefit a minority of depressed people who show particular sensitivity to it. Further research is required to substantiate this.

Fish oils

Description: Fish, particularly oily varieties, are a natural source of omega-3 fatty acids. Fish oils are also available in capsule form as dietary supplements.

Rationale: Polyunsaturated fatty acids are important in nervous system function and fish oils are a major dietary precursor. Low plasma concentrations of a fatty acid found in fish have been associated with low concentrations of a serotonin metabolite in cerebrospinal fluid.¹²⁴ Low concentrations of this metabolite have in turn been associated with depression and suicide.

Quality of evidence: Level III-2 (for unipolar depression).

Review of effectiveness: Countries with a low level of fish consumption have been reported to have a higher prevalence of major depression.¹²⁴ A number of studies have reported a reduced level of omega-3 fatty acids in the plasma or red blood cells of depressed patients.¹²⁵ There are no randomised controlled trials of fish oils as a treatment for unipolar depression. However, there is a randomised trial of omega-3 fatty acids in bipolar disorder; this reported positive effects.¹²⁶

Conclusion: There is currently no evidence to support the effectiveness of this treatment for depression.

Sugar avoidance

Description: Reducing the amount of sucrose in the diet has been proposed to help alleviate depression in some people.

Rationale: It has been proposed that some individuals have a sensitivity to sucrose which leads to depression.¹²² These individuals are said to have symptoms such as feeling fatigued, moody and depressed, with many having headaches, sleeping more than usual, and feeling tense and irritable. Some of these symptoms (eg, sleeping more) are atypical for depression.

Quality of evidence: Level II.

Review of effectiveness: One small, randomised controlled trial has been carried out on patients whose depression was thought to be due to dietary factors.¹²² Patients were randomly assigned either to avoid sugar and caffeine or (as a control) to avoid red meat and artificial sweeteners. Patients assigned to avoid sugar or caffeine showed significantly greater improvement in depressive symptoms. Ten patients were assigned to sugar and caffeine avoidance, and subsequent testing indicated that four were sensitive to sugar. There is no evidence on whether sugar avoidance helps most people with depression. On the contrary, there is some evidence that carbohydrate intake has a short-term effect of improving mood.⁵³

Conclusion: Sugar avoidance might benefit a minority of depressed people. However, further research is required to substantiate this.

Discussion

The complementary and self-help treatments with the best evidence of effectiveness are St John's wort, physical exercise, self-help books involving cognitive behaviour therapy, and light therapy for winter depression. However, none of

these has as much support as antidepressants or face-to-face cognitive behaviour therapy, both of which are standard treatments recommended in clinical practice guidelines.¹²⁷

For example, according to recent meta-analyses, newer antidepressants have been tested on more than 30 000 participants in 315 trials¹²⁸ and cognitive behaviour therapy on 2765 participants in 48 trials.¹²⁹ By contrast, St John's wort has been tested on 2291 participants in 27 trials,³¹ exercise on 724 participants in 14 trials,⁸⁴ and self-help books involving cognitive behaviour therapy on 273 participants in six trials.⁷⁵ Furthermore, while there are some well-designed studies on these complementary and self-help treatments, in general the reported studies are of poorer quality, with common deficiencies being small sample sizes, short follow-up periods, lack of blinding, and failure to use intent-to-treat analysis. We also know little about how some of these self-help treatments perform in special populations such as children and adolescents, the elderly, and perinatal women.

There are a number of other complementary and self-help treatments which have limited evidence to support their effectiveness: acupuncture, light therapy (for non-seasonal depression), massage therapy, negative air ionisation (for winter depression), relaxation therapy, SAME, folate and yoga breathing exercises. Some of these treatments might be effective, but they have received very little research attention. Research on the effectiveness of treatments for depression has tended to focus on a small number of standard treatments and needs to be broadened, particularly in view of the public's more favourable attitudes to some non-standard treatments.

Although some complementary and self-help treatments may be useful, the available evidence is almost entirely confined to patients with mild to moderate depression. However, mild to moderate depression is more prevalent in the community than severe depression. According to data from the National Survey of Mental Health and Wellbeing,¹ the prevalences are 4.4% for mild to moderate and 2.3% for severe depression. For severely depressed people, only conventional medical treatment is supported by evidence.

Given the frequent use of complementary and self-help treatments, it would be prudent for GPs and others treating depressed patients to routinely inquire about the use of these other treatments. An important reason is to prevent potentially harmful interactions with conventional treatments. The Therapeutic Goods Administration has already issued warnings about the use of St John's wort and SAME in conjunction with some prescribed medications, and there might be unknown interactions with other complementary medicines.

Another reason to inquire about use of complementary and self-help treatments is to educate patients to make better choices. If patients wish to use such treatments, it is preferable that they use those best supported by evidence. To assist the education of the public about evidence-based treatments, a consumer guide to treatments for depression is available as a companion to this review.¹³⁰

Acknowledgements

We thank the following people for their help with this project: Trish Jacomb, Betty Kitchener, Ailsa Korten, Jo Medway, Ruth Parslow, Claire Kelly.

References

1. Andrews G, Hall W, Teesson M, Henderson S. The mental health of Australians. Canberra: Mental Health Branch, Commonwealth Department of Health and Aged Care, 1999.
2. Mathers C, Vos T, Stevenson C. The burden of disease and injury in Australia. Australian Institute of Health and Welfare. Canberra: AIHW, 1999. Available at: <<http://www.aihw.gov.au/publications/health/bdia.html>>.
3. Judd LL, Akiskal HS, Paulus MP. The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorder. *J Affect Disord* 1997; 45: 5-18.
4. Andrews G, Sanderson K, Slade T, Issakidis C. Why does the burden of disease persist? Relating the burden of anxiety and depression to effectiveness of treatment. *Bull World Health Organ* 2000; 78: 446-454.
5. Jorm AF, Korten AE, Jacomb PA, et al. "Mental health literacy": a survey of the public's ability to recognise mental disorders and their beliefs about the effectiveness of treatment. *Med J Aust* 1997; 166: 182-186.
6. Jorm AF, Medway J, Christensen H, et al. Public beliefs about the helpfulness of interventions for depression: effects on actions taken when experiencing anxiety and depression symptoms. *Aust N Z J Psychiatry* 2000; 34: 619-626.
7. MacLennan AH, Wilson DH, Taylor AW. Prevalence and cost of alternative medicine in Australia. *Lancet* 1996; 347: 569-573.
8. Kessler RC, Soukup J, Davis RB, et al. The use of complementary and alternative medicines to treat anxiety and depression in the United States. *Am J Psychiatry* 2001; 158: 289-294.
9. Unützer J, Klap R, Sturm R, et al. Mental disorders and the use of alternative medicine: results from a national survey. *Am J Psychiatry* 2000; 157: 1851-1857.
10. Griffiths K, Christensen H. The quality of web-based information on the treatment of depression. *BMJ* 2000; 321: 1511-1515.
11. Ernst E, Rand JI, Stevinson C. Complementary therapies for depression. *Arch Gen Psychiatry* 1998; 55: 1026-1032.
12. Fugh-Berman A, Cott JM. Dietary supplements and natural products as psychotherapeutic agents. *Psychosom Med* 1999; 61: 712-728.
13. Wong HC, Smith M, Boon HS. Herbal remedies in psychiatric practice. *Arch Gen Psychiatry* 1998; 55: 1033-1044.
14. Muskin PR. Complementary and alternative medicine and psychiatry. Washington DC: American Psychiatric Press, 2000.
15. National Health and Medical Research Council. How to use the evidence: assessment and application of scientific evidence. Canberra: NHMRC, 2000.
16. Lingaerde O, Foreland AR, Magnusson A. Can winter depression be prevented by *Ginkgo biloba* extract? A placebo-controlled trial. *Acta Psychiatr Scand* 1999; 100: 62-66.
17. Levine J, Panchalingam K, Rapoport A, et al. Increased cerebrospinal fluid glutamine levels in depressed patients. *Biol Psychiatry* 2000; 47: 586-593.
18. Cocchi R. Antidepressive properties of L-glutamine: preliminary report. *Acta Psychiatr Belg* 1976; 76: 658-666.
19. Kleijnen J, Knipschild P, Ter Riet G. Clinical trials of homeopathy. *BMJ* 1991; 302: 316-323.
20. Lee JR, Hopkins V. What your doctor may not tell you about menopause. New York: Warner Books, 1996.
21. Lawrie TA, Herxheimer A, Dalton K. Oestrogens and progestogens for preventing and treating postnatal depression [Cochrane review]. In: *The Cochrane Library*. Issue 2, 2000. Oxford: Update Software.
22. Van der Meer YG, Loendersloot EW, Van Loenen AC. Effects of high-dose progesterone in post-partum depression. *J Psychosom Obstet Gynaecol* 1984; 3: 67-68.
23. Granger A, Underwood M. Review of the role of progesterone in the management of postnatal mood disorders. *J Psychosom Obstet Gynaecol* 2001; 22: 49-55.
24. Altshuler LL, Hendrick V, Parry B. Pharmacological management of premenstrual disorder. *Harv Rev Psychiatry* 1995; 2: 233-245.
25. Beckmann H, Athen D, Olteanu M, Zimmer R. DL-Phenylalanine versus imipramine: a double-blind study. *Arch Psychiatr Nervenkr* 1979; 227: 49-58.
26. Giannini AJ, Sternberg DE, Martin DM, Tipton KF. Prevention of late luteal phase dysphoric disorder symptoms with DL-phenylalanine in women with abrupt β -endorphin decline: a pilot study. *Ann Clin Psychiatry* 1989; 1: 259-263.
27. Bottiglieri T, Hyland K. S-Adenosylmethionine levels in psychiatric and neurological disorders: a review. *Acta Neurol Scand* 1994; 154 Suppl: 19-26.
28. Bressa GM. S-Adenosyl-1-methionine (SAME) as antidepressant: meta-analysis of clinical studies. *Acta Neurol Scand* 1994; 154: 7-14.
29. Cesarin P. Therapeutic goods regulations. *Commonwealth of Australia Gazette* 2001: S295. Canberra.

30. Nathan P. The experimental and clinical pharmacology of St John's wort (*Hypericum perforatum* L.). *Mol Psychiatry* 1999; 4: 333-338.
31. Linde K, Mulrow CD. St John's wort for depression [Cochrane review]. Issue 1, 2002. Oxford: Update Software.
32. Kim HL, Streltzer J, Goebert D. St John's wort for depression: a meta-analysis of well defined clinical trials. *J Nerv Ment Dis* 1999; 187: 532-538.
33. Harrer G, Schmidt U, Kuhn U, Biller A. Comparison of equivalence between the St John's wort extract LoHyp-57 and fluoxetine. *Arzneimittelforschung* 1999; 49: 289-296.
34. Brenner R, Azbel V, Madhusoodanan S, Pawlowska M. Comparison of an extract of hypericum (LI 160) and sertraline in the treatment of depression: a double-blind, randomized pilot study. *Clin Ther* 2000; 22: 411-419.
35. Schrader E. Equivalence of St John's wort extract (Ze 117) and fluoxetine: a randomized, controlled study in mild-moderate depression. *Int Clin Psychopharmacol* 2000; 15: 61-68.
36. Shelton RC, Keller MB, Gelenberg A. Effectiveness of St John's wort in major depression: a randomized controlled trial. *JAMA* 2001; 285: 1978-1986.
37. Therapeutic Goods Administration. St John's Wort Information sheet for health care professionals. 2000. <<http://www.health.gov.au/tga/docs/html/info.htm>>. Accessed 20 December 2001.
38. Benton D, Cook R. The impact of selenium supplementation on mood. *Biol Psychiatry* 1991; 29: 1092-1098.
39. Gelenberg AJ, Wojcik JD, Falk WE, et al. Tyrosine for depression: a double-blind trial. *J Affect Disord* 1990; 19: 125-132.
40. Hutto BR. Folate and cobalamin in psychiatric illness. *Compr Psychiatry* 1997; 38: 305-314.
41. Morishita S, Sonohara M, Murakami H, et al. Vitamin E treatment of prolonged depression: a report of nine cases. *Int Med J* 2000; 7: 33-36.
42. Stumpf WE, Privette TH. Light, vitamin D and psychiatry. Role of 1,25 dihydroxy-vitamin D3 (soltriol) in etiology and therapy of seasonal affective disorder and other mental processes. *Psychopharmacology* 1989; 97: 285-294.
43. Gloth FM, Alam W, Hollis B. Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder. *J Nut Health Aging* 1999; 3: 5-7.
44. Coppen A, Bailey J. Enhancement of the antidepressant action of fluoxetine by folic acid: a randomised, placebo controlled trial. *J Affect Disord* 2000; 60: 121-130.
45. Godfrey PSA, Toone BK, Cawrney MWP, et al. Enhancement of recovery from psychiatric illness by methylfolate. *Lancet* 1990; 336: 392-395.
46. Coppen A, Chaudhry S, Swade C. Folic acid enhances lithium prophylaxis. *J Affect Disord* 1986; 10: 9-13.
47. Passeri M, Cucinotta G, Abate G. Oral 5'-methyltetrahydrofolic acid in senile organic mental disorders with depression: Results of a double-blind multicentre study. *Aging Clin Expt Res* 1993; 51: 63-71.
48. Guaraldi GP, Fava M, Mazzi F, La Greca P. An open trial of methyltetrahydrofolate in elderly depressed patients. *Ann Clin Psychiatry* 1993; 5: 101-105.
49. Di Palma C, Urani R, Agricola R, et al. Is methylfolate effective in relieving major depression in chronic alcoholics? A hypothesis of treatment. *Curr Ther Res Clin Exp* 1994; 55: 559-568.
50. Bell IR, Edman JS, Morrow FD, et al. Vitamin B1, B2 and B6 augmentation of tricyclic antidepressant treatment in geriatric depression with cognitive dysfunction. *J Am Coll Nutr* 1992; 11: 159-163.
51. Oren DA, Teicher MH, Schwartz PJ, et al. A controlled trial of cyanocobalamin (vitamin B12) in the treatment of winter seasonal affective disorder. *J Affect Disord* 1994; 32: 197-200.
52. Kendell KE, Schnurr PP. The effects of vitamin B6 supplementation on premenstrual symptoms. *Obstet Gynecol* 1987; 70: 145-149.
53. Benton D, Donohoe RT. The effects of nutrients on mood. *Public Health Nutr* 1999; 2: 403-409.
54. Wyatt KM, Dimmock PW, Jones PW, Shaughn O'Brien PM. Efficacy of vitamin B-6 in the treatment of premenstrual syndrome: systematic review. *BMJ* 1999; 318: 1375-1381.
55. Hoes MJAJM, Sijben N. Xanthurenic acid in depression. *J Orthomolec Med* 1987; 2: 129-136.
56. Adams PW, Rose DP, Folkard J, et al. Effect of pyridoxine hydrochloride (vitamin B6) upon depression associated with oral contraception. *Lancet* 1973; 1: 899-904.
57. Cocchi P, Silenzi M, Clabri G, Salvi G. Antidepressant effect of vitamin C. *Pediatrics* 1980; 65: 862.
58. Han JS. Electroacupuncture: an alternative to antidepressants for treating affective diseases? *Int J Neurosci* 1986; 29: 79-92.
59. Allen JJB, Schnyer RN, Hitt SK. The efficacy of acupuncture in the treatment of major depression in women. *Psychol Sci* 1998; 9: 397-401.
60. Röschke J, Wolf C, Müller MJ, et al. The benefit of whole body acupuncture in major depression. *J Affect Disord* 2000; 57: 73-81.
61. Luo H, Meng F, Jia Y, Zhao X. Clinical research on the therapeutic effect of the electroacupuncture treatment in patients with depression. *Psychiatry Clin Neurosci* 1998; 52: S338-S340.
62. Terman M, Terman JS. Treatment of seasonal affective disorder with high-output negative ionizer. *J Altern Complement Med* 1995; 1: 87-92.
63. Terman M, Terman JS, Ross DC. A controlled trial of timed bright light and negative air ionization for treatment of winter depression. *Arch Gen Psychiatry* 1998; 55: 875-882.
64. Wirz-Justice A, Graw P, Kräuchi K, et al. 'Natural' light treatment of seasonal affective disorder. *J Affect Disord* 1996; 37: 109-120.
65. Wirz-Justice A. Beginning to see the light. *Arch Gen Psychiatry* 1998; 55: 861-862.
66. Avery DH, Eder DN, Bolte MA, et al. Dawn simulation and bright light in the treatment of SAD: a controlled study. *Biol Psychiatry* 2001; 50: 205-216.
67. Wileman SM, Eagles JM, Andrew JE, et al. Light therapy for seasonal affective disorder: randomised controlled trial. *Br J Psychiatry* 2001; 178: 311-316.
68. Lee TMC, Chan CCH. Dose-response relationship of phototherapy for seasonal affective disorder: a meta analysis. *Acta Psychiatr Scand* 1999; 99: 315-323.
69. Kripke DF. Light treatment for nonseasonal depression: speed, efficacy, and combined treatment. *J Affect Disord* 1998; 49: 109-117.
70. Field T. Massage therapy effects. *Am Psychol* 1998; 53: 1270-1281.
71. Field T, Morrow C, Valdeon C, et al. Massage reduces anxiety in child and adolescent psychiatric patients. *J Am Acad Child Adolesc Psychiatry* 1992; 31: 125-131.
72. Field T, Grizzle N, Scafidi F, Schanberg S. Massage and relaxation therapies' effects on depressed adolescent mothers. *Adolescence* 1996; 31: 903-911.
73. Zand J. The natural pharmacy: herbal medicine for depression. In: Strohecker J, Strohecker NS, editors. Natural healing for depression. New York: Perigee, 1999.
74. Komori T, Fujiwara R, Tanida M, et al. Effects of citrus fragrance on immune function and depressive states. *Neuroimmunomodulation* 1995; 2: 174-180.
75. Cuipers P. Bibliotherapy in unipolar depression: a meta-analysis. *J Behav Ther Exp Psychiatry* 1997; 28: 139-147.
76. Jamison C, Scogin F. The outcome of cognitive bibliotherapy with depressed adults. *J Consult Clin Psychol* 1995; 63: 644-650.
77. Ackerson J, Scogin F, McKendree-Smith N, Lyman RD. Cognitive bibliotherapy for mild and moderate adolescent depressive symptomatology. *J Consult Clin Psychol* 1998; 66: 685-690.
78. Scogin F, Floyd M, Jamison C, et al. Negative outcomes: what is the evidence on self-administered treatments? *J Consult Clin Psychol* 1996; 64: 1086-1089.
79. Lewinsohn PM, Munoz RF, Youngren M-A, Zeiss AM. Control your depression. New York: Prentice Hall, 1986.
80. Burns DD. Feeling good: the new mood therapy. New York: Morrow, 1980.
81. Stewart NJ, McMullin LM, Rubin LD. Movement therapy with depressed inpatients: a randomized multiple single case design. *Arch Psychiatr Nurs* 1994; 8: 22-29.
82. North TC, McCullagh P, Tran ZV. Effect of exercise on depression. *Exerc Sport Sci Rev* 1990; 18: 379-415.
83. Craft LL, Landers DM. The effect of exercise on clinical depression and depression resulting from mental illness: a meta-analysis. *J Sport Exerc Psychol* 1998; 20: 339-357.
84. Lawlor DA, Hopker SW. The effectiveness of exercise as an intervention in the management of depression: systematic review and meta-regression analysis of randomised controlled trials. *BMJ* 2001; 322: 1-8.
85. Martinsen EW, Medhus A, Sandvik L. Effects of aerobic exercise on depression: a controlled study. *BMJ* 1985; 291: 109.
86. Veale D, Le Fevre K, Pantelis C, et al. Aerobic exercise in the adjunctive treatment of depression: a randomized controlled trial. *J R Soc Med* 1992; 85: 541-544.
87. Klein MH, Greist JH, Gurman AS. A comparative outcome study of group psychotherapy vs. exercise treatments for depression. *Int J Mental Health* 1985; 13: 148-177.
88. McCann L, Holmes DS. Influence of aerobic exercise on depression. *J Pers Soc Psychol* 1984; 46: 1142-1147.
89. Doyne EJ, Ossip-Klein DJ, Bowman ED, et al. Running versus weight lifting in the treatment of depression. *J Consult Clin Psychol* 1987; 55: 748-754.
90. McNeil JK, LeBlanc E, Joyner M. The effect of exercise on depressive symptoms in the moderately depressed elderly. *Psychol Aging* 1991; 6: 487-488.
91. Singh NA, Clements KM, Fiatarone MA. A randomized controlled trial of progressive resistance training in depressed elders. *J Gerontol A Biol Sci Med Sci* 1997; 52A: M27-35.
92. Pinchasov BB, Shurgaja AM, Grishchik OV, Putilov AA. Mood and energy regulation in seasonal and non-seasonal depression before and after midday treatment with physical exercise or bright light. *Psychiatry Res* 2000; 94: 29-42.
93. Blumenthal JA, Babyak MA, Moore KA, et al. Effects of training on older patients with major depression. *Arch Intern Med* 1999; 159: 19-26.
94. Babyak M, Blumenthal JA, Herman S, et al. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. *Psychosom Med* 2000; 62: 633-638.
95. Singh NA, Clements KM, Singh MA. The efficacy of exercise as a long-term antidepressant in elderly subjects: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci* 2001; 56A: M497-M504.
96. Greyson B. Distance healing of patients with major depression. *J Sci Exploration* 1996; 10: 447-465.

97. Field T, Martinez A, Nawrocki T. Music shifts frontal EEG in depressed adolescents. *Adolescence* 1998; 33: 109-116.
98. Lai YM. Effects of music listening on depressed women in Taiwan. *Issues Ment Health Nurs* 1999; 20: 229-246.
99. Chen X. Active music therapy for senile depression. *Chung Hua Shen Ching Ching Shen Ko Tsa Chih* 1992; 25: 252-253 (in Chinese).
100. Zisselman MH, Rovner BW, Shmueli Y, Ferrie P. A pet therapy intervention with geriatric psychiatry inpatients. *Am J Occup Ther* 1996; 50: 47-51.
101. Barker SB, Dawson KS. The effects of animal-assisted therapy on anxiety ratings of hospitalised psychiatric patients. *Psychiatr Serv* 1998; 49: 797-801.
102. Folse EB, Minder CC, Aycock MJ, Santana RT. Animal-assisted therapy and depression in adult college students. *Anthrozoos* 1994; 7: 188-194.
103. Zeiss AM, Lewinsohn PM, Munoz RF. Nonspecific improvement effects in depression using interpersonal skills training, pleasant activity schedules, or cognitive training. *J Consult Clin Psychol*; 47: 427-439.
104. Biglan A, Craker D. Effects of pleasant-activities manipulation on depression. *J Consult Clin Psychol* 1982; 50: 436-438.
105. Reynolds WM, Coats KI. A comparison of cognitive-behavioral therapy and relaxation training for the treatment of depression in adolescents. *J Consult Clin Psychol* 1986; 54: 653-660.
106. Kahn JS, Kehle TJ, Jenson WR, Clark E. Comparison of cognitive-behavioural, relaxation, and self-modeling interventions for depression among middle-school students. *School Psychol Rev* 1990; 19: 196-211.
107. Broota A, Dhir R. Efficacy of two relaxation techniques in depression. *J Pers Clin Stud* 1990; 6: 83-90.
108. Mclean PD, Hakstian AR. Relative endurance of unipolar depression treatment effects: longitudinal follow-up. *J Consult Clin Psychol* 1990; 58: 482-488.
109. Murphy GE, Carney RM, Knesevich MA, et al. Cognitive behaviour therapy, relaxation training, and tricyclic antidepressant medication in the treatment of depression. *Psychol Rep* 1995; 77: 403-420.
110. Bowers WA. Treatment of depressed in-patients. Cognitive therapy plus medication, relaxation plus medication, and medication alone. *Br J Psychiatry* 1990; 156: 73-78.
111. Khumar SS, Kaur P, Kaur S. Effectiveness of shavasana on depression among university students. *Indian J Clin Psychol* 1993; 20: 82-87.
112. Janakiramaiah N, Gangadhar BN, Naga Venkatesha Murthy PJ, et al. Antidepressant efficacy of Sudarshan Kriya Yoga (SKY) in melancholia: a randomized comparison with electroconvulsive therapy (ECT) and imipramine. *J Affect Disord* 2000; 57: 255-257.
113. Brown SA, Schuckit MA. Changes in depression among abstinent alcoholics. *J Stud Alcohol* 1988; 49: 412-417.
114. Davidson KM. Diagnosis of depression in alcohol dependence: changes in prevalence with drinking status. *Br J Psychiatry* 1995; 166: 199-204.
115. Neff JA, Husaini BA. Life events, drinking patterns and depressive symptomatology: the stress buffering role of alcohol consumption. *J Stud Alcohol* 1982; 43: 301-318.
116. Pearlin LI, Radaburgh CW. Economic strains and the coping functions of alcohol. *AJS* 1976; 82: 652-663.
117. Power C, Rodgers B, Hope S. U-shaped relation for alcohol consumption and health in early adulthood and implications for mortality [letter]. *Lancet* 1998; 352: 877.
118. Lipton RI. The effect of moderate alcohol use on the relationship between stress and depression. *Am J Public Health* 1994; 84: 1913-1917.
119. Rodgers B, Kortzen AE, Jorm AF, et al. Non-linear relationships in associations of depression and anxiety with alcohol use. *Psychol Med* 2000; 30: 421-432.
120. Baum-Baicker C. The psychological benefits of moderate alcohol consumption: a review of the literature. *Drug Alcohol Depend* 1985; 15: 305-322.
121. Peele S, Brodsky A. Exploring psychological benefits associated with moderate alcohol use: a necessary corrective to assessments of drinking outcomes? *Drug Alcohol Depend* 2000; 60: 221-247.
122. Christensen L, Burrows R. Dietary treatment of depression. *Behav Ther* 1990; 21: 183-193.
123. Lee MA, Flegel P, Greden JF, Cameron OG. Anxiogenic effects of caffeine on panic and depressed patients. *Am J Psychiatry* 1988; 145: 632-635.
124. Hibbeln JR. Fish consumption and major depression. *Lancet* 1998; 351: 1213.
125. Maidment ID. Are fish oils an effective therapy in mental illness — an analysis of the data? *Acta Psychiatr Scand* 2000; 102: 3-11.
126. Stoll AL, Severus E, Freeman MP. Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. *Arch Gen Psychiatry* 1999; 56: 407-412.
127. US Agency for Health Care Policy and Research. Depression in primary care: volume 2. Treatment of major depression. (Clinical practice guideline no. 5) Rockville, MD: US Department of Health and Human Services, 1993. (AHCPR Publication No. 93-0551.)
128. Williams JW, Mulrow CD, Chiquette E, et al. A systematic review of newer pharmacotherapies for depression in adults: evidence report summary. *Ann Intern Med* 2000; 132: 743-756.
129. Gloaguen V, Cottraux J, Cucherat M, Blackburn IM. A meta-analysis of the effects of cognitive therapy in depressed patients. *J Affect Disord* 1998; 49: 59-72.
130. Jorm AF, Christensen H, Griffiths KM, et al. Help for depression: what works (and what doesn't). Canberra: Centre for Mental Health Research, 2001. □