Effectiveness of treatments for depression in older people

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ABSTRACT

Objective: To conduct a systematic review of the evidence for the effectiveness of a range of possible treatments for depression in older people.

Data sources: Literature search using the PubMed, PsycInfo and Cochrane Library databases.

Data synthesis: Treatments that have been suggested to be effective for depression were grouped under three categories: medical treatments, psychological treatments, and lifestyle changes/alternative treatments. We describe each treatment, review the studies of its effectiveness in people aged ≥60 years, and give a rating of the level of evidence.

Conclusions: The treatments with the best evidence of effectiveness are antidepressants, electroconvulsive therapy, cognitive behaviour therapy, psychodynamic psychotherapy, reminiscence therapy, problem-solving therapy, bibliotherapy (for mild to moderate depression) and exercise. There is limited evidence to support the effectiveness of transcranial magnetic stimulation, dialectical behaviour therapy, interpersonal therapy, light therapy (for people in nursing homes or hospitals), St John's wort and folate in reducing depressive symptoms.

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Depression is a major health problem that affects many older people, causing significant distress and disability, exacerbating existing medical conditions, and resulting in earlier death and higher use of services.[1] Estimates of the prevalence of depression among elderly people living in the community vary widely, from less than 1% to 35%.[2]

Depression in older people can be distinguished from that in younger adults by a different symptom profile and possible additional causes. In depressed older adults, depressed mood may be less commonly reported, while somatic symptoms (such as loss of appetite, lack of energy, irritability, sleeplessness, worrying, and aches and pains) are more prominent. Elderly depressed people are also more likely to have psychotic delusions than younger people.[3] This profile has prompted the development of a separate instrument, the Geriatric Depression Scale,[4] to measure depression in older people. Some aetiological pathways are also different in older people: in addition to psychosocial and genetic factors, late-life depression is also associated with cerebrovascular disease and its associated risk factors (high blood pressure, diabetes, smoking and increased serum lipid levels).[5] This additional pathway has given rise to the term "vascular depression" to describe late-onset episodes.

In this review we summarise the evidence for the effectiveness of a range of proposed treatments for depression in older people, including medical, psychological and alternative therapies and lifestyle changes. Unlike earlier reviews,[6-9] which have focused only on medical or psychological therapies for depression, our review considers all reported interventions, using the same strict methodology.

METHOD

Following the method previously described,[10,11] we performed a search (up to 30 November 2004) of the PubMed, PsycInfo and Cochrane Library databases, using the terms (depressi* OR dysthym* OR mood OR affective) AND (elder* OR old* OR late-life). A general search of these terms was supplemented with a review of each treatment type from a list compiled in an earlier study[10] to see if any of the effectiveness studies had involved older people.

Our review covered any studies of people aged 60 years or older, although most studies looked at the ≥65-years age group. We looked firstly at meta-analyses to locate relevant studies, secondly at randomised controlled trials (RCTs), or, if these were unavailable, at other types of studies. Articles were included only if they reported treatment of people with major depression or a high level of depressive symptoms. Occasionally, studies on depression symptoms in non-clinical populations (not selected for major depression or a high level of symptoms) are mentioned if they form an important part of the literature, but such studies were not used in rating the effectiveness of treatments.

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The evidence was evaluated using the National Health and Medical Research Council levels of evidence,[12] with "Level V" ("no evidence, minimal evidence such as testimonials, single case studies, controlled studies of non-clinical samples only") added to the scheme to allow for even weaker types of evidence, as was done in previous studies in this series.[10,11] 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 rigorously and found to be ineffective or, conversely, evaluated by weaker methods but found to be highly effective. For this reason, a conclusion about the effectiveness of each treatment, based on the evidence, is given at the end of each review.

RESULTS

Interventions have been grouped under the three categories of medical treatments, psychological treatments and lifestyle changes/alternative therapies. Information on safety is provided where this is an issue. Interventions for which there was no evidence in the literature of effectiveness *in older people* are listed in Box 1.

Medical treatments

Antidepressant medication

Description: Classes of drugs used to treat depression.

Quality of evidence: I.

Review of effectiveness: Antidepressants have been well tested for use in older people. A recent review of 17 RCTs concluded that three classes of antidepressants — tricyclic antidepressants, selective serotonin reuptake inhibitors and monoamine oxidase inhibitors — are effective for treating older people, even those who are hospitalised with severe physical illnesses.[13] Side effects, including increased risk

1 Treatments identified as being used for depression, but for which no evidence was found on depression in older people (aged ⩾ 60 years)

Medicines and remedies

Biotin, black cohosh (*Actaea racemosa* and *Cimicifuga racemosa*), borage (*Borago officinalis*), brahmi (*Bacopa monniera*), Californian poppy (*Eschscholtzia californica*), cat's claw (*Uncaria tomentosa*), catnip (*Nepeta cataria*), chamomile (*Anthemis nobilis*), chaste tree berry (*Vitex agnus castus*), Chinese medicinal musrooms (reishi) (*Ganoderma lucidum*), choline, chromium, coenzyme Q10, cowslip (*Primula veris*), damiana (*Turnera aphrodisiaca*), dandelion (*Taraxacum officinale*), flax seeds (linseed) (*Linum usitatissimum*), γ-aminobutyric acid (GABA), gingko (*Gingko biloba*), ginseng (*Panax ginseng*), glutamine, hawthorn (*Crataegus oxyacantha*), homoeopathy, hops (*Humulus lupulus*), hyssop (*Hyssopus officinalis*), inositol, lecithin, lemon balm (*Melissa officinalis*), L-glutamine, L-tyrosine, melatonin, milk thistle (*Silybum marianum*), mistletoe (*Viscum album*), motherwort (*Leonurus cardiaca*), nettles (*Urtica dioica*), nicotinamide, oats (*Avena sativa*), para-aminobenzoic acid (PABA), pantothenic acid, peppermint (*Mentha piperita*), phenylalanine, potassium, rehmannia (*Rehmannia glutinosa*), *S*-adenosylmethionine (SAMe), schizandra (*Schizandra chinensis*), selenium, Siberian ginseng (*Eleutherococcus senticosus*), skullcap (*Scutellaria lateriflora*), spirulina (*Spirulina maxima*, *Spirulina platensis*), St Ignatius bean (*Ignatia amara*), taurine, tension tamer, tissue salts, vervain (*Verbena officinalis*), wild yam (*Dioscorea villosa*), wood betony (*Stachys officinalis*, *Betonica officinalis*), yeast, zinc, zizyphus (*Zizyphus spinosa*).

Lifestyle and alternative treatments

Acupuncture, air ionisation, alcohol (for relaxation), aromatherapy, adequate sleep, avoidance of certain foods (barley, rye, wheat, dairy foods), caffeine avoidance, dance and movement, distraction techniques, ketogenic diet, marijuana avoidance, meditation, pets, pleasant activities, relaxation therapy, sugar avoidance, t'ai chi, yoga.

of falls and of overdose, need to be considered before a particular medication is chosen. The risk of relapse is high when medication is discontinued, and maintenance doses may be required.[14]

Conclusion: Antidepressants have sound evidence of effectiveness for use in depressed older people.

Electroconvulsive therapy

Description: Electroconvulsive therapy (ECT) involves delivering a brief electric current to the brain to produce a cerebral seizure.

Quality of evidence: I.

Review of effectiveness: From two reviews,[15,16] four RCTs were located. The only study that compared ECT with placebo (sham ECT) in older people[17] showed that ECT was effective. ECT has been widely used to treat severe depression in older people, and retrospective studies have concluded that it is reasonably safe to use, even in patients aged over 80 years.[14] Possible side effects of the treatment are memory deficit, confusion, cardiovascular problems and an increased risk of falls. ECT requires undergoing a general anaesthetic, with its attendant risks.

Conclusion: ECT is supported by a high level of evidence to show that it is an effective treatment, although potential side effects restrict its suitability mainly to people with severe depression.

Oestrogen therapy

Description: Oestrogen is usually supplied in tablet form, but is also available in the form of a skin patch, cream, gel, injection, implant or suppository. It is usually given with progestogen to reduce the risk of endometrial cancer.

Quality of evidence: II.

Review of effectiveness: One study of women who had had hysterectomies showed a decrease in depressed mood after 6 months of oestrogen treatment. However, the number of women was very small ($n = 12$) and they were relatively young.[18] The same effect has not been seen in women after natural menopause: one RCT of postmenopausal women using 0.1 mg/day estradiol skin patches found no greater improvement in depression symptoms compared with the placebo group after 8 weeks.[19] Oestrogen treatment increases the risk of cancer of the uterus and may increase the risk of breast cancer and thrombosis. It can also cause a number of other problems, such as breast tenderness and breakthrough bleeding.

Conclusion: The only RCT of oestrogen as a therapy for depression after natural menopause failed to find an effect, although it might be helpful after hysterectomy.

Testosterone therapy

Description: Testosterone can be administered orally, by injection, as skin patches or as a gel.

Quality of evidence: III-3.

Review of effectiveness: One small study[20] ($n = 16$) showed that testosterone replacement for 8 weeks quickly reduced depression in older men, but there was no control condition for comparison. The improvement was similar whether the men received 100 mg or 200 mg testosterone cypionate per week. Testosterone treatment is associated with various health risks such as acne, sleep apnoea or hepatic dysfunction. Men with prostate cancer should not have testosterone therapy, as it may accelerate growth of the cancer.

Conclusion: There is no convincing evidence that testosterone is an effective treatment for depression in older men.

Transcranial magnetic stimulation

Description: Transcranial magnetic stimulation (TMS) involves stimulating specific regions of the brain by passing strong magnetic pulses through the skull. When applied in trains of pulses it is named repetititive TMS.

Quality of evidence: II.

Review of effectiveness: Three RCTs of TMS in older people have shown no effects of TMS at 2 weeks.[21-23] One further RCT reported modest positive outcomes on depression in patients with refractory depression and stroke compared with sham treatment.[24] Some patients in these trials responded well. TMS sometimes produces a headache or discomfort on the scalp, and, in very rare cases, can produce an epileptic fit.

Conclusion: The bulk of the evidence for TMS shows no effect on depressive symptoms in older people.

Psychological treatments

Cognitive behaviour therapy

Description: Cognitive behaviour therapy (CBT) (or "cognitive therapy") is an active, time-limited therapy that aims to change the thinking and behaviour that cause or maintain depression.

Quality of evidence: I.

Review of effectiveness: Five RCTs in older people showed that CBT is effective for treating depression in later life compared with

waiting list (ie, being on a waiting list for treatment), no treatment, usual care or pill placebo.[6] However, a recent study of older adults recovering from stroke found that CBT was no more effective than no treatment.[25] A review of studies comparing CBT with antidepressant medication and other psychological treatments for depression found that CBT consistently had the largest effect sizes.[26]

Conclusion: CBT has shown to be an effective treatment for depressed older people, although stroke patients may not benefit.

Dialectical behaviour therapy

Description: Dialectical behaviour therapy can be delivered in groups or individually. The aim of the therapy is to reduce rigid or extreme responses in favour of being more flexible. The areas concentrated on relate to styles of trying to solve problems, accepting reality, relating to others and maintaining a sense of self.

Quality of evidence: II.

Review of effectiveness: One study of 34 depressed people aged 60 or older found that dialectical behaviour therapy plus antidepressant medication was more effective than antidepressant medication alone.[27]

Conclusion: One small study supports the effectiveness of dialectical behaviour therapy as an adjunct to antidepressant medication.

Interpersonal therapy

Description: Interpersonal therapy is a manual-based, time-limited therapy with a focus on current interpersonal relationships. Any of four areas may be targeted: disputes with others, insufficient social support, long-term grief following the loss of a loved one, and difficulty adapting to a role change.

Quality of evidence: II.

Review of effectiveness: One study has shown that interpersonal therapy together with placebo pills is more effective than placebo pills alone.[28] Interpersonal therapy has also been evaluated as an adjunct to antidepressant medication: in a study of depression in older people who had recently suffered the death of a spouse, these treatments in combination were more effective than antidepressants alone.[29]

Conclusion: The evidence suggests that interpersonal psychotherapy is an effective treatment for depression in older people, either alone or as an adjunct to antidepressant medication.

Problem-solving therapy

Description: Problem-solving therapy aims to teach depression sufferers effective problem-solving skills. Problems can range from major adverse life events, such as divorce, the death of a family member, or a serious medical condition, to smaller everyday problems, such as locking the keys in the car.

Quality of evidence: II.

Review of effectiveness: Four RCTs investigated the effectiveness of problem-solving therapy for older adults. Three found that problem-solving therapy was better than other therapies and better than no treatment,[30-32] but the other trial found no significant difference compared with a placebo pill.[33]

Conclusion: There is some good evidence for the effectiveness of problem-solving therapy for depression in older adults. However, in one large trial it was ineffective.

Psychodynamic psychotherapy

Description: Psychodynamic psychotherapy focuses on understanding the unique internal dynamics within a person that influence current relationships and everyday life.

Quality of evidence: II.

Review of effectiveness: Six RCTs of psychodynamic therapy or brief dynamic therapy for older adults have shown that it is an effective treatment for depression.[6] Another study showed that 4 months of psychodynamic therapy was just as effective as CBT, and that 70% of people who had received the psychotherapies were in remission at 2-year follow-up.[34]

Conclusion: Psychodynamic psychotherapy is well supported as a helpful treatment for depression in older people.

Reminiscence and life review

Description: Reminiscence and life review techniques involve going back over one's life and remembering particular days and events. The two therapies are similar, although reminiscence tends to be more about remembering pleasant events spontaneously, while life review therapy is more structured and involves an evaluation of one's life.

Quality of evidence: I.

Review of effectiveness: A recent meta-analysis of 23 studies concluded that, for older people, reminiscence and life review are effective in reducing depression.[35] Of these, 13 RCTs had a no-treatment control group. Another RCT found that autobiographical memory practice reduced depression compared with usual care.[36] While the evidence for an effect is good, one comparative study found that group life-review was not as effective as problem-solving therapy.[31]

Conclusion: Life review and reminiscence are well supported as effective treatments for depression in older people.

Bibliotherapy (self-help books)

Description: Bibliotherapy involves reading books or using the Internet or computer programs to find out about depression and learn how to reduce symptoms. It is usually based on CBT. Self-help books commonly used in studies of effectiveness include *Feeling good* (Burns, 1980), *Control your depression* (Lewinsohn et al, 1986), *Beating the blues* (Tanner and Ball, 1989) and *Change your thinking* (Edelman, 2002).

Quality of evidence: II.

Review of effectiveness: Four RCTs evaluated bibliotherapy for depression in older adults.[37] Three of these found it to be more effective than either waiting list or placebo control conditions. The fourth found that bibliotherapy was as helpful as therapy provided by a professional. No trials have tested whether bibliotherapy is helpful for older people with severe depression.

Conclusion: Bibliotherapy is an effective treatment for older people with mild to moderate depression.

Lifestyle changes and alternative therapies

Alcohol avoidance

Description: Alcohol avoidance means reducing or stopping consumption of alcohol, to avoid intoxication.

Quality of evidence: V.

Review of effectiveness: There have been no trials of alcohol avoidance as a treatment for depression in older people. Studies of older people show that excessive drinking is associated with depression, although whether the alcohol problem is a cause or a result of the depression is unclear.[38,39]

Conclusion: Although excessive drinking and drinking problems are associated with depression in older people, there have been no studies evaluating alcohol avoidance as a treatment for depression.

Exercise

Description: There are two main types of exercise: cardiovascular activity that exercises the heart and lungs (such as running or brisk walking) and resistance training that strengthens muscles (also called weight training or strength training).

Quality of evidence: II.

Review of effectiveness: We identified four RCTs[40-43] testing five exercise interventions in older people with depression. In two studies, aerobic exercise was found to be significantly more effective than health education and waiting list at lowering depression scores.[40,41] An exercise class for the over 60s, involving endurance, muscle strengthening and stretching elements, was also found to be more effective than a health education control.[42] Evidence from studies of progressive resistance training have not been consistent. One found that resistance exercise was no more effective than a health education control,[40] while another smaller study found that resistance training was effective, even at 26-month follow-up.[43]

Conclusion: There is evidence that various types of physical exercise improve mood and reduce depression in older people.

Fish oils (omega-3 fatty acids)

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.

Quality of evidence: V.

Review of effectiveness: We did not find any trials of fish oils as a treatment for depression in older people. Three studies found a correlation between low omega-3 levels in the body and depression in older people.[44-46] A very large study of older men in Finland found no association between the dietary intake of omega-3 fatty acids or fish consumption and depression.[47]

Conclusion: There have been no trials of fish oils as a treatment for depression in older people.

Light therapy

Description: Light therapy involves patients being exposed to bright light for about an hour each day. This may be artificial light, or sunlight obtained from spending a period of the day outside.

Quality of evidence: II.

Review of effectiveness: Two RCTs, one involving small numbers (n=10), demonstrated that light therapy (> 5000 lux) compared with no treatment or weak light therapy (300 lux) significantly reduced depression in long-term care residents and those in rehabilitation hospitals.[48,49] Light therapy can produce mild mania or insomnia.

Conclusion: For older adults in hospitals or nursing homes, light therapy looks promising, but needs further study.

Massage therapy

Description: Massage therapy involves sessions of manual manipulation of soft tissue, often by a trained massage therapist.

Quality of evidence: III-3.

Review of effectiveness: The only study involving older adults examined 10 elderly volunteers with mild depressive symptoms who received massages three times a week for 3 weeks, as well as giving massages to infants three times a week for 3 weeks, in a crossover design.[50] Giving and receiving massage were both effective in reducing reported depressive symptoms, but *giving* massages was the more effective of the two.

Conclusion: Without stronger evidence from studies involving a larger group of subjects, massage therapy can not be recommended as a treatment for depression in older people.

Music therapy

Description: Music therapy involves listening to music, with a view to lifting mood.

Quality of evidence: V.

Review of effectiveness: There have not been any studies of the effect of music therapy alone on depression in older people. However, it can be a component of an effective program — one RCT found that music, combined with CBT (a proven treatment for depression), gentle exercise and relaxation, had positive effects on depression in older people.[51]

Conclusion: There is no evidence at present that listening to music by itself reduces depression.

St John's wort

Description: St John's wort (*Hypericum perforatum*) is a herb available in tablet, capsule and liquid forms from supermarkets, chemists and health food shops.

Quality of evidence: II.

Review of effectiveness: Three trials involving older people have shown that St John's wort reduces symptoms of depression to the same extent as antidepressants, although one study of severely depressed older people found that St John's wort was effective only in the short term.[52] No studies of older people have compared St John's wort to placebo treatment. In older people, St John's wort can have side effects (eg, dizziness, fatigue), although less often than antidepressant drugs.

Conclusion: St John's wort can be a useful treatment for older people with mild to moderate depression.

Vitamins

Description: Vitamins are organic chemicals that are required in small amounts for the proper functioning of the body. They are present in foods, and also available as a supplement from pharmacies, health food shops and supermarkets.

Quality of evidence: Folate: II (for patients with Alzheimer's disease); III-3 (for others). Other B vitamins: II. Vitamins C, D and E: V.

Review of effectiveness: **Folate.** One RCT found that methylfolate is as effective as trazodone (a serotonin agonist) for patients who have both depression and Alzheimer's disease.[53] There is also some evidence for an effect on people who do not have Alzheimer's disease: an open pre–post trial (1-week placebo washout) of methylfolate in older patients with depressive disorder showed an 81% response rate among completers and a marked reduction in

depression scores.[54] One trial looking at the effectiveness of antidepressants found that high baseline serum levels of folate predicted a better response to sertraline but not to nortriptyline,[55] suggesting that folate may boost the effectiveness of selective serotonin reuptake inhibitors.

Other B vitamins. The evidence for effectiveness of other B vitamins in depression is mixed. One short, small RCT compared a combination of B vitamins (B_1, B_6 and B_{12}) and tricyclic antidepressants with placebo and tricyclic antidepressants in older people.[56] Although the results were described as containing "promising trends", the effects on mood were not significant. A study of older women found that serum vitamin B_{12} levels were not significantly lower in those with depression, but there were significantly more B_{12}-deficient women in the depressed groups: 15% of those with no depression, 17% of those with mild depression and 27% of those with severe depression.[57] Similarly, vitamin B_{12} deficiency was related to depressive disorders in a study of community residents in Rotterdam.[58] In two other community surveys, no association was found between vitamin B_{12} levels and depression.[59,60]

Vitamins C, D and E. Serum vitamin C level was found to be unrelated to depression in older people.[59] Vitamin D serum levels were not significantly different in groups of patients with major depression, schizophrenia and healthy controls.[61] Vitamin E was not related to depressive symptoms in older Rotterdam residents,[62] but another study found that baseline vitamin E status protected against the development of depression over 4 years in men.[63]

Conclusion: There is some evidence for the effectiveness of folate as a treatment for depression in older people. There is no convincing evidence for the effectiveness of other B vitamins, and there have been no studies of the effectiveness of vitamins C, D and E for treating depression.

DISCUSSION

An overview of the evidence available for each treatment is shown in Box 2. Our review shows that there are a variety of therapies with a sound evidence base to choose from. Older people with depressive symptoms have treatment options from all three categories (medical, psychological and lifestyle changes/alternative therapies), at least for mild to moderate depression.

Most treatments that were found to be effective for older adults overlap with those that are currently recommended for adults in general.[64] This similarity of recommended treatments does not, however, suggest that treatments do not need to be tested for older adults. Given the different aetiological pathways and the different presentation of depression in older people, it is important that the full range of possible treatments be evaluated for use by this population. Reminiscence/life review and testosterone therapy are treatments specifically formulated for older people, and others may be found to be especially effective in this age group. In the case of late-onset vascular depression, trials of treatments for cerebrovascular disease would be worthwhile.

Treatments for depression that have been shown to work in other age groups, but have not been tested in older people, include alcohol avoidance, negative air ionisation for seasonal winter depression, *S*-adenosylmethionine treatment and yoga breathing exercises. Testing of older people needs to be broadened to include these possible treatments, particularly in view of the public's more favourable attitudes to some non-standard treatments.

2 Conclusions on the effectiveness of treatments for late-life depression

Treatment	Evidence level*	Conclusion
Medical treatments		
Antidepressant medication	I	Sound evidence of effectiveness
Electroconvulsive therapy	I	Sound evidence of effectiveness, but only appropriate in extreme circumstances
Oestrogen	II	No effect found
Testosterone	III-3	No convincing evidence
Transcranial magnetic stimulation	II	No convincing evidence
Psychological treatments		
Cognitive behaviour therapy	I	Sound evidence of effectiveness, but not for stroke patients
Dialectical behaviour therapy	II	Evidence of effectiveness as adjunct to antidepressant medication
Interpersonal therapy	II	Some evidence of effectiveness
Problem-solving therapy	II	Some evidence of effectiveness
Psychodynamic psychotherapy	II	Sound evidence of effectiveness
Reminiscence and life review	I	Sound evidence of effectiveness
Bibliotherapy	II	Sound evidence of effectiveness for mild to moderate depression
Lifestyle changes and alternative therapies		
Alcohol avoidance	V	No evidence
Exercise	II	Evidence of effectiveness
Fish oils	V	No convincing evidence
Light therapy	II	Evidence of effectiveness for people in hospitals or nursing homes
Massage therapy	III-3	No convincing evidence
Music therapy	V	No evidence
St John's wort	II	Evidence of effectiveness for mild to moderate depression
Vitamins		
Folate	II	Some evidence of effectiveness for patients with Alzheimer's disease
	III-3	No convincing evidence for patients without Alzheimer's disease
Other B vitamins	II	No convincing evidence
Vitamins C, D and E	V	No evidence

* Based on National Health and Medical Research Council levels of evidence,[12] with the addition of "Level V" for even weaker types of evidence.

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COMPETING INTERESTS

None identified.

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