

*Full Length Research Paper*

# **Non-drug strategies in the management of depression: A comprehensive study of systematic review and meta-analysis of randomised controlled trials**

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**Between 5 to 10% of the population experience depression at any time in any year, needing psychiatric or psychosocial intervention. The World Health Organization has reported that depression's financial burden globally ranked fourth in 2000, and will increase by 2020 to be the second most costly disease. This paper focus on the range of non-drug strategies available to patients, other than prescribed pharmacological treatments, which could be helpful in treating depression.**

**Key words:** Systematic review, meta-analysis, depression, non-drug, psychological therapies, exercise and lifestyle interventions, complementary and alternative treatments.

## **INTRODUCTION**

Depression is a global health problem. According to the World Health Organization, it affects about 121 million people worldwide, and those numbers are increasing. It is estimated to be the leading cause of mental disability worldwide and is predicted to be the 2nd leading cause of all health disability by 2020. Depressive disorders affect as many as 18.8 million American adults or about 9.5% of the U.S. population age 18 and older in any given year, according to the National Institute of Mental Health. Though the global estimates are not available, depression costs more than US\$ 83 billion annually in medical treatment and lost productivity in work place to US economy, according to a published report (Michael, 2011).

The management of depression depends on its severity, and treatment includes non-pharmacological and pharmacological approaches or both. The non-pharmacological approaches play a significant role in the management of depression individually as well as in addition to pharmacological treatment. Sometimes, these

are preferred over pharmacological approaches due to their non-harmful and non addictive effect. This paper identifies and examines the non-drug strategies for the management of depression. These include psychological therapies, exercise and lifestyle interventions, and complementary and alternative treatments. It also provides evidence based an assessment of these interventions for depression in adult population.

## **METHODS**

This paper focus on systematic review and randomised controlled trial (RCT) evidence of effectiveness, with searches extended to identify observational studies only where appropriate. Therapies commonly available to patients without prescriptions were selected for inclusion. Studies were excluded where there was no formal diagnosis by International Classification of Disease (ICD) 9, ICD 10, Diagnostic Statistical Manual (DSM)-III or DSM-IV, or use of a recognized, validated and reliable measurement scale specifically for depressive symptoms. Further, the studies in patient groups with clear indicators of severe depression or with significant psychological and/or physical comorbidities were also excluded.

A systematic review of the literature was carried out using an unambiguous search strategy. Databases searched include: Pubmed, Medline, Embase, Cinahl, PsycINFO, AMED, and the Cochrane Library. The year range covered was 1998 to 2010 with

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variations depending on topic. Internet searches were also carried out on various websites.

## RESULTS

Results of the systematic review and meta-analysis of RCTs are broadly classified and detailed into psychological therapies, exercise and lifestyle interventions, and complementary and alternative treatments along with evidence based assessment of these interventions.

## PSYCHOLOGICAL THERAPIES

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

### Behavioural activation

Behavioral activation is a brief, structured, goal-focused therapeutic approach to treating acute depression that seeks to alleviate depression by promoting an individual's contact with sources of reward through increasing activation, improving problem solving, and decreasing avoidance and other barriers to activation (Dimidjian and Davis, 2009). A meta-analysis of 34 randomised controlled studies with 2055 participants found behavioural activation to be effective in reducing depressive symptoms in adults and older adults compared to treatment as usual and waiting list control, and as effective as cognitive therapy (Mazzucchelli et al., 2009). This is consistent with the conclusions of other studies incorporating behavioural activation therapy as part of a larger meta-analysis in adults and older patients (Cuijpers et al., 2006, 2007).

### Cognitive behavioural therapy

Cognitive behavioural therapy (CBT) is a psychotherapeutic approach, a talking therapy, which aims to solve problems concerning dysfunctional emotions, behaviors and cognitions through a goal-oriented, systematic procedure. The title is used in diverse ways to designate behavior therapy, cognitive therapy, and to refer to therapy based upon a combination of basic behavioral and cognitive research (Dimidjian and Davis, 2009). There is strong and consistent meta-analysis and systematic review evidence that CBT is more effective

than either treatment as usual or waiting list control in the treatment of depression in adults and older adults and is at least as effective as antidepressant medication. For those studies where follow up was examined, CBT was at least as effective as antidepressant medication over six months to two years follow up. In some studies CBT was more effective than other psychological therapies whilst other studies suggest CBT has similar effectiveness to other systematic therapies such as psychodynamic therapy and interpersonal therapy (Cuijpers et al., 2006; Churchill et al., 2001; Hensley et al., 2004; Leichsenring, 2001; Mackin and Arean, 2005; Pincus et al., 2006).

In another systematic review, patients receiving individual CBT were more likely to improve and had fewer symptoms as follow up than patients receiving group CBT (Churchill et al., 2001). A systematic review of CBT in adults with major depressive disorder who had not responded to at least one course of antidepressant medication identified two studies providing adequate data for interpretation. Although there was benefit of CBT (15 to 30 sessions) in treatment-resistant depression, the evidence base is insufficient to support a recommendation in this patient group (McPherson et al., 2005).

### Counselling

Counselling is the skilled and principled use of relationships which develop self knowledge, emotional acceptance and growth, and personal resources. The overall aim is to live more fully and satisfyingly. Counselling may be concerned with addressing and resolving specific problems, making decisions, coping with crises, working through inner feelings and inner conflict, or improving relationships with others. The counsellor's role is to facilitate the patient's work in ways that respect the patient's values, personal resources, and capacity for self determination (Michael and Gillian, 2001). In the literature the term 'counselling' encompasses a variety of approaches. An RCT compared GP treatment as usual with GP treatment as usual plus psychodynamic or cognitive behavioural counselling (average 6 sessions, range 1 to 16 sessions) in patients with depression. At 6, 12 and 36 months follow up there were no significant differences between the study groups in Beck Depression Inventory scores. Diagnostic selection criteria were unclear and there were variations in the counselling intervention (Simpson et al., 2000, 2003; Corney and Simpson, 2005).

Another RCT had patient preference arms and compared randomised antidepressant treatment with randomised counselling, preference antidepressant and preference counselling. The recommended number of counselling sessions was six. GPs were guided to prescribe one of three antidepressants (Bedi et al., 2000;

Chilvers et al., 2001). There was no clear superiority of any treatment approach at eight weeks. At 12 months follow up, generic counselling was as effective as antidepressants but antidepressants may result in more rapid recovery and are likely to be chosen by those who are more severely depressed.

### **Marital therapy**

Marital therapy or couple-focused therapy has the twofold aim of modifying negative interaction patterns and increasing mutually supportive aspects of couple relationships, thus changing the interpersonal context linked to depression (Barbato and D'Avazo, 2007). A systematic review identified eight studies evaluating the effect of marital therapy on depression (Barbato and D'Avazo, 2007). A variety of treatment models were subsumed within the marital therapy approach, including CBT, emotion-focused, interpersonal and systemic therapy. A variety of control comparisons were used, including CBT, interpersonal therapy, drug therapy, combined individual and drug therapy and waiting list. Duration of treatment ranged from 10 to 20 weeks and follow up ranged from post-test to two years. Studies were characterized by small sample size, lack of intention to treat analysis and high numbers could not follow up. The review concluded there was no evidence to support marital therapy being any more or less effective than one to one therapies or drug therapy in the treatment of depression, even when associated with marital distress. In comparison to no/minimal treatment the outcome for depression was better in the marital therapy group, although this was based on only two small studies. Marital therapy should be considered where the current relationship is contributing to the depression, or where involvement of a partner is considered to be of potential therapeutic benefit.

### **Family therapy**

Family therapy helps people in a close relationship to help each other. It enables family members to express and explore difficult thoughts and emotions safely, to understand each other's experiences and views, appreciate each other's needs, build on family strengths and make useful changes in their relationships and their lives (Allison et al., 2003). Studies of the effect of family therapy on depressive symptoms have been conducted in very specific patient populations and the results are not easily generalized. In one poor quality study, twelve sessions of cognitive behavioural family intervention were as effective as 12 sessions of behavioural family intervention in alleviating depressive symptoms in mothers who have a child with conduct disorder (Sanders

and McFarland, 2000).

### **Hypnotherapy**

Hypnotherapy is any therapeutic approach using hypnosis as a main technique, for example, to promote imaginal re-exposure or relaxation (Alladin and Alibhai, 2007). One RCT with methodological limitations found that CBT supplemented by hypnotherapy produced a significantly larger reduction in depressive symptoms than CBT alone. This effect was sustained at six and 12 month follow up. It is unclear whether the interventions were equivalent in terms of duration of therapy offered to patients (Alladin and Alibhai, 2007).

### **Interpersonal therapy**

Interpersonal therapy (IPT) is a time-limited intervention, which aims to reduce symptoms by working on improving the quality of the patient's interpersonal relationships. IPT focuses on specific interpersonal problem areas such as grief, role transition and interpersonal disputes. A positive therapeutic alliance is encouraged and a range of therapeutic strategies are employed to encourage the open expression of affect and problem resolution. Patient literacy is not required (Stuart and Robertson, 2003). A systematic review examining achievement of complete remission in major depression found that IPT, CBT and medication were equally effective (Casacalenda et al., 2002). A further systematic review of nine studies reported consistent evidence that IPT, delivered according to the standard manual of over 12 to 20 sessions, is superior to placebo and similar in effectiveness to antidepressant medication (prescribed at therapeutic doses) and to CBT in patients with depression (de Mello et al., 2005). A subsequent RCT comparing IPT with CBT concluded that the therapies are equally effective for depression. For severe depression CBT showed slightly higher levels of symptom reduction at end of treatment than IPT (Luty et al., 2007).

### **Mindfulness based cognitive therapy**

Mindfulness-based cognitive therapy is a brief group intervention that seeks to prevent depressive relapse by promoting mindful attention, acceptance, and skillful action to help individuals interrupt habitual cognitive and effective patterns associated with risk of relapse (Dimidjian and Davis, 2009). A systematic review identified two RCTs showing that mindfulness based cognitive therapy conducted in a group setting (8 x 2-2.5 h sessions) reduced relapse in chronic depression (three or more depressive episodes) by over 50% during a one

year follow up period, compared to treatment as usual. There was no reduction in relapse for patients having experienced one or two episodes of depression (Coelho et al., 2007).

### **Music therapy**

Music therapy is a therapeutic approach where music-making forms the primary basis for communication (Maratos et al., 2008). A Cochrane review of five small and diverse studies concluded that music therapy on its own or as an adjunct to psychological therapies, is acceptable to people with depression and is associated with improvements in mood. Due to less number of studies, it is not possible to be confident of its effectiveness (Maratos et al., 2008).

### **Problem solving therapy**

Problem solving therapy (PST) is a brief focused psychological intervention that is delivered by an individual trained in problem solving approaches. These are often highly individualized and have a pragmatic focus, in which the professional and individual work through a series of defined steps to clarify the person's problems, desired goals, generate potential solutions and help to implement the chosen solution (Cuijpers et al., 2007). A well conducted meta-analysis of PST in depression found that, in general, PST was more effective than control interventions. There was significant variation in the outcome measures used and there was large heterogeneity. Overall effect size (ES) varied according to the type of analysis: ES = 0.34, when it was assumed that all interventions were equivalent (fixed effects model), ES = 0.83, when it was assumed the interventions differed in some way (random effects model). This indicates that PST has varying effects on depression and may be considered as a treatment option for patients with depression (Cuijpers et al., 2007).

### **Psychodynamic psychotherapy**

Psychodynamic psychotherapy is based on psychodynamic theories of development and of the mind and includes attention to unconscious as well as conscious mental processes. The approach places emphasis on the importance of the therapeutic relationship, including transference and counter transference, are difficulties from the past and can be repeated in the therapeutic relationship as well as in current relationships and therefore understood and changed. The therapy involves both expressive and supportive elements. By allowing the patient to express

thoughts and feelings freely in the sessions with the therapist the patient can become more objective and effect desired change (Leichsenring, 2001). A number of variants of psychodynamic psychotherapy are used in studies, making comparisons difficult. One systematic review identified six studies comparing short term psychodynamic psychotherapy with CBT for outpatients with major depression and found the two therapies to be equally effective in the treatment of depression, although results were considered to be preliminary due to the small number of trials (Leichsenring, 2001).

### **Reminiscence therapy**

Reminiscence therapy involves a progressive return to an awareness of past experiences, both successful and unsuccessful, so that salient life experiences may be re-examined and re-integrated. The life review process gives older people opportunities to place their accomplishments in perspective, to resolve lingering conflicts, and to find new significance and meaning in their lives, thereby relieving the despair and depression that often accompany ageing (Watt and Cappeliez, 2000). Two studies of reminiscence therapy in older adults with depression were identified (Klausner et al., 1998; Watt and Cappeliez, 2000). Reminiscence therapy was compared with goal-focused psychotherapy and active socialization group as the control condition. Results were equivocal and studies were generally of poor methodological quality.

### **Art therapy**

Art therapy is a form of psychotherapy that uses art media as its primary mode of communication (Shirley, 2001). No evidence specific to depression was identified on the use of art therapy.

### **Cognitive behavioural analysis system of psychotherapy**

Cognitive behavioural analysis system of psychotherapy (CBASP) is an integrative model that combines behavioural, cognitive, psychodynamic and interpersonal procedures. It was developed specifically for treatment of chronic forms of depression and focuses primarily on helping the depressed person to understand how their behaviour can influence the outcome of problematic interpersonal situations. Specific examples of such situations, including the therapeutic relationship are analyzed in detail in order to improve interpersonal skills and teach more effective engagement with the social environment (McCullough, 2000). No evidence specific to

depression was identified on the use CBASP therapy.

### **Cognitive analytic therapy**

Cognitive analytic therapy is a brief integrative therapy comprising elements of cognitive behavioural and psychodynamic therapies in an active, structured and collaborative approach, based on written and diagrammatic reformulations of the presenting difficulty (Denman, 2001). No evidence specific to depression was identified on the use cognitive analytic therapy.

### **Eye movement desensitization and reprocessing**

Eye movement desensitization and reprocessing (EMDR) therapy is used for post-traumatic conditions in which the client is asked to hold in mind the image of the trauma, a negative self cognition, negative emotions and related physical sensations. While doing so the client is instructed to move his or her eyes quickly and laterally back and forth. Other forms of left-right alternating stimulation (auditory) may be used. This procedure continues until desensitisation of troubling material is complete and positive self cognitions have replaced the previous negative self cognition (Shapiro, 2001). No evidence specific to depression was identified on the use EMDR therapy.

### **Neurolinguistic programming**

Neurolinguistic programming (NLP) is a therapeutic technique to detect and re-program unconscious patterns of thought and behaviour in order to alter psychological responses (Lisa, 2008). No evidence specific to depression was identified on the use NLP therapy.

## **EXERCISE AND LIFE STYLE MODIFICATIONS**

### **Exercise**

Exercise is a subset of physical activity, which is any movement of the body that results in energy expenditure rising above resting level, and includes activities of daily living, domestic chores, gardening and walking. Exercise is undertaken to improve health or as part of sports or leisure time activities including swimming, jogging, brisk walking, going to the gym, tennis, football and cricket. Evidence from systematic reviews and meta-analyses consistently supports structured exercise in a range of environments; home, community, health care settings, leisure center etc. as an effective treatment in reducing symptoms of depression. Exercise (both aerobic, for

example, Walking and jogging and anaerobic, for example, weight training) reduces depressive symptoms in patients with mild to moderate depression and is as effective as antidepressant medications. There is a large evidence base for aerobic exercise than for anaerobic exercise (Babyak et al., 2000; Blumenthal et al., 2007; Dunn et al., 2002, 2005; Mather et al., 2002; Nabkasorn et al., 2006; Singh et al., 2001).

A Cochrane review of 23 trials (n = 907) found a large and statistically significant clinical effect of exercise (measured post-treatment) when compared to no treatment or control intervention. Further, in comparisons of effectiveness with antidepressant medication and CBT there was no difference between exercise and the established interventions (Mead et al., 2008). The benefits of exercise have generally been shown to be independent of social group effect (Dunn et al., 2005).

### **Lifestyle modifications**

No good quality evidence was identified on the effect of reducing alcohol consumption and caffeine intake on depressive symptoms.

## **COMPLEMENTARY AND ALTERNATIVE THERAPIES**

### **Acupuncture**

Acupuncture is a family of procedures involving the stimulation of anatomical locations on or in the skin by a variety of techniques. There are a number of different approaches to diagnosis and treatment in acupuncture that incorporate medical traditions from China, Japan, Korea, and other countries. Four good quality systematic reviews of poor quality RCTs of acupuncture in patients with depression were identified (Smith, 2005; Mukaino et al., 2005; Leo and Ligot, 2007; Hao et al., 2008). Results were inconclusive and studies had a number of methodological limitations.

### **Animal assisted therapy**

Animal assisted therapy is a therapy that uses dogs or other pets to improve the physical and mental health of patients with certain acute or chronic diseases. There is evidence from one systematic review that the introduction of animal assisted activities may have beneficial effects on the severity of depressive symptoms in older people resident in nursing homes and psychiatric institutions. The degree to which the benefits found are a result of animal contact or human contact with the animal facilitator is unclear and requires further investigation (Souter and Miller, 2007).

## Homeopathy

Homeopathy is a system of medicine which is based on treating the individual with highly diluted substances given mainly in tablet form, which trigger the body's natural system of healing. In a good quality systematic review only two RCTs were identified, one of poor quality and one in which only six patients completed the study. This review concluded that the evidence for the effectiveness of homeopathy in depression is limited due to lack of clinical trials of high quality (Pilkington et al., 2005).

## Light therapy

Light therapy involves the therapeutic exposure to full-spectrum artificial light that simulates sunlight, used to treat various conditions such as seasonal affective disorder. A Cochrane review of light therapy for non-seasonal depression identified 20 RCTs comparing bright light with inactive placebo treatments for non-seasonal depression. The review found that bright light may confer modest benefits on severity of depression symptoms in the very early stages of treatment of people with depressive disorder in hospital and long term care settings (Tuunainen et al., 2004). A subsequent good quality systematic review reported that trials evaluating light therapy as a stand-alone intervention in non-seasonal depression had inconsistent results (Even et al., 2008).

## Massage therapy

Massage therapy involves the manipulation of the soft tissues of the body - the muscles, tendons and ligaments. A systematic review of massage therapy for depression identified 17 RCTs ( $n = 786$ ) from 246 retrieved references. All seventeen RCTs were of moderate quality and showed positive effect of massage therapy on depressed people with a mean quality score of 6.4 ( $SD = 0.85$ ). Limitations of these RCTs were lack of standardized protocols of massage therapy, various depression rating scales, and ill-defined target populations (Hou et al., 2010).

## Yoga

Yoga is an ancient system of breathing practices, physical exercises and postures, and meditation, intended to integrate the practitioner's body, mind, and spirit. A systematic review of five RCTs examined the effectiveness of different forms of yoga in patients with depression ranging in severity from mild to severe

(Pilkington et al., 2005). All trials reported positive benefits of yoga interventions on the severity of self reported or assessor-rated symptoms of depression. Basic details of trial methodology were poorly reported and a meta-analysis was not attempted due to the diversity of outcome measures, absence of assessor blinding in all but one of the studies, and inadequate information on participant characteristics. There were no details on method of randomization, compliance or attrition rates.

## Aromatherapy

Aromatherapy is a therapy based on the use of very concentrated "essential" oils from the flowers, leaves, bark, branches, rind or roots of plants with purported healing properties (van der Watt and Janca, 2008). No applicable evidence was identified on the use of aromatherapy as stand-alone treatment for patients with depression.

## Emotional freedom technique

Emotional freedom technique is an emotional, needle-free version of acupuncture (Waite and Holder, 2003). No applicable evidence was identified on the use of emotional free technique as stand-alone treatment for patients with depression.

## Reflexology

Reflexology involves massage of reflex areas found in the feet and the hands (Ernst, 2009). No applicable evidence was identified on the use of reflexology as stand-alone treatment for patients with depression.

## Reiki

Reiki is hands-on alternative healing technique that involves the exchange of energy between practitioner and patient to restore mental, physical, emotional, and spiritual balance (Lee et al., 2008). No applicable evidence was identified on the use of Reiki as stand-alone treatment for patients with depression.

## Tai chi chuan

Tai chi chuan is a Chinese exercise system that uses slow, smooth, body movements to achieve a state of relaxation of both body and mind (Wang et al., 2010). No applicable evidence was identified on the use of Tai chi

chuan as stand-alone treatment for patients with depression.

### Thought field therapy

Thought field therapy involves tapping with the fingers at meridian points on the upper body and hands (Callahan, 1995). No applicable evidence was identified on the use of thought field therapy as stand-alone treatment for patients with depression.

### Conclusions

In the present review, a number of non-drug strategies available in the management of depression were identified and reviewed. Among psychological therapies, behavioural activation, individual CBT and IPT is recommended as a treatment option for patients with depression. Mindfulness based cognitive therapy in a group setting may be considered as a treatment option to reduce relapse in patients with depression who have had three or more episodes. Whereas, problem solving therapy and short term psychodynamic psychotherapy may be considered as a treatment option in depressed patients. Structured exercise may be considered as a treatment option for patients with depression. No applicable evidences were identified on which to base a recommendation for complementary and alternative therapies.

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