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Depression: Augmenting current treatments with low cost strategies.

By

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Key points

- Depression is a huge public health concern and will be the second biggest global burden of disease by year 2020.
- Main treatment modalities of depression are effective but have limitations.
- Exercise and eco-therapies are lesser known interventions for depression but they are effective, inexpensive, non-invasive and have little side effects and this has implication for nursing practice.

Abstract

Depression has profound social, economic and personal consequences for the affected individual and it shows no signs of abating in the general population. There are several treatment modalities available for this debilitating illness but; effective as they are, these treatments have pitfalls. Antidepressants are the most common form of treatment for depression; they are relatively cheap, effective but induces uncomfortable side effects some of which can be life threatening. These side effects include cardio-toxicity, weight gain, the serotonin syndrome, sexual dysfunction, dry mouth and urinary retention. Electroconvulsive therapy has been used in the treatment of depression since the late 1930 and is effective particularly in severe depression. It is quick acting but its use tend to evoke moral and ethical debates. Psychological therapies have been used since the 9th century AD and are effective and have little side effects but they are relatively expensive and there is a long waiting list in the NHS for these therapies. Emerging evidence suggest a place for the use of exercise to improve depressive symptoms. The article discusses evidence in support of exercise and eco-therapy in particular to alleviate symptoms of depression and promote recovery. This has implications for mental health nursing practice.

Introduction

Depression is a significant public health issue and is present in 10% of the population (Cassano and Fava 2002). The World Health Organisation(WHO) estimates that depression affects approximately 350 million people worldwide and will be the leading cause of global burden of

disease in developed countries by 2020(WHO 2008). Depression has many consequences; first, the affected individual may suffer distressing psychological symptoms and may function poorly at work, school and within the family. Second, depression is often a chronic condition which imposes a high economic burden for the individual, their family as well as society. The WHO estimates that depression costs the NHS over £43 billion between 2006 and 2007 alone (WHO 2008). In combination with anxiety and other common mental health disorders, depression is responsible for the largest proportion of certified sickness absence in the UK (Henderson *et al.* 2011). It is frequently co-morbid with many physical illnesses such as cardiovascular disease, diabetes, and cancer. Depression can significantly influence the outcome of these illnesses. This is because the adverse health risk behaviours and psychobiological changes associated with depression increase the risk for these chronic medical disorders and morbidity(Penninx *et al.* 2013). Conversely, biological changes such as elevation of proinflammatory factors, hypothalamic-pituitary axis changes, autonomic and metabolic changes seen during physical illness have a strong association with depression (Katon 2011; Muller 2014). Further, depression is associated with a higher risk of obesity, sedentary lifestyle, smoking (Tjora *et al.* 2014), and poor adherence to medication (DiMatteo *et al.* 2000). At its worst, depression can lead to suicide (Beghi and Rosenbaum 2010). The WHO estimates that suicide due to depression is responsible for one million deaths every year and therefore its public health importance is obvious. For this reason, there has been an increase in the number of effective treatment modalities.

Several treatments options are available for the treatment of depression and these include pharmacological, psychological and Electro-convulsive Therapy (ECT). However, many of these treatments are expensive, not readily available to patients or have a high cost to benefit ratio as in pharmacotherapy and ECT. This article seeks to examine advantages and disadvantages of current treatment modalities and how they compare with emerging low cost interventions. Specifically, the article discusses the use of exercise and eco-therapy to improve physical and psychological wellbeing of depressed individuals. First, the article evaluates the use of antidepressant pharmacotherapy in the treatment of depression.

Pharmacotherapy

For nearly 60 years, antidepressants have been the first-line treatment for various forms of depression and their use is by far the most common (Kirsch 2008). The Health and Social Care Information Centre reports that prescriptions for anti-depressants are at record levels in England, with 50 million antidepressants dispensed in 2012 alone(hscic 2013). In financial terms, this translates to approximately £77 billion a year (hscic 2013). However, like any other treatment, antidepressants have advantages and disadvantages that largely depend on the type of antidepressants the individual takes. A key advantage of antidepressants is that they are effective in boosting mood in a significant proportion of people with depression and they are cost effective (Barbui *et al.* 2003). A relatively recent randomised controlled trial determined the short-term efficacy of antidepressants in major depressive disorder and found that they are efficacious in all age groups(Gibbons *et al.* 2012b). However in spite of these advantages, antidepressants treatment has some pitfalls.

Antidepressants induce serious side effects and this has been associated with non-adherence with medication (Usher *et al.* 2013), poorer social function (Serretti and Mandelli 2010; Rayner *et al.* 2011). Common side effects of antidepressants include, cardiac arrhythmias, constipation, insomnia, serotonin syndrome, movement disorders, serotonin discontinuation syndrome and sexual dysfunction (Kennedy and Rizvi 2009; Baldwin and Foong 2013). A key side effect of antidepressants with long term ramifications is weight gain.

In a meta-analysis of 116 eligible the studies on the relationship between antidepressants and weight gain, Serretti and Mandelli (2010) found that amitriptyline, mirtazapine, and paroxetine were associated with the greatest risk of weight gain which heightens the risk of cardiovascular disorders, diabetes and hypertension. More importantly, antidepressants are associated with suicidal ideation in young people particularly in adolescents.

Since 2003, governments in Europe and North America have issued a series of advisories culminating in a black box warning for all antidepressants prescribing for those under the age 18 years. Some investigators have contested the association between suicidality and the use of antidepressants in children (Gibbons *et al.* 2012a). Gibbons et al (2012) found no evidence of increased suicidal ideation in young patients on fluoxetine or venlafaxine treatment but found that

young people on these antidepressants showed no significant improvement in their symptoms. Put differently, the authors concluded that antidepressants have little or no effect in young persons. In spite of this dissent, the bulk of evidence in the extant literature convincingly suggests that first-line prescription of antidepressants for children under the age of 18 year old is not advisable (Sparks and Duncan 2013).

The superiority of antidepressants over other forms of treatment in the treatment and recovery of depression has been called into question (Kirsch 2008). The largest open label pragmatic study, the Sequenced Treatment Alternatives to Relieve Depression(Warden *et al.* 2007) found that only 28%-33% of patients, remitted after 12 weeks of adequate trial on a single antidepressant; switching to another antidepressant or augmentation with a second drug was often necessary(Warden *et al.* 2007). Other studies have directly compared the effectiveness of antidepressants and psychological therapies and found no particular advantages for antidepressants. For example, a Cochrane systematic review of 10 studies with a study population of 1235 adolescents found limited evidence for the superiority of antidepressants over psychological therapies. Instead, the review concluded that psychological and antidepressant therapies or a combination of these have limited efficacy in adolescents and children (Cox *et al.* 2012). However, a Cochrane review of 5 studies found that adding psychotherapy to antidepressants improves outcome in people with depression (Jakobsen *et al.* 2012). The small sample size (total 365 participants) from this review limits the generalizability of the finding. Overall, it appears that despite their effectiveness in treating depression, antidepressants may not be suitable for everyone as they have the propensity to compromise the quality of life and the general well-being of individuals with depression. Further, antidepressants may not be effective in relieving symptoms of depression in some people. For mild to moderate depression, some guidelines favour psychotherapy over antidepressants (NICE 2009). Again like antidepressants psychological therapies have advantages and disadvantages and we will discuss these.

Psychological therapies

Although the value of psychological therapies is undoubted, the evidence base for its effect size is less solid than that for antidepressants. A recent Cochrane systematic review of twenty five trials

with 955 participants concluded that there is low to moderate-quality evidence that support the effectiveness of psychological therapies in the treatment of depression (Shinohara *et al.* 2013). Further, meta-analytic review that examined effect sizes of 117 trials found that all forms of therapies including CBT are only effective in approximately 42% of cases. The investigators concluded that the effects of psychological therapies in adults with depression seem to be overestimated considerably because of publication bias (Cuijpers *et al.* 2010). This finding is also supported by another Meta analytic review of twenty one studies that found Cognitive Behavioural Therapy and antidepressants to be modestly effective (Roshanaei-Moghaddam *et al.* 2011).

The UK government has invested significantly in psychological therapies within the NHS and this is perhaps long overdue. The large scale program, Improving Access to Psychological Therapies (IAPT) spent over £300 million in its first phase roll-out and will spend a further £400 million by 2015 (DoH 2011). Due to the current bias towards CBT, evidence suggests that a significant proportion of patients are facing long waiting lists (Richards *et al.* 2012). Moreover, there is significant variation in how patients are initially allocated to treatment, and patient whom are referred directly to high intensity services face long waiting lists therefore, limiting access to treatment and resulting in no service (Richards *et al.* 2012). This is likely to increases a person's risk of a deteriorating mental health, increasing hospitalisations and risk for suicide. One option for patients who face barriers in accessing CBT, is to pay privately for sessions but the hourly cost of talking therapy varies between £40 and £100 (NHS 2013). The Department of Health (2011), suggest that people suffering with mild to moderate depression may receive between 6 and 10 sessions, and up to 20 sessions for serious depression. Because of barriers to accessing healthcare, this could translate to costs ranging from £200 to £2000 per course for the individual who chooses to pay privately and this is clearly prohibitive for most people. For those whose depression is resistant, (ECT) may be indicated.

Electro-convulsive therapy

In the UK, electro convulsive therapy has been used to treat depression and other conditions since 1939. More than 70 years since its introduction, electroconvulsive therapy (ECT) remains the most

effective somatic treatment in mental health, with unsurpassed efficacy and remarkable safety (Petrides *et al.* 2011). It is a viable treatment option when antidepressants and psychotherapy have failed or if the individual presents with psychotic or catatonic symptoms. It is also indicated when rapid relief of symptoms is required because of suicide risk or deterioration of medical conditions (Petrides *et al.* 2011). An early systematic review and meta-analysis of 6 studies found that ECT is an effective short-term treatment for depression, and is probably more effective than antidepressants(The UK ECT review group 2003). In terms of the risk to benefit ratio of ECT, questions have centred on its propensity to induce long term memory loss (Fraser *et al.* 2008; Ingram *et al.* 2008) concentration problems, and confusion (Read *et al.* 2004). Moreover, another source of concern is despite its high efficacy, there is a significant relapse rate after treatment (Trevino *et al.* 2010). Because of the side effects it induces and its mode of action is unclear, debate has also centred on whether ECT treatment can be ethically justified (Ottosson 1985). Given the possible adverse effects related to pharmacological treatment, the high cost of psychological therapies and controversies surrounding ECT, it is important to investigate other treatment strategies such as exercise.

There has been emerging evidence, supporting the use of practical, low cost, therapies that require minimum or no training for the professional. Because of reduced spending in the NHS as a result of current global financial crisis, the use of these therapies is particularly timely (Appleby 2013). The following section discusses evidence supporting the use of exercise and eco-therapy in particular as adjunct to current treatment modalities for depression to aid outcome and recovery.

Exercise and eco-therapies for depression

In general, evidence in the extant literature suggest that physical exercise has favourable effects on physical and mental health (Matta Mello *et al.* 2013). In the last 30 years, a number of studies have sought to establish whether exercise could be regarded as an alternative to antidepressants. Results of cross-sectional and longitudinal studies are more consistent in indicating that aerobic exercise training has antidepressant and anxiolytic effects and protects against harmful consequences of stress. Moreover, increased physical activity has been consistently shown to be associated with improved physical health, life satisfaction, cognitive functioning, and psychological well-being (Carek *et al.* 2011). This is because physical exercise promotes changes in the human brain due to increases in metabolism, oxygenation and blood flow in the brain. It also modulates major brain neurotransmitters that are associated with an individual's state of alertness (norepinephrine), the pleasure and reward system (dopamine) and the level of anxiety (serotonin). Other neurochemical factors that may be released during physical activities include trophic factors, opioids and endocannabinoids which promote a sense of euphoria and well-being, anxiolytic effects, sedation and decreased sensitivity to pain in humans (Dietrich and McDaniel 2004).

Physical exercise compares favourably to antidepressant medications as a first-line treatment for mild to moderate depression and has been shown to improve depressive symptoms when used alone or adjunct to other treatments (Cooney *et al.* 2013a). Evidence also suggest it is effective and cost-efficient treatment alternative for a variety of disorders including anxiety (Cooney *et al.* 2013b). A recent systematic review of 13 studies found a strong effectiveness of exercise combined with antidepressants in the treatment of major depression (Mura *et al.* 2014). Additionally, a Cochrane systematic review of thirty nine studies with a total number of 2326 participants found that physical exercise appears to be equally effective as psychological or pharmacological therapies in treating symptoms of depression but cautioned that a larger number of studies is required to be conclusive (Cooney *et al.,* 2013).

Further evidence confirms that even gentle exercise such as walking has additional beneficial effects that include weight loss (Thompson *et al.* 2011a; Beebe *et al.* 2005), reducing the risk of obesity (Turk *et al.* 2009), cardiovascular disease, diabetes mellitus (Praet and van Loon 2009) and reducing the risk of certain cancers (Courneya and Friedenreich 2011). Depression has a strong association with the above mentioned disorders and therefore; the use of physical exercise to relieve depression is timely.

There is evidence to suggest that, exercising in natural environments offer greater benefits than exercising indoors (Thompson *et al.* 2011a; Pretty *et al.* 2005) and this finding has brought about the notion of Green Exercise or Eco-therapy (Pretty *et al.* 2005). Eco-therapy is the implementation of interventions such as walking, relaxation and creative activity, aimed at improving physical, psychological and social functioning using green spaces (Davis and Atkins 2004). A recent systematic review of nine studies found that compared to exercising indoors, exercising in natural environments such as parks or taking country walks is associated with greater feelings of revitalization and positive engagement, decrease in tension, confusion, anger, depression and increased energy. The review further reported that, those who participated in outdoor activities reported greater enjoyment and satisfaction and declared a greater intent to repeat the activity later. Those who participated in indoor exercise did not report the same level of satisfaction (Thompson *et al.* 2011b). This finding is buttressed by a more recent study of 708 participants that compared

the effects of walking exercise in a natural environment as opposed to walking exercise in an urban environment (Marselle *et al.* 2013). The investigators found that, group walks in farmland were significantly associated with less perceived stress, more positive mood, and greater mental well-being than walks in urban environments (Marselle *et al.* 2013). They concluded that outdoor walking group programs could be endorsed through "green prescriptions" to improve psychological and emotional well-being, as well as physical activity. Similarly, MIND (UK)commissioned a qualitative study of 109 participants engaging in eco-therapy and 90% of these reported that exercising in natural environments positively affected their mental health profoundly (MIND 2007). Some of the participant comments included,

"*It improves my depression, helps me be more motivated and gives me satisfaction in doing things. Since starting the project I have been able to improve on my quality of life. Coming here has made me overcome most of my problems*." Another comment included, "*I am more relaxed, have better focus of mind, greater coordination and greater self-esteem*"

Apart from the effects of eco-therapy in improving symptoms of depression, it may promote positive human behaviour and relationships in regaining personal identity, which may have been lost due to illness and possibly, during admission to inpatient hospital services. MIND (UK) have presented evidence on the impact and cost-effectiveness of eco-therapy suggesting that introducing five people with mental health issues to eco-therapy saves the state more than £25,000 per year in costs (MIND 2013). However, other investigators have questioned the clinical utility of exercise (Krogh *et al.* 2011).

In a systematic review of 13 trials with a total number of 687 participants, Krogh and colleagues concluded that exercise interventions may have a small, short-term beneficial effect in relieving symptoms of depression. They further asserted that there was no evidence that this small effect continued beyond 10 weeks (Krogh *et al.* 2011). However, findings from this review were limited by the relatively small sample size and caution is required when interpreting these findings. An additional pitfall of physical exercise pertains to its intensity. An excessive level of exercise can have adverse effects, such as overtraining (Armstrong and VanHeest 2002). Diagnoses of various mental disorders are surprisingly common among athletes who have been subjected to overtraining, fatigue, competition-related stress, injuries, failure and retirement (Schaal *et al.* 2011). On balance however, contemporary evidence support the use of physical exercise either alone or as an adjunct in the treatment of depression. Overall, this has implications for clinical for mental health nursing.

Implications for mental health nursing practice

From a historical perspective, many mental health institutions were often situated in pleasant gardens and beautiful landscape thus offering the many advantages of eco-therapy. Perhaps the main obvious benefit of exercise and eco-therapy is that it is cost effective. Whilst conventional treatments like antidepressants and psychological therapies are relatively costly and have unpleasant side effects as in the case of antidepressants, exercise and eco-therapy are relatively inexpensive. For depressed patients who may be non-adherent with antidepressants because of side effects, mental health nurses may actively encourage patients to take up exercise and prescribe eco-therapy as part of the care package. Unlike antidepressants, exercise or eco-therapy has minimal or no adverse side effects, yet it has the potential to be at least as effective.

Concerns have been raised about the unavailability of psychological therapies and waiting lists for CBT can be up to four years in some instances (MIND 2007). To counter this service deficiency, mental health nurses can play a critical role in enhancing the recovery process for those on a waiting list by usefully engaging them in eco-therapy and exercise. Unlike many psychological therapies that require the professional to be trained usually at a considerable cost to the service provider, eco-therapy requires little or no additional training for the professional. An important factor of exercise and eco-therapy is that it is non-invasive and likely to induce a sense of empowerment and control in the individual. With these factors in mind, eco-therapy may improve the overall functioning of a person in recovery and offer a better quality of life in promoting the bio-psychosocial model particularly for those with depression (Frankel *et al.* 2003).

Mental health nurses can encourage those patients who may be averse ECT treatment to take up eco-therapy and exercise as an alternative therapy. To overcome the high relapse rate that people experience after ECT, mental health nurses can encourage patients to take up exercise and eco-therapy as prophylactic measure after ECT treatment. Unlike ECT, exercise does not invoke similar moral and ethical questions. Specifically, eco-therapy improves mental wellbeing and meets outcomes across five government-identified areas for action (MIND 2013). It uses a life course approach, allowing people to develop skills and positive social relationships. It allows them to build

strength and resilience with benefits for individuals and communities. Importantly, it promotes health holistically and enables people to build self-esteem and confidence levels (MIND 2013).

Conclusion

Current treatment modalities for depression show effectiveness but they have pitfalls for a variety of reasons. High financial cost as in the case of psychological therapies, adverse side effects as in antidepressant treatment are all important pitfalls. Though effective ECT, it is short acting and poses moral and ethical questions. There is emerging evidence however to support the use of low cost interventions to augment existing treatment of depression. Eco-therapy and physical exercise are two alternative interventions that may proffer advantages to the individual with depression and mental; health nurses can implement these strategies as part of an armamentarium to militate against the ravages of depression. It is non-invasive, low cost and requires little or no further training for the mental health nurse. Critically, the benefits accrued by exercise and eco-therapy go beyond the treatment of depression.

Reference List

Appleby, J. What are we spending on the English NHS? 2013. Kings Fund. 15-3-0014.
Ref Type: Online Source

Armstrong LE, VanHeest JL (2002) The unknown mechanism of the overtraining syndrome: clues from depression and psychoneuroimmunology. Sports Med. **32,** 185-209.

Baldwin DS, Foong T (2013) Antidepressant drugs and sexual dysfunction
1. Br.J Psychiatry **202,** 396-397.

Barbui C, Percudani M, Hotopf M (2003) Economic evaluation of antidepressive agents: a systematic critique of experimental and observational studies
30. J Clin.Psychopharmacol. **23,** 145-154.

Beebe LH, Tian L, Morris N, Goodwin A, Allen SS, Kuldau J (2005) Effects of exercise on mental and physical health parameters of persons with schizophrenia
2. Issues Ment.Health Nurs. **26,** 661-676.

Beghi M, Rosenbaum JF (2010) Risk factors for fatal and nonfatal repetition of suicide attempt: a critical appraisal
1. Curr.Opin.Psychiatry **23,** 349-355.

Carek PJ, Laibstain SE, Carek SM (2011) Exercise for the treatment of depression and anxiety
7. Int.J Psychiatry Med **41,** 15-28.

Cassano P, Fava M (2002) Depression and public health: an overview
3. J Psychosom.Res **53,** 849-857.

Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, McMurdo M, Mead GE (2013a) Exercise for depression
1. Cochrane.Database.Syst.Rev. **9,** CD004366.

Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, McMurdo M, Mead GE (2013b) Exercise for depression
1. Cochrane.Database.Syst.Rev. **9,** CD004366.

Courneya KS, Friedenreich CM (2011) Physical activity and cancer: an introduction. Recent Results Cancer Res. **186,** 1-10.

Cox GR, Callahan P, Churchill R, Hunot V, Merry SN, Parker AG, Hetrick SE (2012) Psychological therapies versus antidepressant medication, alone and in combination for depression in children and adolescents
1. Cochrane.Database.Syst.Rev. **11,** CD008324.

Cuijpers P, Smit F, Bohlmeijer E, Hollon SD, Andersson G (2010) Efficacy of cognitive-behavioural therapy and other psychological treatments for adult depression: meta-analytic study of publication bias
5. Br.J Psychiatry **196,** 173-178.

Davis, K. M and Atkins, S. S. Creating and teaching a course in ecotherapy: we went to the woods. Journal of Humanistic Couselling Education and Development 43, 211-218. 2004.
Ref Type: Journal (Full)

Dietrich A, McDaniel WF (2004) Endocannabinoids and exercise. Br.J.Sports Med. **38,** 536-541.

DiMatteo MR, Lepper HS, Croghan TW (2000) Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence
1. Arch.Intern.Med **160,** 2101-2107.

DoH (2011) '
Talking therapies: A four-year plan of action.' Department of Health,London

Frankel, R. M, Quill, T. E, and McDaniel, S. H. The Biopsychosocial approach: past,present,future. 2003. Rochester, University of Rochester Press.
Ref Type: Edited Book

Fraser LM, O'Carroll RE, Ebmeier KP (2008) The effect of electroconvulsive therapy on autobiographical memory: a systematic review
1. J ECT. **24,** 10-17.

Gibbons RD, Brown CH, Hur K, Davis J, Mann JJ (2012a) Suicidal thoughts and behavior with antidepressant treatment: reanalysis of the randomized placebo-controlled studies of fluoxetine and venlafaxine
8. Arch.Gen.Psychiatry **69,** 580-587.

Gibbons RD, Hur K, Brown CH, Davis JM, Mann JJ (2012b) Benefits from antidepressants: synthesis of 6-week patient-level outcomes from double-blind placebo-controlled randomized trials of fluoxetine and venlafaxine
6. Arch.Gen.Psychiatry **69,** 572-579.

Henderson M, Harvey SB, Overland S, Mykletun A, Hotopf M (2011) Work and common psychiatric disorders
2. J R.Soc.Med **104,** 198-207.

hscic. Prescriptions dispersed in the community. 2013.
Ref Type: Online Source

Ingram A, Saling MM, Schweitzer I (2008) Cognitive side effects of brief pulse electroconvulsive therapy: a review
7. J ECT. **24,** 3-9.

Jakobsen JC, Hansen JL, Simonsen E, Gluud C (2012) The effect of adding psychodynamic therapy to antidepressants in patients with major depressive disorder. A systematic review of randomized clinical trials with meta-analyses and trial sequential analyses
4. J Affect.Disord. **137,** 4-14.

Katon WJ (2011) Epidemiology and treatment of depression in patients with chronic medical illness
6. Dialogues.Clin.Neurosci. **13,** 7-23.

Kennedy SH, Rizvi S (2009) Sexual dysfunction, depression, and the impact of antidepressants
15. J Clin.Psychopharmacol. **29,** 157-164.

Kirsch I (2008) Antidepressant drugs 'work', but they are not clinically effective
6. Br.J Hosp.Med (Lond) **69,** 359.

Krogh J, Nordentoft M, Sterne JA, Lawlor DA (2011) The effect of exercise in clinically depressed adults: systematic review and meta-analysis of randomized controlled trials. J.Clin.Psychiatry **72,** 529-538.

Marselle MR, Irvine KN, Warber SL (2013) Walking for well-being: are group walks in certain types of natural environments better for well-being than group walks in urban environments?
1. Int.J Environ.Res Public Health **10,** 5603-5628.

Matta Mello PE, Cevada T, Sobral Monteiro-Junior R, Teixeira GT, da Cruz RE, Lattari E, Blois C, Camaz DA (2013) Neuroscience of exercise: from neurobiology mechanisms to mental health. Neuropsychobiology **68,** 1-14.

MIND (2007) 'Ecotherapy-the green agenda for mental health.' MIND publishers,London

MIND (2013) 'Feel better outside feel better inside: ecotherapy for mental well being resilience and recovery.' Mind,London

Muller N (2014) Immunology of major depression
4. Neuroimmunomodulation. **21,** 123-130.

Mura G, Moro MF, Patten SB, Carta MG (2014) Exercise as an add-on strategy for the treatment of major depressive disorder: a systematic review
1. CNS.Spectr. 1-13.

NHS. Can I get free counselling or therapy? 2013. London, National Health Service, England.
Ref Type: Online Source

NICE. The Nice guidelines on the teratment and management of depression(updated edition). National Health Service . 2009. NHS.

Ref Type: Electronic Citation

Ottosson JO (1985) Use and misuse of electroconvulsive treatment. Biol.Psychiatry **20,** 933-946.

Penninx BW, Milaneschi Y, Lamers F, Vogelzangs N (2013) Understanding the somatic consequences of depression: biological mechanisms and the role of depression symptom profile 43. BMC.Med **11,** 129.

Petrides G, Tobias KG, Kellner CH, Rudorfer MV (2011) Continuation and maintenance electroconvulsive therapy for mood disorders: review of the literature. Neuropsychobiology **64,** 129-140.

Praet SF, van Loon LJ (2009) Exercise therapy in type 2 diabetes
1. Acta Diabetol. **46,** 263-278.

Pretty J, Peacock J, Sellens M, Griffin M (2005) The mental and physical health outcomes of green exercise
1. Int.J Environ.Health Res **15,** 319-337.

Rayner L, Price A, Evans A, Valsraj K, Hotopf M, Higginson IJ (2011) Antidepressants for the treatment of depression in palliative care: systematic review and meta-analysis
1. Palliat.Med **25,** 36-51.

Read J, Mosher LR, Bentall R (2004) 'Models of madness: Psychological, social and biological approaches to schizophrenia.' (Routledge: London)

Richards DA, Bower P, Pagel C, Weaver A, Utley M, Cape J, Pilling S, Lovell K, Gilbody S, Leibowitz J, Owens L, Paxton R, Hennessy S, Simpson A, Gallivan S, Tomson D, Vasilakis C (2012) Delivering stepped care: an analysis of implementation in routine practice
2. Implement.Sci. **7,** 3.

Roshanaei-Moghaddam B, Pauly MC, Atkins DC, Baldwin SA, Stein MB, Roy-Byrne P (2011) Relative effects of CBT and pharmacotherapy in depression versus anxiety: is medication somewhat better for depression, and CBT somewhat better for anxiety? Depress.Anxiety. **28,** 560-567.

Schaal K, Tafflet M, Nassif H, Thibault V, Pichard C, Alcotte M, Guillet T, El HN, Berthelot G, Simon S, Toussaint JF (2011) Psychological balance in high level athletes: gender-based differences and sport-specific patterns. PLoS.One. **6,** e19007.

Serretti A, Mandelli L (2010) Antidepressants and body weight: a comprehensive review and meta-analysis
2. J Clin.Psychiatry **71,** 1259-1272.

Shinohara K, Honyashiki M, Imai H, Hunot V, Caldwell DM, Davies P, Moore TH, Furukawa TA, Churchill R (2013) Behavioural therapies versus other psychological therapies for depression
11. Cochrane.Database.Syst.Rev. **10,** CD008696.

Sparks JA, Duncan BL (2013) Outside the Black Box: Re-assessing Pediatric Antidepressant Prescription
1. J Can.Acad.Child Adolesc.Psychiatry **22,** 240-246.

The UK ECT review group (2003) Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. The Lancet **8,** 799-808.

Thompson CJ, Boddy K, Stein K, Whear R, Barton J, Depledge MH (2011a) Does participating in physical activity in outdoor natural environments have a greater effect on physical and mental wellbeing than physical activity indoors? A systematic review
3. Environ.Sci.Technol. **45,** 1761-1772.

Thompson CJ, Boddy K, Stein K, Whear R, Barton J, Depledge MH (2011b) Does participating in physical activity in outdoor natural environments have a greater effect on physical and mental wellbeing than physical activity indoors? A systematic review
3. Environ.Sci.Technol. **45,** 1761-1772.

Tjora T, Hetland J, Aaro LE, Wold B, Wiium N, Overland S (2014) The association between smoking and depression from adolescence to adulthood
1. Addiction.

Trevino K, McClintock SM, Husain MM (2010) A review of continuation electroconvulsive therapy: application, safety, and efficacy
1. J ECT. **26,** 186-195.

Turk MW, Yang K, Hravnak M, Sereika SM, Ewing LJ, Burke LE (2009) Randomized clinical trials of weight loss maintenance: a review
4. J Cardiovasc.Nurs. **24,** 58-80.

Usher K, Park T, Foster K, Buettner P (2013) A randomized controlled trial undertaken to test a nurse-led weight management and exercise intervention designed for people with serious mental illness who take second generation antipsychotics
41. J Adv.Nurs. **69,** 1539-1548.

Warden D, Rush AJ, Trivedi MH, Fava M, Wisniewski SR (2007) The STAR*D Project results: a comprehensive review of findings
1. Curr.Psychiatry Rep. **9,** 449-459.

WHO. The global burden of disease. 2008. Geneva, WHO.
Ref Type: Online Source