

# **Safer Treatments for Depression and Anxiety**

A Guide to the Controlled Research on Alternatives to  
Pharmaceuticals

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Much of this information is available at [www.phonecounseling.net](http://www.phonecounseling.net)

“Although the world is full of suffering, it is also full of the overcoming of it.”

-- Helen Keller

*Thanks to Brian, Annie and Larry.*

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# Introduction

In 2008 I started seeing a successful graphic designer who was suffering from depression. He had been prescribed an SSRI a year earlier and had experienced a manic episode as a result. He was off of the medication when our therapy began and seeking alternative treatments. Every week he was asking me what I knew about a new herbal remedy, dietary supplement or gadget. I would research them to the best of my ability, and while it was outside of my scope of practice to recommend for or against any of them, I could tell him what the research seemed to say. My client kept a mood chart and experimented with many different treatments, eventually settling with psychotherapy, multivitamins, eating a few more vegetables and moderate weight lifting.

Through this experience, I realized that people suffering from depression are faced with the overwhelming task of deciphering mountains of conflicting claims about which treatments are effective and which are quackery. As a result, I began compiling this guide and made it available online. I now present it in booklet form for mental health professionals hoping that it will be able to help them and their clients to make more informed choices.

Pharmaceutical companies spend billions of dollars each year to convince doctors and their patients that medications are the best (or only) treatment for depression. However, research overwhelmingly shows that this is not the case. This guide is an attempt to review the evidence on some of the most popular depression treatment options. While not every alternative treatment has strong evidence behind it, several do. My hope is that this guide helps you discern which ones are which.

As a psychotherapist, I cannot recommend any treatment other than therapy because it would be outside of the scope of my license. However, I believe all therapists, social workers, doctors and dietitians can better serve their clients by having a clearer understanding of which alternative treatments are supported by evidence and which aren't.

Alternative treatments that do have strong supporting evidence have been included in the section I'm calling "First Tier Treatments." The other section is comprised of treatments that have been well-researched but the evidence is weak, and those that have not yet been tested enough for a conclusion to be warranted. It should go without saying that a lack of evidence does not indicate anything negative about the potential quality of the treatment.

I created this guide by doing an exhaustive literature review on MEDLINE and Google Scholar for peer-reviewed controlled outcome studies of popular alternative treatments for depression. When there were not enough of those, I included other study designs. I sifted through thousands of studies assessing the strengths of their designs and paid specific attention to conflicting data. This document could be much longer than it is, but I chose

only to include representative studies that give the reader the best overall picture of the state of the research. Therefore, when I found many similar studies with similar results, I included just one. When I found conflicting results, I made sure to include them, while contextualizing which results were more common. At times, I offer interpretations for mixed results, but I try to clearly distinguish my guesses from facts.

This project is a work in progress and I welcome all feedback.

## **Prevalence of Alternative Treatments for Depression**

While use of pharmaceuticals for depression has been growing at an alarming rate, complementary and alternative medicine (CAM), which includes many of the treatments discussed in this guide, remains extremely popular. While the larger and more encompassing studies are now quite old, newer research suggests that these treatments are not declining in popularity. I believe it is still safe to assume that at least half of people diagnosed with panic or depression are using some form of CAM and that these treatments are at least as popular as pharmaceuticals. The number today could be much higher given the growth of the alternative medicine industry, but we don't have solid data. It is also still likely that most people using these treatments are not being seen by an alternative practitioner.

Psychotherapy is not considered a CAM in the literature, so the percentage of people using non-pharmaceutical treatments is much greater than the numbers here.

### **Research**

**Kessler. R. et al. The Use of Complementary and Alternative Therapies to Treat Anxiety and Depression in the United States. *Am J Psychiatry* 158:289-294, February 2001.**

In a survey of 2,055 people (1997–1998) that obtained information on the use of 24 complementary and alternative therapies, it was found that 56.7% of those with panic and 53.6% of those with severe depression reported using complementary and alternative therapies in the past 12 months. Only 20.0% of those with anxiety attacks and 19.3% of those with severe depression visited a complementary or alternative therapist. 65.9% of people who had been seen by a conventional provider for anxiety attacks and 66.7% of those seen by a conventional provider for severe depression also used complementary and alternative therapies. Found that complementary and alternative therapies are used more than conventional therapies by people with self-defined panic attacks and severe depression. Most patients visiting conventional mental health providers for these problems also use complementary and alternative therapies.

**Wu, P. et al. Use of Complementary and Alternative Medicine Among Women With Depression: Results of a National Survey. *Psychiatr Serv* 58:349-356, March 2007.**

In a telephone survey of 3,068 women, 54% of those with depression reported past-year use of complementary and alternative medicine. Participants' most commonly cited reasons for use of these therapies were wanting treatments to be based on a "natural approach," wanting treatments to be congruent with their own values and beliefs, and past experiences in which conventional medical therapies had caused unpleasant side effects or had seemed ineffective.

**Tindle, H. et al. Trends in use of complementary and alternative medicine by US. *Alternative Therapies in Health and Medicine*, 2005 (Vol. 11) (No. 1) 42-49.**

Using the Alternative Health/Complementary and Alternative Medicine supplement to the 2002 National Health Interview Survey (NHIS, n=31,044) and a 1997 national survey (n=2,055), inquired into trends in the use of alternative therapies in the US between 1997 and 2002. Found that the most commonly used were herbal therapy (18.6%, representing over 38 million people) followed by relaxation techniques (14.2%, representing 29 million people) and chiropractic (7.4%, representing 15 million people). The greatest relative increase in CAM use between 1997 and 2002 was seen for herbal medicine (12.1% vs.18.6%, respectively), and yoga (3.7% vs. 5.1%, respectively), while the largest relative decrease occurred for chiropractic (9.9% to 7.4%, respectively).

**Bausell, B et al. Demographic and Health-Related Correlates of Visits to Complementary and Alternative Medical Providers. *Medical Care*. 39(2):190-196, February 2001.**

Individuals in poorer health and those suffering from mental, musculoskeletal, and metabolic disorders also tended to be more likely to have visited a CAM provider.

**Kessler, R. Prevalence and Treatment of Mental Disorders, 1990 to 2003. *NEJM*. Volume 352:2515-2523 June 16, 2005 Number 24.**

Using the National Comorbidity Survey (NCS) conducted between 1990-1992 (n=5388) and the NCS Replication conducted between 2001-2003 (n=4319) looked at the prevalence of different treatments for psychological problems. Found a small decrease in alternative therapies between the early 90's and 2003 and a large increase in psychiatric services.

**Russinova, Z. Wewiorski, N. Cash, D. Use of Alternative Health Care Practices by Persons With Serious Mental Illness: Perceived Benefits. October 2002, Vol 92, No. 10 | *American Journal of Public Health* 1600-1603.**

In a survey of 157 people with various diagnoses (bipolar disorder 45%, schizophrenia spectrum disorder 25%, and depressive disorder 25%) found that 86% used multiple treatments. That same percentage were using medications. The most frequently reported alternative practices were religious/spiritual activities (50%), meditation (43%), massage (31%), yoga (20%), guided imagery (18%), herbs (16%), chiropractic (13%), and nutritional supplements (13%).

# Overview of First Tier Treatments

## **Counseling and Therapy**

Psychotherapy is the most well-researched treatment for depression and no treatment has been found to be more effective. While a huge percentage of psychotherapy research suffers from poor design and bias, there is also a lot of solid research out there. One of the most consistently supported findings is that qualities such as positive regard and client reports of feeling understood are more predictive of positive outcome than any technique. What is sadly lacking in the research are reliable ways for therapists to strengthen those qualities in themselves.

## **Exercise as Depression Treatment**

Over the past 20 years there have been hundreds of studies on exercise and depression. From all this evidence it has become clear that exercise is at least as effective as medication, if not more so. Several types of exercise have been studied and no one form has been shown to be more effective than others. However, high intensity exercise (such as sprinting or interval training) has been shown to raise beta-endorphin levels at rates higher than moderate intensity exercise.

## **Nutrition and Supplements as a Treatment for Depression**

Since the beginning of controlled research in mental health, nutritional treatments have been shown to be effective for even the most severe psychological problems. In fact, there is evidence that many people's depression could be actually caused by a vitamin deficiency or other dietary imbalance. Therefore, a blood test checking vitamin levels in addition to thyroid levels would be reasonable for someone experiencing depression.

## **Sunlight and Lightbox Treatment for Depression**

Light therapy (also called phototherapy) is often the fastest acting treatment for depression, achieving results four times faster than drugs. There is evidence that depression can be caused by a vitamin D deficiency, and sufficient exposure to sunlight or bright full-spectrum artificial lights can cure that deficiency. Sunscreen blocks the skin's ability to produce vitamin D, and should never be used in conjunction with light therapy.

## **Negative Ions and Nature as a Depression Treatment**

In natural settings such as near the ocean or in a forest, the level of negative ions in the air is many thousand times greater than in urban or suburban settings. Artificially generating negative air ions is a relatively new and promising treatment. It has been tested in conjunction with light therapy as well as alone and has shown consistently positive results.

It seems to follow that spending time in a natural setting would offer similar benefits, but this has not been sufficiently studied.

## **Social Support and Depression**

Having enough social support is absolutely vital for both physical and mental health. While people who are more introverted may prefer to spend a good percentage of their time alone, we are social animals who need to feel cared for and connected to other people. However, for many of us, finding enough social support is easier said than done. Luckily, there are options such as support groups and internet tools like MeetUp.com for people whose social network is not strong enough.

## **Meaning and Spirituality**

Why can some people live through the most difficult circumstances and remain positive and healthy? In the past 20 years, research has found that one important answer to this question is meaning. If we can make sense out of our lives in a positive way and we interpret our difficulties as opportunities for growth, we become much less likely to experience psychological symptoms. Spirituality is one important way that people find meaning. This section discusses spiritual and non-spiritual ways to create meaning in life and reviews the research.

## **Volunteering and Service**

The research supporting the benefits of volunteering is some of the strongest of any depression treatment. People of all ages who volunteer show significant improvements in mood whether or not they had been experiencing depression. This section reviews the research as well as providing some resources to find volunteering opportunities.

# Specific Recommended Treatments

## Therapy and Counseling

After decades of research on psychotherapy, a few things have become very clear. Therapy is at least as effective as any other treatment for depression and adding complimentary treatments to therapy is helpful to some but not to others.

### Therapy Outcome Research In Brief

Over the past 50 years, researchers have learned a great deal about what makes someone a good therapist. They have found that what matters most are qualities such as whether he or she is a good listener, easy to connect with, and says what he or she means. One of the most important characteristics in a therapist is being unconditionally accepting.

Surprisingly, research has consistently shown that level of training has little effect on a therapist's skill. This means that whether you have a PhD or no advanced degree at all, it does not predict how effective you will be at helping people feel better. Similarly, theoretical orientation (cognitive-behavioral, psychodynamic, eclectic, etc.) does little to predict whether a therapist will be very good. While more than one thousand forms of psychotherapy exist, very few have been adequately studied and there is not good evidence that any are more or less effective than any others.

### Therapy vs. Medications

It has been well-established that medications do not out-perform psychotherapy as a treatment of depression. There is some debate as to whether combined treatment with drugs and therapy is superior to therapy alone. However, I have been unable to find any studies comparing therapy and drugs to therapy and placebo-drugs. Looking at the rest of the evidence on antidepressants, one can reasonably assume that drugs would not add any additional effect beyond placebo when combined with therapy. Some studies have found that therapy out-performs therapy and drugs over the long-term.

### Research

**Leslie A. Robinson, Jeffrey S. Berman, and Robert A. Neimeyer. Psychotherapy for the Treatment of Depression: A Comprehensive Review of Controlled Outcome Research. Psychological Bulletin. 1990, Vol. 108, No. 1, 30--49.**

A huge metaanalysis of all available controlled studies on treatments of depression. It found psychotherapy to be superior to medication, and therapy with medication to be equal to therapy alone.

**Antonuccio, David O.; Danton, William G.; DeNelsky, Garland Y. Psychotherapy versus medication for depression: Challenging the conventional wisdom with data. Professional Psychology: Research and Practice. 1995 Dec Vol 26(6) 574-585.**

Found that therapy is more effective than medications when patient-rated measures are used and long-term follow-up is considered.

**Wampold, B. (2001). The Great Psychotherapy Debate: Models, Methods and Findings. Laurence Erlbaum: New York.**

Reviews the evidence on what makes psychotherapy effective. Supports a common factors model over treatment modalities.

## **Exercise as a Depression Treatment**

For more than 20 years, studies have consistently shown that exercise is at least as effective as medications for treating depression. The most commonly studied forms of exercise for depression treatment have been jogging and lifting weights, and when compared, both have been found to be equally helpful. Some studies suggest that higher intensity, short-term exercise (such as sprinting) would have a larger effect because it releases more beta-endorphins, which are linked to elevated moods. Other research suggests that no additional benefit is gained from exercising at more than moderate intensity or more than three times a week. What is clear is that beginning to exercise has an equal or better chance at improving depression compared to drugs.

### **Beginning to exercise**

There are two main issues to think about in beginning to exercise to improve mood. The first is how to exercise safely. In general, it is safest to get some supervision from a trainer at a gym or to talk to your doctor. Second, in order to stick with it, it is important to have support. This can mean exercising with a friend, going to a gym where one feels comfortable, or talking with supportive people about successes in exercising.

To learn about higher intensity exercise (the kind that has been shown to raise your beta-endorphin levels in a much shorter amount of time), one can look up "high intensity interval training." If one is new to exercise, they should definitely have the supervision of a trainer or doctor for exercising at high intensity.

### **Research**

**Blumenthal, J; Babyak, M; Moore, K; Craighead, W; Herman, S; Khatri, P; Waugh, R; Napolitano, M; Forman, L; Appelbaum, M; Doraiswamy, P.; K. Krishnan, R. Effects of Exercise Training on Older Patients With Major Depression. Arch Intern Med. 1999;159:2349-2356.**

One hundred fifty-six men and women diagnosed with major depression (age,  $\geq 50$  years) were assigned randomly to a program of aerobic exercise, medication (sertraline hydrochloride), or combined exercise and medication. In this study, medication led to a more rapid initial therapeutic response than exercise, but after 16 weeks of treatment exercise was equally effective in reducing depression. There was no placebo medication control.

**Michael Babyak, PhD, James A. Blumenthal, PhD, Steve Herman, PhD, Parinda Khatri, PhD, Murali Doraiswamy, MD, Kathleen Moore, PhD, W. Edward Craighead, PhD, Teri T. Baldewicz, PhD and K. Ranga Krishnan, MD. Exercise Treatment for Major Depression: Maintenance of Therapeutic Benefit at 10 Months. Psychosomatic Medicine 62:633-638 (2000)**

This was a follow-up of the study above. After 4 months people in all three groups exhibited significant improvement; the proportion of people who no longer met diagnostic criteria for major depression and had an HRSD score  $< 8$  was comparable across the three treatment conditions. After 10 months, however, remitted subjects in the exercise group had significantly lower relapse rates ( $p = .01$ ) than subjects in the medication group. Exercising on one's own during the follow-up period was associated with a reduced probability of depression diagnosis at the end of that period (odds ratio = 0.49,  $p = .0009$ ).

**A . Dunn , M . Trivedi , J . Kampert , C . Clark , H . Chambliss. Exercise treatment for depression: Efficacy and dose response. American Journal of Preventive Medicine , Volume 28 , Issue 1 , Pages 1 - 8**

Participants were randomized to one of four aerobic exercise treatment groups that varied total energy expenditure (7.0 kcal/kg/week or 17.5 kcal/kg/week) and frequency (3 days/week or 5 days/week) or to exercise placebo control (3 days/week flexibility exercise). The main effect of energy expenditure in reducing Hamilton scores at 12 weeks was significant. Adjusted mean Hamilton scores at 12 weeks were reduced 47% from baseline for the high-intensity group, compared with 30% for low-intensity and 29% for control. There was no main effect of exercise frequency at 12 weeks.

**Salmon, P. Effects of physical exercise on anxiety, depression, and sensitivity to stress: A unifying theory. Clinical Psychology Review. Volume 21, Issue 1, February 2001, Pages 33-61**

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.

**Schwarz, L. et al. Changes in beta-endorphin levels in response to aerobic and anaerobic exercise. Sports Med. 1992**

Exercise-induced increases in the peripheral beta-endorphin concentration are mainly associated both with changes in pain perception and mood state. Published studies reveal that incremental graded and short term anaerobic exercise lead to an increase in beta-endorphin levels.

**MH Klein, JH Greist, AS Gurman, RA Neimeyer, DP. A comparative outcome study of group psychotherapy vs. exercise treatments for depression. International Journal of Mental Health, 1985.**

Found that group therapy, jogging and weight lifting all have equivalent effect sizes for decreasing measures of depression.

## **Nutritional Treatments for Depression**

For more than 50 years psychiatrists have been researching nutritional treatments to treat psychological problems, often with impressive results. The body of research is overwhelmingly clear that diet not only affects mood, but that inadequate nutrition and vitamin deficiency may be the cause of some people's depression.

A small percentage people have a metabolic condition that causes difficulties absorbing certain vitamins from food and they can require much higher doses in order to get adequate vitamin levels in their blood. This means that some people can be experiencing vitamin deficiencies even though they are eating a healthy diet and must take supplements. Therefore, it can make sense for someone experiencing depression to get their blood tested to see if they are deficient in any vitamins, especially folate, niacin, B12 and D.

### **Trying to eat better**

Social support is important in trying to change one's diet. As you will read below, many common foods (such as sugar) have drug effects and can be very difficult to give up. Overeaters Anonymous can be a source of support for someone trying to change their diet.

### **Important Foods and Supplements for Depression**

The information below is not meant to constitute a recommended diet. It is a list of foods that have been shown to have a negative correlation with depression, either directly or indirectly.

**Green leafy vegetables:** These are by far the most nutritious foods, including spinach, kale, collards, chard and lettuce. They are an excellent source of folate and stimulate the body to produce its own powerful antioxidants. Dr. Joel Fuhrman recommends having at least one bunch of greens or one head of lettuce each day. This is much more than most Americans eat, but it may dramatically improve one's health and mood.

**Omega-3 fats:** These fats play an important role in our brains and their positive effect on mood has considerable (although not unanimous) evidence. People who are depressed can get a therapeutic dose of Omega-3's by taking 3 grams of high quality fish oil each day. Other sources include fresh wild salmon, algae-based DHA, ground flax seeds and walnuts.

**Beans especially chickpeas and black-eyed peas:** They are the best dietary source of folate.

**Starchy roots such as potatoes, parsnips and carrots:** Countries with high intake of these foods have a much lower incidence of depression.

**Vitamin D:** It can be difficult to get enough vitamin D from the sun, especially if you live somewhere that is not sunny year round. One may want to take a supplement, in which case it should be known that the most absorbable form of vitamin D is cholecalciferol.

**B Vitamins including Folate:** It can be a good idea to take a B12 supplement. Other vitamins can interfere with absorption of B12, so many doctors recommend taking it on its own. It also needs to mix with saliva in order to be metabolized, so the ideal form is a small pill called a 'sublingual' that you just hold under your tongue until it dissolves. MTHF is the most absorbable form of folate.

**Antioxidants including Vitamin E:** Fruits such as pomegranate and blueberries are good sources of antioxidants. Vitamin E is found in many seeds and nuts.

**Zinc:** Several studies have shown a correlation between zinc deficiencies and depression, but others have failed to show this. Some studies suggest that zinc is a potentially effective treatment for depression, but others do not.

### **Substances One May Want to Avoid**

- Sugar.
- Caffeine.
- Alcohol.
- Dairy.
- Cholesterol
- Fried foods.
- Binge eating or eating to cope with negative feelings

## Research

### - Omega 3 Fats

**Peet, M. International variations in the outcome of schizophrenia and the prevalence of depression in relation to national dietary practices: an ecological analysis. The British Journal of Psychiatry (2004) 184: 404-408**

The diets in New Zealand, Canada, Germany, France, USA, USSR, Taiwan and Japan were correlated with their rates of depression. With regard to depression, the strongest association was between a high dietary intake of fish and seafood and reduced prevalence of depression.

**Mamalakis G, Tornaritis M, Kafatos A. Depression and adipose essential polyunsaturated fatty acids. Prostaglandins Leukot Essent Fatty Acids. 2002;67(5):311-8.**

Depressed people have lower levels of the Omega-3 fat DHA in their fatty tissues compared to others.

**Peet M, Stokes C. Omega-3 fatty acids in the treatment of psychiatric disorders. Drugs. 2005;65(8):1051-9.**

EPA is more effective than DHA for treating depression.

**Maesa, M. Smithd, R. Christophee, A. Cosynsc, P. Desnydera, R. Meltzerb, H. Fatty acid composition in major depression: decreased  $\omega$ 3 fractions in cholesteryl esters and increased C20:4 $\omega$ 6/C20:5 $\omega$ 3 ratio in cholesteryl esters and phospholipids. Journal of Affective Disorders. Volume 38, Issue 1, 26 April 1996, Pages 35-46**

People diagnosed with major depression had significantly higher Omega 6/Omega 3 ratios compared to healthy volunteers and people with minor depression. People with major depression showed significantly lower total Omega 3 polyunsaturated fatty acids. These findings suggest an abnormal intake or metabolism of essential fatty acids in conjunction with decreased formation of cholesteryl esters in major depression.

**Lucas M; et al. Dietary intake of n-3 and n-6 fatty acids and the risk of clinical depression in women: a 10-y prospective follow-up study. The American Journal Of Clinical Nutrition [Am J Clin Nutr] 2011 Jun; Vol. 93 (6), pp. 1337-43.**

A huge study that followed over 50,000 women (ages 50-77) for 10 years. Found no relationship between dietary Omega 3 intake from fish and depression. Did find that alpha-linolenic acid (ALA, from Omega 3 rich vegetable sources) did protect from depression.

- **Vitamin D**

**Gloth FM 3rd, Alam W, Hollis B. Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder. J Nutr Health Aging. 1999;3(1):5-7.**

All subjects receiving vitamin D improved in all outcome measures. Subjects receiving vitamin D improved more than those receiving phototherapy.

**Shipowick, C. D. Moore, C. B. Corbett, C. Bindler, R. Vitamin D and depressive symptoms in women during the winter: a pilot study. Appl Nurs Res. 2009 Aug; 22 (3): 221-5.**

Vitamin D supplementation led to higher levels of the vitamin in the blood and decreases in depression scores. No placebo control.

**Jorde, R. Sneve, M. Figenschau, Y. Svartberg, J. Waterloo, K. Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: randomized double blind trial. J Intern Med. 2008 Dec; 264 (6): 599-609.**

Placebo controlled study found vitamin D had specific antidepressive effects.

**Penckofer, S. Kouba, J. Byrn, M. Estwing Ferrans, C. Vitamin D and depression: where is all the sunshine? Issues Ment Health Nurs. 2010 Jun; 31 (6): 385-93.**

Concluded that detecting vitamin D deficiency and addressing it would be a cost-effective response to depression.

- **Folate, Niacin and other B Vitamins**

**Bolander-Gouaille, C. Treatment of depression: time to consider folic acid and vitamin B12. Journal of Psychopharmacology, Vol. 19, No. 1, 59-65 (2005)**

Both low folate and low vitamin B12 status have been found in studies of depressed people, and an association between depression and low levels of the two vitamins is found in studies of the general population. There is now substantial evidence of a common decrease in serum/red blood cell folate, serum vitamin B12 and an increase in plasma homocysteine in depression. The authors suggest supplements of both folic acid (800 µg daily) and vitamin B12 (1 mg daily) to improve treatment outcome in depression.

**Raymond T. P. Paul, Anne P. McDonnell, Dr Christopher B. Kelly. Folic acid: neurochemistry, metabolism and relationship to depression. Human Psychopharmacology: Clinical and Experimental. Volume 19 Issue 7, Pages 477 - 488**

A recently discovered genetic variant (5,10 MTHFR) leading to altered folic acid metabolism may explain why some individuals are vulnerable to the effects of folic acid deficiency, despite adequate intake.

**Tommi Tolmunena, Jukka Hintikka, Anu Ruusunen, Sari Voutilainen, Antti Tanskanen, Veli-Pekka Valkonen, Heimo Viinamäki, George A. Kaplan, Jukka T. Salonen. Dietary Folate and the Risk of Depression in Finnish Middle-Aged Men: A Prospective Follow-Up Study. Psychother Psychosom 2004;73:334-339**

Studied the association between dietary folate and recovery from depression in Finnish men. The group was recruited between 1984 and 1989 and followed until the end of 2000, and it consisted of 2,313 men aged between 42 and 60 years from eastern Finland. Results: The mean intake of folate in the whole cohort was 256 µg/day (SD = 76). Those below the median of energy-adjusted folate intake had higher risk of depression (RR 3.04, 95% CI: 1.58, 5.86) during the follow-up period than those who had a folate intake above the median.

**Alpert JE, Fava M. Nutrition and depression: the role of folate. Nutr Rev. 1997 May;55(5):145-9.**

Depressive symptoms are the most common neuropsychiatric manifestation of folate deficiency. Conversely, borderline low or deficient serum or red blood cell folate levels have been detected in 15-38% of adults diagnosed with depressive disorders.

**Martha S. Morris, Maurizio Fava, Paul F. Jacques, Jacob Selhub, Irwin H. Rosenberg. Depression and Folate Status in the US Population. Psychother Psychosom 2003;72:80-87**

Healthy subjects whose red blood cell folate concentrations had been measured were determined to have no depression (n = 2,526), major depression (n = 301), or dysthymia (n = 121) using a diagnostic interview schedule. Low folate status was detectable in depressed members of the general US population.

**Young, S. The use of diet and dietary components in the study of factors controlling affect in humans: a review. J Psychiatry Neurosci. 1993 November; 18(5): 235-244.**

Reviews the effects of diet on depression, especially folate and complex carbohydrates.

#### **- Antioxidants Including Vitamin E**

**Tsuboi H, Shimoi K, Kinae N, Oguni I, Hori R, Kobayashi F. Depressive symptoms are independently correlated with lipid peroxidation in a female population: comparison with vitamins and carotenoids. J Psychosom Res. 2004; 56(1): 53-8**

Oxidated fats, such as any fat or oil that has been used for cooking, increases chances for depression. Antioxidants neutralize these oxidated fats.

**Maes, M. Lower serum vitamin E concentrations in major depression Another marker of lowered antioxidant defenses in that illness. Journal of Affective Disorders , Volume 58 , Issue 3 , Pages 241 - 246.**

Major depression is associated with defective antioxidant defenses. Vitamin E is the major fat soluble antioxidant in the body. Patients with major depression had significantly lower serum vitamin E concentrations than healthy controls.

- Zinc

**Amani R; Saeidi S; Nazari Z; Nematpour S. Correlation between dietary zinc intakes and its serum levels with depression scales in young female students. Biological Trace Element Research [Biol Trace Elem Res] 2010 Nov; Vol. 137 (2), pp. 150-8.**

In a random sampling of 308 female college students, identified 28 suffering from depression. Compared dietary zinc intake and zinc blood levels between them and 28 non-depressed. Found that depressed had one-third less zinc in diet and in blood.

**Cope EC; Levenson CW. Role of zinc in the development and treatment of mood disorders. Current Opinion In Clinical Nutrition And Metabolic Care [Curr Opin Clin Nutr Metab Care] 2010 Nov; Vol. 13 (6), pp. 685-9.**

Reviews clinical studies and animal lab studies to show that zinc deficiency may play a role in depression and that supplementation could be an effective treatment.

**Irmisch G; Schlaefke D; Richter J. Zinc and fatty acids in depression. Neurochemical Research [Neurochem Res] 2010 Sep; Vol. 35 (9), pp. 1376-83.**

Found no difference in zinc levels in the blood of depressed and non-depressed people.

**DiGirolamo AM; et al. Randomized trial of the effect of zinc supplementation on the mental health of school-age children in Guatemala. The American Journal Of Clinical Nutrition [Am J Clin Nutr] 2010 Nov; Vol. 92 (5), pp. 1241-50.**

Compared zinc and placebo. Found that zinc supplements increased blood levels of zinc more than placebo but did not beat placebo in improving depressive symptoms.

- Sugar and Caffeine

**Peet, M. International variations in the outcome of schizophrenia and the prevalence of depression in relation to national dietary practices: an ecological analysis. The British Journal of Psychiatry (2004) 184: 404-408**

The diets in New Zealand, Canada, Germany, France, USA, USSR, Taiwan and Japan were correlated with their rates of depression. Found that a greater consumption of refined sugar is associated with a greater prevalence of depression. Conversely, high intake of starchy roots was associated with a reduced prevalence of depression.

**Carlo Colantuoni, Pedro Rada, Joseph McCarthy, Caroline Patten, Nicole M. Avena, Andrew Chadeayne, and Bartley G. Hoebel. Evidence That Intermittent, Excessive Sugar Intake Causes Endogenous Opioid Dependence Obes Res. 2002;10:478-488.**

Intermittent excessive intake of sugar led to physical addiction in rats, marked by strong withdrawal symptoms. Withdrawal symptoms could be triggered after high sugar doses by either fasting or an opioid blocker, Naloxone.

**Lenoir, M. et al. Intense Sweetness Surpasses Cocaine Reward. PLoS ONE 2(8): e698. doi:10.1371/journal.pone.0000698**

Found that 94% rats prefer water sweetened with saccharin—an intense calorie-free sweetener—to cocaine. The preference for saccharin was not attributable to its unnatural ability to induce sweetness without calories because the same preference was also observed with sucrose, a natural sugar. Finally, the preference for saccharin was not surmountable by increasing doses of cocaine and was observed despite either cocaine intoxication, sensitization or intake escalation—the latter being a hallmark of drug addiction.

**Lee MA, Flegel P, Greden JF, Cameron OG. Anxiogenic effects of caffeine on panic and depressed patients. Am J Psychiatry. 1988 May;145(5):632-5.**

Found that people who have been diagnosed with depression report that caffeine makes them feel anxious at a level higher than people who are not feeling depressed.

- **Dairy**

**Peet, M. International variations in the outcome of schizophrenia and the prevalence of depression in relation to national dietary practices: an ecological analysis. The British Journal of Psychiatry (2004) 184: 404-408**

The diets in New Zealand, Canada, Germany, France, USA, USSR, Taiwan and Japan were correlated with their rates of depression. It was found that a high intake of dairy products was associated with an increased prevalence of depression.

- **Alcohol**

**Brown SA, Schuckit MA. Changes in depression among abstinent alcoholics. J Stud Alcohol 1988; 49: 412-417.**

Heavy drinkers experienced a dramatic decrease in depressive symptoms upon abstaining from alcohol.

**Worthington J, Fava M, Agustin C, Alpert J, Nierenberg AA, Pava JA, Rosenbaum JF. Consumption of alcohol, nicotine, and caffeine among depressed outpatients. Relationship with response to treatment. Psychosomatics. 1996 Nov-Dec;37(6):518-22.**

Found that even moderate levels of alcohol consumption interfered with depression treatment.

**S . Gilman. A longitudinal study of the order of onset of alcohol dependence and major depression. Drug and Alcohol Dependence , Volume 63 , Issue 3 , Pages 277 - 286**

This study followed more than 14,000 consumers of community mental health services and found that when someone begins to drink heavily, they are likely to meet criteria for Major Depression within the next year. The converse is also true.

**Jürgen Rehm, Robin Room, Kathryn Graham, Maristela Monteiro, Gerhard Gmel & Christopher T. Sempos. The relationship of average volume of alcohol consumption**

**and patterns of drinking to burden of disease: an overview. *Addiction*. Volume 98 Issue 9, Pages 1209 - 1228**

Found that alcohol consumption correlated to several serious health problems from major depression to various forms of cancer.

**David W. Oslin, M.D., Ira R. Katz, M.D., Ph.D., William S. Edell, Ph.D., and Thomas R. Ten Have, Ph.D. Effects of Alcohol Consumption on the Treatment of Depression Among Elderly Patients. *Am J Geriatr Psychiatry* 8:215-220, August 2000**

Found that decreasing alcohol use, even for moderate drinkers, lead to an improvement for elderly people with depression.

**Davidson KM. Diagnosis of depression in alcohol dependence: changes in prevalence with drinking status. *Br J Psychiatry* 1995; 166: 199-204.**

Eighty-two alcohol-dependent in-patients were tested and during the episode of drinking which led to admission, a diagnosis of major depression was found in the majority of patients (67%). Once detoxification from alcohol took place, only the minority (13%) met criteria for major depression. This suggests that alcohol use could cause depression that remits upon abstinence.

#### - **Cholesterol**

**Weidner, G. et al. Improvements in hostility and depression in relation to dietary change and cholesterol lowering. *The Family Heart Study. Ann-Intern-Med.* 1992 Nov 15; 117(10): 820-3.**

Those who consumed a low-fat, high complex-carbohydrate diet at the end of the study showed significantly greater improvements in depression (P = 0.044; difference in improvement, 2.9 points) and aggressive hostility (P = 0.035; difference in improvement, 3.3 points) as well as a reduction in their plasma cholesterol levels (P = 0.024; difference in improvement, 2.7%) compared with those who ate a high-fat "American diet."

#### - **Fried Foods**

**Tsuboi H, Shimoi K, Kinae N, Oguni I, Hori R, Kobayashi F. Depressive symptoms are independently correlated with lipid peroxidation in a female population: comparison with vitamins and carotenoids. *J Psychosom Res.* 2004; 56(1): 53-8**

Oxidated fats, such as any fat or oil that has been used for frying, increases chances for depression. Antioxidants neutralize these oxidated fats.

- **Eating to cope with negative feelings**

**Musante, G. Costanzo, P. Friedman, K. The comorbidity of depression and eating dysregulation processes in a diet-seeking obese population: A matter of gender specificity. *International Journal of Eating Disorders*. (1998). Volume 23 Issue 1, Pages 65 - 75.**

This sample consisted of 1,184 self-admitted patients enrolled in a residential weight loss program between 1990 and 1995. Subjects were administered several questionnaires including (a) the Beck Depression Inventory, (b) 5-point scales of eating-related foci, and (c) 7-point scales of subject's confidence in their eating control under various circumstances. For obese females, negative-emotion disrupted eating and binge-purge behaviors were prominent predictors of depression. For males, eating induced by experiences of social or physical inadequacy and fasting relating to eating behaviors were the depression-relevant variables.

## **Sunlight and Lightboxes**

Light therapy (also called phototherapy) has been studied as a treatment for seasonal depression for more than 20 years. More recently it has been established as an effective treatment for nonseasonal depression as well. Several studies have shown lightboxes can achieve significant relief from depression more than four times faster than medication. They are particularly effective for people over 65.

### **What kind of light to use**

Both natural sunlight and commercial lightboxes have been shown to treat depression effectively. When thinking about whether to purchase an artificial lightbox, one should know that sunlight reaches levels of 100,000 lux, while the most powerful home lightboxes produce only about one-tenth that amount of light. However, being able to be exposed to bright lights while indoors is more convenient for many people, and depending on one's latitude, the sun may only be high enough to be able to produce vitamin D for a few hours around midday.

Therapeutic exposure to a 10,000 lux lightbox is 30 minutes a day. Some studies indicate that doing light therapy as close to dawn as possible increases effectiveness, while others suggest that time of day is not important. When choosing to use sunlight, one half hour on a clear day at midday is ideal.

Whether using natural sunlight or a lightbox, it is very important that one does not use any sunscreen. Sunscreen blocks your body's ability to produce vitamin D, which is believed to play an important role in causing and treating depression. Some evidence suggests that vitamin D supplements are more effective than light therapy.

## Research

**Terman, M; Terman, J. Light Therapy for Seasonal and Nonseasonal Depression: Efficacy, Protocol, Safety, and Side Effects. *CNS Spectr.* 2005;10(8):647-663.**

Bright light therapy is well recognized as an extremely effective treatment for seasonally-related depression, specifically Seasonal Affective Disorder. Treatment ranges from 2,500 to 10,000 lux for 2 hours to .5 hours respectively. For major depression, light therapy produces results after one only week that medications do not achieve until 4-16 weeks. Light therapy is particularly effective with elderly people.

**G . Lambert , C . Reid , D . Kaye , G . Jennings , M . Esler. Effect of sunlight and season on serotonin turnover in the brain. *The Lancet*, Volume 360 , Issue 9348 , Pages 1840 - 1842**

The rate of production of serotonin by the brain was directly related to the prevailing duration of bright sunlight ( $r=0.294$ ,  $p=0.010$ ), and rose rapidly with increased luminosity. Supports the notion that changes in release of serotonin by the brain underlie mood seasonality and seasonal affective disorder.

**Isabel C. Sumaya. Beth M. Rienzib, Jess F. Deegan, Ilb and Donald E. Mossa. Bright Light Treatment Decreases Depression in Institutionalized Older Adults: A Placebo-Controlled Crossover Study. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 56:M356-M360 (2001).**

Scores on the Global Depression Scale (GDS) remained unchanged during the placebo (low light) and control conditions, but depression scores decreased significantly during the 10,000 lux treatment (pretest GDS M = 15 vs posttest GDS M = 11,  $p < .01$ ). After the 10,000 lux treatment, 50% of the participants no longer scored in the depressed range. Improvement during the 10,000 lux condition was positively correlated ( $r = .62$ ,  $p < .05$ ) to baseline GDS scores, where participants with higher GDS scores experienced greater improvement following the 10,000 lux treatment.

**Charmane I. Eastman, PhD; Michael A. Young, PhD; Louis F. Fogg, PhD; Liwen Liu, PhD; Patricia M. Meaden, PhD. Bright Light Treatment of Winter Depression: A Placebo-Controlled Trial. *Arch Gen Psychiatry.* 1998;55:883-889.**

After 3 weeks of treatment, morning light produced more of the complete or almost complete remissions than placebo. By 1 criterion (24-item SIGH-SAD score  $<50\%$  of baseline and  $\leq 8$ ), 61% of the patients responded to morning light, 50% to evening light, and 32% to placebo after 4 weeks of treatment.

**Avery DH, Bolte MA, Dager SR, Wilson LG, Weyer M, Cox GB, Dunner DL. Dawn simulation treatment of winter depression: a controlled study. Am J Psychiatry. 1993 Jan;150(1):113-7.**

The 2-hour, 250-lux dawn simulation resulted in Hamilton depression scale scores that were significantly lower than scores after the 30-minute, 0.2-lux dawn simulation.

**Joan Arehart-Treichel. In Treating Nonseasonal Depression, Let the Light Shine In. Psychiatr News Sept, 2005 Volume 40, Number 17, page 14.**

Found that light was somewhat more effective in people who had been exposed to light during the winter than in subjects who had been exposed to light in months outside of winter, but the difference was not significant.

**Gloth FM 3rd, Alam W, Hollis B. Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder. J Nutr Health Aging. 1999;3(1):5-7.**

All subjects receiving vitamin D improved in all outcome measures. Subjects receiving vitamin D improved more than those receiving phototherapy.

**B.-E. Thalén, B.F. Kjellman, L. Mørkrid, R. Wibom, L. Wetterberg. Light treatment in seasonal and nonseasonal depression. Acta Psychiatrica Scandinavica. Volume 91 Issue 5, Pages 352 - 360.**

Depressed patients with seasonal pattern improved significantly more than those with a nonseasonal pattern to light therapy. There were no significant differences in outcome when light treatment was given in the morning or in the evening, and not between patients with and without atypical symptoms such as carbohydrate craving or increased appetite.

**Daniel F. Kripke. Light treatment for nonseasonal depression: speed, efficacy, and combined treatment. Journal of Affective Disorders. Volume 49, Issue 2, May 1998, Pages 109-117.**

Light treatment of nonseasonal depression produces net benefits in the range of 12–35%, often within 1 week. Showed that light therapy's value for nonseasonal and seasonal depression are comparable. Light appears to produce faster antidepressant benefits than medication.

## **Negative Ions and Nature**

In natural settings such as near the ocean or in a forest, the level of negative ions in the air is many thousand times greater than in urban or suburban settings. Artificially creating negative ions has been shown to be an effective and fast acting treatment for depression.

It would seem to follow that spending time in natural settings might yield similar results, although it has not been demonstrated empirically.

## Research

**Goel, N. Terman, M. Terman, J. Macchi, M. Stewart, J. Controlled trial of bright light and negative air ions for chronic depression. *Psychological Medicine*. 35(7):945-955, July 2005.**

Subjects were 24 women and 8 men, ages 22-65 years (mean age +/- S.D., 43.7 + 12.4 years), diagnosed with major depression. Found that people recovered at rates of 53.7% for bright light and 51.1% for high-density ions v. 17.0% for low-density ions. The presence or severity of atypical symptoms did not predict response. Both bright light and negative air ions are effective for treatment of chronic depression.

**Terman, M. Terman, J. Ross, D. A Controlled Trial of Timed Bright Light and Negative Air Ionization for Treatment of Winter Depression. *Arch Gen Psychiatry*. 1998;55:875-882.**

Subjects with seasonal affective disorder (n=158) were randomly assigned to 6 groups for 2 consecutive treatment periods, each 10 to 14 days. Light treatment sequences were morning-evening, evening-morning, morning-morning, and evening-evening (10000 lux, 30 min/d). Two other groups received either high density ions or low density (which was the placebo). Low-density ion response was shown to be inferior to all other groups, with no other group differences. The only sequence effect was that the response to evening light was reduced when preceded by treatment with morning light. Stringent remission criteria, however, showed significantly higher response to morning than evening light, regardless of treatment sequence. Bright light and high-density negative air ionization both appear to act as specific antidepressants in patients with seasonal affective disorder. Whether clinical improvement would be further enhanced by their use in combination or as complements to other treatments awaits investigation.

**Terman, M, Terman, J. Controlled Trial of Naturalistic Dawn Simulation and Negative Air Ionization for Seasonal Affective Disorder. *Am J Psychiatry* 163:2126-2133, December 2006**

The subjects were 99 adults (77 women and 22 men) with season affective disorder (94 cases) and bipolar II disorder (five cases). Five parallel groups received 1) dawn simulation (0.0003–250 lux in the pattern of May 5 at 45° north latitude); 2) a dawn light pulse (13 minutes, 250 lux, with an illuminant dose of 3.25x10<sup>3</sup> lux-minutes matched to the simulated dawn); 3) postawakening bright light (30 minutes, 10,000 lux); 4) negative air ionization at high flow rate (93 minutes, 4.5x10<sup>14</sup> ions/second); or 5) ionization at low flow rate (93 minutes, 1.7x10<sup>11</sup> ions/second). The symptoms were assessed over 3 weeks with the Hamilton Depression Rating Scale—Seasonal Affective Disorder Version. Results were bright light, 57.1%; dawn simulation, 49.5%; dawn pulse, 42.7%; high-density ions, 47.9%; and low-density ions, 22.7% (significantly lower than the others). Contrary to the authors' hypothesis, analysis of variance failed to find superiority of dawn simulation to the dawn pulse or bright light. However, the dawn pulse led to a pattern of residual or exacerbated depressive symptoms similar to those seen in low-density ion nonresponders. Naturalistic dawn simulation and high-density ionization are active

antidepressants that do not require the effort of postawakening bright light therapy. They can be considered candidate alternatives to bright light or medication.

**Goel, N. Etwaroo, G. Bright light, negative air ions and auditory stimuli produce rapid mood changes in a student population: a placebo-controlled study. *Psychological Medicine*. 36(9):1253-1263, September 2006.**

One hundred and eighteen subjects, 69 women and 49 men (mean age + S.D., 19.4+1.7 years), were randomly assigned to one of four conditions: bright light (10000 lux; n = 29), auditory stimuli (60 dB; n = 30), or high-density (4.5 x 10<sup>14</sup> ions/s flow rate; n = 29) or low-density (1.7 x 10<sup>11</sup> ions/s; n = 30; placebo control) negative ions. Exposure was for 30min on three consecutive evenings between 1900 and 2100 hours. Mood and alertness assessments, using standardized scales, occurred before, and 15 and 30 min during exposure. The Beck Depression Inventory classified subjects as depressed ( $\geq 10$ ; n = 35) or non-depressed ( $< 10$ ; n = 83). The three active stimuli, but not the low-density placebo, reduced depression, total mood disturbance (a global affect measure) and/or anger within 15-30 min. Neither time of year nor intensity of depressive symptoms affected response to stimuli. The auditory stimulus, bright light and high-density ions all produced rapid mood changes - with small to medium effect sizes - in depressed and non-depressed subjects, compared with the low-density placebo, despite equivalent pre-study expectations. Thus, these stimuli improve mood acutely in a student sample, including a subset with depressive symptoms.

**Goel, N; Terman, M; Terman, Juan S; Macchi, M; Stewart, J. Controlled trial of bright light and negative air ions for chronic depression. *Psychological Medicine*. 35(7):945-955, July 2005.**

SIGH-SAD score improvement was 53.7% for bright light and 51.1% for high-density ions v. 17.0% for low-density ions. Remission rates were 50%, 50% and 0% respectively. The presence or severity of atypical symptoms did not predict response to either treatment modality, nor were phase advances to light associated with positive response. Both bright light and negative air ions are effective for treatment of chronic depression. Remission rates are similar to those for SAD, but without a seasonal dependency or apparent mediation by circadian rhythm phase shifts.

**Krueger, A. Kotaka, S. The effects of air ions on brain levels of serotonin in mice. *International Journal of Biometeorology*. Volume 13, Number 1 / June, 1969.**

Mice were exposed for 12, 24, 48 and 72 hrs to 3 different concentrations of small positive or negative air ions: 2-4 x 10<sup>3</sup> ions/cm<sup>3</sup>, 3-4 x 10<sup>4</sup> ions/cm<sup>3</sup> or 3.5-5 x 10<sup>5</sup> ions/cm<sup>3</sup>. Brain serotonin levels of these mice showed statistically significant differences as early as 12 hours from those of untreated mice. They did not persist after 12 hours. Unclear if untreated mice were handled in a similar way.

**Morton, L. Kershner, J. Differential negative air ion effects on learning disabled and normal-achieving children. International Journal of Biometeorology. Volume 34, Number 1 / March, 1990.**

Forty normal-achieving and 33 learning disabled (LD) children were assigned randomly to either a negative ion or placebo test condition. On a dichotic listening task using consonant-vowel (CV) combinations, both groups showed an ion-induced increase in the normal right ear advantage (REA).

## **Social Support**

The amount of social support in a person's life not only has an enormous effect on their mental health, but on their physical health as well. Every form of illness and emotional distress is worsened by not having enough social support.

Research has helped us to learn quite a bit about social support. First, not all “social support” is positive. Some is problematic and can have a negative effect, such as a close-knit but hostile family. Social support can be understood as having a certain level of depth (how intimate a connection is) and breadth (how many people someone interacts with). Both depth and breadth are important. Finally, some research suggests that the main ways that social support contributes to our well-being is by giving us a sense of belonging and self-worth.

### **Ways to Increase Social Support**

In trying to increase social support, we can be aware that we are ultimately looking for a sense of belonging and self-worth. Some relationships will be better at meeting those needs, so more energy should be put there.

One of the most well-researched avenues to increase social support is to become a volunteer.

Support groups are another excellent way of reaching out for people who are shy. They provide an easier way to meet people for those who dislike unstructured social events. Also, websites such as MeetUp.com can be helpful in finding activity partners and are a good way to meet new people.

Research has found that using the internet for information about health problems can help people feel more social support and less lonely.

## Research

**C. S. Aneshensel and J. D. Stone. Stress and depression: a test of the buffering model of social support. Arch Gen Psych. Vol. 39 No. 12, December 1982.**

Among a large community sample (n=1,000) of Los Angeles County adults interviewed in 1979, perceived support were negatively related to depressive symptoms. Data suggested that social support, instead of merely protecting an individual against the negative impact of stress, may itself be important in ameliorating depressive symptoms. Moreover, assuming that lack of perceived or actual social support is not just a manifestation of depression itself, data suggested that the lack of social support contributes to the creation of depressive symptoms.

**LK George, DG Blazer, DC Hughes and N Fowler. Social support and the outcome of major depression. The British Journal of Psychiatry 154: 478-485 (1989).**

One hundred and fifty middle-aged and elderly adults with a diagnosis of major depression were assessed initially as in-patients, and were re-interviewed 6-32 months later. Both size of social network and subjective social support were significant predictors of depressive symptoms at follow-up, with baseline depression scores and other predictors of outcome statistically controlled. Subjective social support was most strongly associated with major depression; this effect was significantly stronger for middle-aged than older adults, and for men than women. Differences in the effects of marital status, size of social network, and subjective social support also suggest the importance of distinguishing between involvement in and quality of interpersonal relationships.

**MOHR D. C. ; CLASSEN C. ; BARRERA M. JR ; The relationship between social support, depression and treatment for depression in people with multiple sclerosis. Psychological medicine. vol. 34, no3, pp. 533-541.**

Studies have been fairly consistent in finding a relationship between social support and depression. This study examined the effects of treatment for depression on social support among patients with multiple sclerosis (MS). Treatment for depression was associated with significant increases in perceived social support, utilized social support and satisfaction with support, as well as reduction in need for emotional support. There were no significant changes in structural support or need for physical support.

**Ornish, D. (1998). Love and Survival. HarperCollins: New York.**

Reviews a large body of research relating various measures of intimacy to various health outcomes. Shows a consistent connection between breadth and depth of social support and overall health.

**Revenson, T. et al. Social support as a double-edged sword: the relation of positive and problematic support to depression among rheumatoid arthritis patients. Soc Sci Med. 1991;33(7):807-13.**

This study differentiated between positive and problematic social support in patients recently diagnosed with rheumatoid arthritis. Found that positive support

decreased depression, while problematic support increased it. A positive X problematic support interaction suggested that the costs of problematic support do not cancel out the benefits of positive support. Patients who reported both little support and a greater degree of problematic interactions experienced the highest level of symptoms. Emphasized the need to consider positive and negative aspects of support transactions conjointly in assessing their stress-reducing and health-protective potential.

**Holahan CK, Holahan CJ. Self-efficacy, social support, and depression in aging: a longitudinal analysis. J Gerontol. 1987 Jan;42(1):65-8.**

Showed that self-efficacy relating to social support (the belief that one has the capability to build a supportive social network) predicts levels of social support and depression one year later.

**Russell DW, Cutrona CE. Social support, stress, and depressive symptoms among the elderly: test of a process model. Psychol Aging. 1991 Jun;6(2):190-201.**

Effects of social support, negative life events, and daily hassles on depressive symptoms were assessed in 301 adults aged 65 or older, in person 3 times at 6-month intervals and by mail questionnaires every month over a 12-month period. Social support and initial levels of depressive symptoms predicted the number of daily hassles but not number of major life events.

**Prince, M. et al. Social Support Deficits, Loneliness and Life Events as Risk Factors for Depression in Old Age. Psychological Medicine. 27(2):323-332, March 1997.**

There was a strong, graded, relationship between the number of social support deficits (SSDs) and depression. Number of SSDs also related to age, handicap, loneliness and use of homecare services. Loneliness was itself strongly associated with depression; odds ratio 12.

**Dean A, Kolody B, Wood P. Effects of social support from various sources on depression in elderly persons. J Health Soc Behav. 1990 Jun;31(2):148-61.**

Although global measures of social support demonstrate significant effects on psychological and physical well-being, the differential significance of various support sources is largely unknown. Spouse, friends, and adult children were found to rank in descending order of importance; other relatives showed no effect. Low support may have stronger effects than unavailability of sources.

**Logsdon MC, McBride AB, Birkimer JC. Social support and postpartum depression. Res Nurs Health. 1994 Dec;17(6):449-57.**

Women with low-risk first pregnancy (n=105) were surveyed 1 month before and 1 month after delivery. In multiple regression, two social support discrepancy measures, prenatal depression and postpartal closeness to husband, correlated with postpartal depression (positively and negatively, respectively) and accounted for nearly 40% of its variance.

**Bolton W, Oatley K. A longitudinal study of social support and depression in unemployed men. Psychol Med. 1987 May;17(2):453-60.**

Interviews were conducted with 49 men just after they had become unemployed, and with a matched sample of 49 employed men. Follow-up interviews took place 6-8 months later. At follow-up 20 originally unemployed men were still without work, and were significantly more depressed than the employed. In a multiple regression analysis there was a significant employment X social support interaction that indicated depression scores at follow-up were higher in those who remained unemployed and who had little social contact with others in the month before losing their jobs. Depression becomes likely when people lose a source of social interaction that is important to their sense of worth, and have no alternative means of experiencing this worth in other relationships.

**Symister, P. Friend, R. The influence of social support and problematic support on optimism and depression in chronic illness: A prospective study evaluating self-esteem as a mediator. Health psychology. 2003, vol. 22, no2, pp. 123-129.**

Eighty-six end-stage renal disease patients were assessed twice for social support, problematic support, and self-esteem. Adjustment was assessed twice by depression and optimism. Mediation analyses indicated that social support operated through self-esteem to influence optimism cross-sectionally and prospectively and depression cross-sectionally. Social support was associated with high self-esteem, which in turn increased optimism and was related to decreased depression.

**Fogel, J. et al. Internet use and social support in women with breast cancer. Health Psychology. Vol 21(4), Jul 2002, 398-404.**

The authors investigated the potential psychological benefits of Internet use for medical information by breast cancer patients. Of the 251 women approached, 188 were successfully interviewed (74.9%). Forty-two percent used the Internet for medical information related to breast health issues and did so for an average of 0.80 hr per week. The Interpersonal Support Evaluation List and the UCLA Loneliness Scale, with results controlled for covariates, showed that Internet use for breast health issues was associated with greater social support and less loneliness than Internet use for other purposes or nonuse. Breast cancer patients may obtain these psychological benefits with only a minimal weekly time commitment.

**Hagerty, B. Williams, A. The Effects of Sense of Belonging, Social Support, Conflict, and Loneliness on Depression. Nursing Research. 48(4):215-219, July/August 1999.**

A sample of clients diagnosed with major depressive disorder and students in a midwestern community college participated in the study by completing questionnaires. Social support had only an indirect effect on depression, and this finding supported the buffer theory of social support. Sense of belonging was a better predictor of depression.

# Spirituality and Meaning

Our ability to create satisfactory meaning out of the events in our lives has been well-established as a factor in mental health. Spirituality is often defined in terms of the meaning and purpose attributed to life, illness, death and other existential concerns. When defined in this way, spirituality has been shown to be strongly protective against depression.

Conversely, measures of how religious someone is, based on attending services or strength of beliefs (whether or not they are associated with an institutionalized religion), generally are not. In fact, many studies have found a slight increase in the likelihood of someone being depressed if they invest a lot of meaning in religious practices. The exception seems to be depression that religion protects against depression caused by poor health in elderly people.

People receiving treatment for depression often rate their spirituality as one of the most important parts of their recovery. Much of the research on spirituality and depression has been focused on elderly or terminally ill people, although similar results have been found for college students and the middle-aged.

## Developing Positive Meaning and Spirituality

Most of the research on involving meaning and spirituality is focused on how important it is for mental health. There is little controlled research on effective ways to improve these qualities. One thing we do know is that thinking about the meaning of events in life or of life itself does no harm. I often recommend that clients reflect on their lives, experiences and other aspects of life that trouble them and try to find some positive meaning in them. Reading books or talking with people who have a strong sense of meaning and purpose in their lives can be helpful as well.

It can also be helpful to develop a ritual or habit around self-care. Depression is very responsive to anything that one believes will be of help, so wholehearted belief is important to make treatment work.

## Research

**Nelson, C. et al. Spirituality, Religion, and Depression in the Terminally Ill . *Psychosomatics* 43:213-220, June 2002.**

This study examined the impact of spirituality and religiosity on depressive symptom severity in a sample of terminally ill patients with cancer and AIDS. A strong negative association was observed between the FACIT Spiritual Well-Being scale and the Hamilton Depression Scale, but no such relationship was found for religiosity, because more religious individuals had somewhat higher depression scores. Similar patterns were observed for the FACIT subscales, finding a strong negative association between the meaning and peace subscale (which corresponds

to the more existential aspects of spirituality) and depression scores, whereas a positive, albeit nonsignificant, association was observed for the faith subscale (which corresponds more closely to religiosity). These results suggest that the beneficial aspects of religion may be primarily those that relate to spiritual well-being rather than to religious practices per se. Implications for clinical interventions and palliative-care practice are discussed.

**Breitbart, W. Spirituality and meaning in supportive care: spirituality- and meaning-centered group psychotherapy interventions in advanced cancer. Supportive Care in Cancer. Volume 10, Number 4 / May, 2002.**

As concepts of adequate supportive care expand beyond a focus on pain and physical symptom control, existential and spiritual issues such as meaning, hope and spirituality in general have received increased attention from supportive care clinicians and clinical researchers. This paper reviews the topics of spirituality and end-of-life care, defines spirituality, and suggests measures of spirituality that deal with two of its main components: faith/religious beliefs and meaning/spiritual well-being. These two constructs of spirituality are reviewed in terms of their role in supportive care.

**Cooper, L. et al. How Important Is Intrinsic Spirituality in Depression Care? A Comparison of White and African-American Primary Care Patients. J Gen Intern Med. 2001 September; 16(9): 634–638.**

Used a cross-sectional survey to compare the views of African-American and white adult primary care patients (n=76) regarding the importance of various aspects of depression care. Patients were asked to rate the importance of 126 aspects of depression care (derived from attitudinal domains identified in focus groups) on a 5-point Likert scale. Intrinsic spirituality was rated 6 by both African Americans and whites.

**MCCOUBRIE R. DAVIES A. Is there a correlation between spirituality and anxiety and depression in patients with advanced cancer? Supportive care in cancer. 2006, vol. 14, no4, pp. 379-385.**

Religion and spirituality are generally recognized as having different meanings - religion entailing a relationship with a higher being, while spirituality can be thought of in terms of meaning and purpose in life. A significant negative correlation was found between both anxiety and depression scores and overall spiritual well-being scores (n=85;  $p < 0.0001$ ). When the subscale scores were analysed individually, a significant negative correlation was found between the existential well-being scores and the anxiety and depression scores ( $p < 0.001$ ). However, no correlation was found between the religious well-being scores and anxiety or depression.

**Wink, P. et al. Religion as Moderator of the Depression-Health Connection. Research on Aging, Vol. 27, No. 2, 197-220 (2005).**

When spirituality is measured as adherence to noninstitutionalized religious beliefs and practices, it does not protect against depression. Religiousness did protect against depression associated with poor health in an elderly population.

**Ellermann, C. Reed, P. Self-Transcendence and Depression in Middle-Age Adults. Western Journal of Nursing Research, Vol. 23, No. 7, 698-713 (2001).**

Self-transcendence has been found to be an important correlate of mental health in older adults and adults facing the end of life. This relationship was also found in middle-aged adults.

**Reker, G. Personal meaning, optimism, and choice: existential predictors of depression in community and institutional elderly. The Gerontologist, Vol 37, Issue 6 709-716, 1997.**

Showed that choice/responsibility, social resources, and physical health predicted depression in community elderly; personal meaning, optimism, social resources, and physical health predicted depression in institutionalized elderly. In both samples, the existential variables accounted for unique variance in depression over and above that accounted for by traditional measures. The important role of existential constructs in transcending personal and social losses and feelings of depression are discussed.

**Fehring RJ, Brennan PF, Keller ML. Psychological and spiritual well-being in college students. Res Nurs Health. 1987 Dec;10(6):391-8.**

In two separate studies of 95 and 75 college students, several tests were administered. Found that spiritual well-being, existential well-being, and spiritual outlook showed strong inverse relationships with negative moods suggesting that spiritual variables may influence psychological well-being.

**Blinderman, C. Existential issues do not necessarily result in existential suffering: lessons from cancer patients in Israel. Palliative Medicine, Vol. 19, No. 5, 371-380 (2005).**

A qualitative assessment of 40 patients with advanced cancer was undertaken through an interview process addressing the following themes: autonomy, dignity/body image, social isolation, coping mechanisms, guilt/past disappointments, spiritual health, meaning, hope and death/dying. The findings of this study indicate that existential concerns are endemic in this patient population, but that significant distress is relatively uncommon.

**Neimeyer, R. (ed.) Meaning Reconstruction and the Experience of Loss. APA: Washington DC (2001).**

Focuses on the importance of creating meaning out of losses in order to process them healthily. Reviews a large body of research supporting this claim.

# Volunteering and Service for Depression

Although most of the research has focused on how volunteering benefits people over 65, it has also been shown to have a strong effect on relieving depression and improving well-being for all adults. Volunteering is especially helpful for people experiencing depression and chronic medical conditions such as pain.

Volunteering has been shown to help overall health, life functioning, one's sense of optimism and control. It does not seem to make a difference whether you volunteer with one organization or several, nor what cause you volunteer for. However there is some evidence that people over 65 benefit more from volunteering for religious causes, while this finding does not seem to hold for people under 65.

## Ways to Find Volunteering and Service Opportunities

There are several services online that help find volunteer opportunities by location and interest.

- VolunteerMatch.org
- HUD Volunteering Clearinghouse.
- Network for Good.

## Research

**Li, Y. Ferraro, K. Volunteering and Depression in Later Life: Social Benefit or Selection Processes? *Journal of Health and Social Behavior*, Volume 46, Number 1, March 2005 , pp. 68-84(17).**

Depression was shown to be associated with a subsequent increase in formal volunteering, suggesting voluntarism as a means of compensation. Functional health problems, not depression, emerged as the important barrier to volunteering.

**Li, Y. Ferraro, K. Volunteering and Depression: The Effect of Social Causation or Selection?" Paper presented at the annual meeting of the American Sociological Association, Atlanta Hilton Hotel, Atlanta, GA, Aug 16, 2003.**

Addresses these questions with three waves of data from a national sample of older people. Multi-group structural-equation models for complete and incomplete data were used to estimate the joint causal relationship between volunteer work and depression. The results reveal a beneficial effect of formal volunteering on depression, but not for informal helping. In addition, a sample selection effect was detected and accounted for in the analysis — depressed persons and non-volunteers were less likely to complete the panel study. Depression was shown to be associated with a subsequent increase in formal volunteering.

**Wheeler, J. Gorey, K. Greenblatt, B. The beneficial effects of volunteering for older volunteers and the people they serve : A meta-analysis. International journal of aging & human development. 1998, vol. 47, no1, pp. 69-79 (2 p.3/4).**

This meta-analysis of thirty-seven independent studies provided the means of inferring not only that elder volunteers' sense of well-being seemed to be significantly bolstered through volunteering, but also that such relatively healthy older people represent a significant adjunct resource for meeting some of the service needs of more vulnerable elders, as well as those of other similarly vulnerable groups such as disabled children.

**Lum, T. The Effects of Volunteering on the Physical and Mental Health of Older People. Research on Aging, Vol. 27, No. 1, 31-55 (2005).**

Longitudinal data from the 1993 and 2000 panels of the Asset and Health Dynamics Among the Oldest Old Study (AHEAD) were used to measure health and mental health outcomes of people over age 70 who volunteered at least 100 hours in 1993. The findings provide empirical support to earlier claims that volunteering slows the decline in self-reported health and functioning levels, slows the increase in depression levels, and improves mortality rates for those who volunteer.

**Morrow-Howell, N. et al. Effects of Volunteering on the Well-Being of Older Adults. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences 58:S137-S145 (2003).**

This study re-analyzed data from the Americans' Changing Lives Study. It found that older adults who volunteer and who engage in more hours of volunteering report higher levels of well-being. This positive effect was not moderated by social integration, race, or gender. There was no effect of the number of organizations for which the older adult volunteered, the type of organization, or the perceived benefit of the work to others.

**Musick, M. Wilson, J. Volunteering and depression: the role of psychological and social resources in different age groups. Social Science & Medicine. Volume 56, Issue 2, January 2003, Pages 259-269.**

Found that, for the elderly, volunteering for religious causes is more beneficial for mental health than volunteering for secular causes.

**Arnstein, P. et al. From chronic pain patient to peer: Benefits and risks of volunteering. Pain Management Nursing. Volume 3, Issue 3, September 2002, Pages 94-103.**

This study found that improvements in pain, disability, and depression were reported immediately after training and after volunteering for several months without evidence of harm for a sample of chronic pain patients who did peer volunteering.

**Helmes, E. Govindan, A. Differences between Older Adult Volunteers and Non-volunteers in Depression and Self-efficacy. Australian Journal on Volunteering, Volume 12 Issue 2 (2007).**

Levels of self-efficacy and depression were contrasted among 87 older volunteers and 84 non-volunteers on measures of self-efficacy, depression, years of education and age. The results found that self-efficacy, depression and age all discriminated significantly between volunteers and non-volunteers. The present study highlights the importance volunteering may have in fostering self-efficacy in older people, and while exploratory in nature, it has important implications for promoting independent functioning in later life and improving the quality of life of older people.

**Mellor, D. et al. Volunteering and Well-Being: Do Self-Esteem, Optimism, and Perceived Control Mediate the Relationship? Journal of Social Service Research, Volume 34, Issue 4 August 2008 , pages 61 - 70.**

Using personal well-being as a more positive measure of well-being than absence of depression, this study further explored the possible mediating role of self-esteem, optimism, and perceived control in the relationship between volunteer status and well-being. Participants (n=1,219) completed a 97-item survey as part of the Australian Unity Wellbeing project. Variables measured included personal well-being, self-esteem, optimism, and a number of personality and psychological adjustment factors. Analyses revealed that perceived control and optimism, but not self-esteem, mediated the relationship between volunteer status and personal well-being.

# Other Specific Treatments

## 5-HTP and Other Amino Acids

The relationship between neurotransmitters and mood is complicated often misunderstood. While it is clear that serotonin and norepinephrine have something to do with depression, it is hard to say what that relationship is exactly. It has been well established that people who are depressed are likely to have low levels of these chemicals in their blood. However, when researchers artificially drop the level of serotonin in the blood of a depressed person who has never used antidepressants, it has no effect on their mood at all. When the same serotonin is dropped in healthy subjects, it usually has only a small effect on their mood.

This seems to indicate one of two things. Either low serotonin is a side-effect of depression (rather than a cause) or that it can cause depression only in certain people. There is some reason to believe that a genetic polymorphism could be involved in what makes serotonin affect some people's mood more than others. However, there are many people with this gene who are not depressed.

5-HTP and tyrosine are amino acids that are the main building blocks for serotonin and norepinephrine respectively, and there has been interest in using them to treat depression.

From the current research, it is not clear that increasing the levels of these amino acids in your blood has any positive effects beyond placebo. (It should be remembered that placebo is a highly effective treatment for depression.) The current research is not of high enough quality to make a determination and further research is needed.

Given what we know about serotonin, the most likely effective use for 5-HTP would be specifically for people with genetically-determined low transcription of that neurotransmitter. However, there have not yet been any studies to test this hypothesis.

Someone who does have this certain genetic polymorphism, could potentially be helped by supplementing 5-HTP. However, the evidence for this treatment is not nearly as strong as those listed in the "First Tier Treatments" section of this booklet.

## Research

### - Amino Acids as Treatment

**Meyers, S. Use of Neurotransmitter Precursors for Treatment of Depression. *Altern Med Rev* 2000;5(1):64-71.**

Reviewed available evidence on precursors to serotonin (tryptophan and 5-HTP) and norepinephrine (L-phenylalanine and tyrosine) to treat depression. Found the evidence to be conflicting and insufficient to make a conclusion about their efficacy.

**Kelly Shaw, Jane Turner, Christopher Del Mar. Are tryptophan and 5-hydroxytryptophan effective treatments for depression? A meta-analysis. *Australian and New Zealand Journal of Psychiatry*. Volume 36 Issue 4, Pages 488 - 491.**

While there is some evidence of superiority to placebo, this review found that the quality of research investigating 5-HTP and tryptophan is too poor to discern if they have any specific antidepressant properties.

**Tyrosine and L-Phenylalanine Supplements. *Nutr Health*. 1984;3(3):163-73.**

Reviews the theory behind advocating for neurotransmitter precursors in the treatment of depression and its relationship to the neurotransmitter theories of depression. Mentions that the supposed effectiveness of SSRI's is largely responsible for the neurotransmitter theory of depression.

**Thomson, J. The treatment of depression in general practice: a comparison of L-tryptophan, amitriptyline, and a combination of L-tryptophan and amitriptyline with placebo. *Psychol Med*. 1982 Nov;12(4):741-51.**

One hundred and fifteen patients from 5 general practices participated in a 12-week, double-blind study comparing L-tryptophan, amitriptyline, L-tryptophan-amitriptyline combination and placebo in the treatment of depression. Analysis of total score on the Hamilton Depression Scale and a global rating of depression showed that all 3 active treatments were more effective than placebo.

### - The Relationship Between Amino Acids and Depression

**Neumeister, A. et al. Association Between Serotonin Transporter Gene Promoter Polymorphism (5HTTLPR) and Behavioral Responses to Tryptophan Depletion in Healthy Women With and Without Family History of Depression. *Arch Gen Psychiatry*. 2002;59:613-620.**

Serotonin transporter gene promoter polymorphism (5HTTLPR)-dependent low transcriptional activity of the human serotonin transporter gene may be a genetic susceptibility factor for depression. This study looked at the behavioral responses to tryptophan depletion (TD) in healthy women with and without a first-degree family history of depression and examined the relationship to 5HTTLPR alleles. The TD induced a robust decrease of plasma tryptophan levels in all women irrespective of family history of depression or 5HTTLPR genotypes. The s/s genotype of the 5HTTLPR was associated with an increased risk of developing depressive symptoms

during TD irrespective of family history. In contrast, individuals with the l/l genotype did not develop depressive symptoms, irrespective of family history. Finally, s/l subjects without family history showed a mood response that was intermediate between the s/s and l/l subjects, while s/l subjects with a family history of depression showed the same depressiogenic effect of TD as seen in the s/s subjects.

**Åberg-Wistedt, A. Serotonergic 'vulnerability' in affective disorder: a study of the tryptophan depletion test and relationships between peripheral and central serotonin indexes in citalopram-responders. *Acta Psychiatrica Scandinavica*. Volume 97 Issue 5, Pages 374 - 380.**

A double-blind study of the tryptophan depletion (TD) challenge was performed on a sample consisting of 20 patients with a major depressive disorder in clinical remission after citalopram treatment. TD was induced by the intake of 43 g of an amino acid mixture containing the five large neutral amino acids. The control group received the same mixture, to which 2.3 g tryptophan had been added. Five of the 12 challenged patients showed a worsening of depressive symptoms during the day of the test. In contrast, there was no mood alteration in the eight control patients. Baseline Cortisol levels were significantly higher in responders to TD compared to those in non-responders and controls. Thus low mood appeared to be associated with low serotonin precursor availability as well as with high Cortisol levels.

## **Acupuncture for Depression**

The research on acupuncture for depression is promising, but unclear. While there have been several controlled trials of acupuncture for depression, none have had an excellent study design.

Acupuncture has been found to be as effective as medications in treating depression in most trials. However, it does not seem to matter which points in the body receive the acupuncture needles (whether they are acupuncture points associated with depression, acupuncture points not associated with depression or just random points). There is also some evidence that electro-acupuncture might be more effective than traditional acupuncture for depression, but this could be due to enhanced placebo response.

Acupuncture does not yet have solid evidence for depression, but it might be effective and has positive side-effects, including relaxation and strengthening the immune system.

## Research

**Röschke, J. The benefit from whole body acupuncture in major depression. *Journal of Affective Disorders*, Volume 57, Issue 1 - 3, Pages 73 - 81.**

A single-blind placebo-controlled study that looked at the efficacy of acupuncture applied in conjunction with drug treatment for major depression. The study included 70 inpatients with a major depressive episode in three different treatment groups: verum acupuncture, placebo acupuncture and a control group. All three groups were pharmacologically treated with the antidepressant mianserin. Patients who experienced acupuncture improved slightly more than patients treated with mianserin alone. However, no differences between placebo and verum acupuncture were detected.

**Allen, J. Schnyer, R. Hitt, S. The Efficacy of Acupuncture in the Treatment of Major Depression in Women. *Psychological Science*. Volume 9 Issue 5, Pages 397 - 401.**

The effectiveness of acupuncture as a treatment for major depression was examined in 38 women, randomly assigned to one of three treatment groups. Specific treatment involved acupuncture treatments for symptoms of depression; nonspecific treatment involved acupuncture for symptoms that were not clearly part of depression; a wait-list condition involved waiting without treatment for 8 weeks. Results from this small sample suggest that acupuncture can provide significant symptom relief in depression, at rates comparable to those of psychotherapy or pharmacotherapy.

**Luo H, Clinical research on the therapeutic effect of the electro-acupuncture treatment in patients with depression. *Psychiatry Clin Neurosci*. 1998 Dec;52 Suppl:S338-40.**

Electroacupuncture (EA) stimulation has been found to influence the brain (norepinephrine metabolism in experimental animals). Preliminary clinical research has shown that EA treatment is as effective as medication for patients with depression. In this study, two consecutive clinical studies on the treatment of depression with EA are conducted. The first study was double blind placebo controlled, in which 29 depressed inpatients were recruited. Patients were randomly divided into three groups: EA + placebo; amitriptyline; and EA + amitriptyline. They received EA and/or amitriptyline treatment for 6 weeks. The Hamilton Rating Scale for Depression, Clinical Global Impression and ASBERG scales for the side effect of antidepressants were used to evaluate the therapeutic efficacy and side effects. Based on the results and research protocol of the first study, a multi-centered collaborative study was conducted, in which 241 inpatients with depression were recruited. Patients were randomly divided into two treatment groups: the EA + placebo and the amitriptyline groups. The results from both studies showed that the therapeutic efficacy of EA was equal to that of amitriptyline for depressive disorders ( $P > 0.05$ ). Electro-acupuncture had a better therapeutic effect for anxiety somatization and cognitive process disturbance of depressed patients than amitriptyline ( $P < 0.05$ ). Moreover, the side effects of EA were much less than that of amitriptyline ( $P < 0.001$ ). The article suggested that EA treatment

was an effective therapeutic method for depressive disorders. Particularly, it was a treatment of choice for depressed patients who were unable to comply with the classic antidepressants because of their side effects. The possible mechanism of EA treatment is discussed.

**Smith CA, Hay PP. Acupuncture for depression. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD004046.**

This review examined the efficacy and adverse effects of acupuncture for depression by reviewing studies on six databases. Inclusion criteria included all published and unpublished randomised controlled trials comparing acupuncture with sham acupuncture, no treatment, pharmacological treatment, other structured psychotherapies (cognitive behavioural therapy, psychotherapy or counselling), or standard care. Meta analysis was performed using relative risk for dichotomous outcomes and weighted mean differences for continuous outcomes, with 95% confidence intervals. Primary outcomes were reduction in the severity of depression, measured by self rating scales, or by clinician rated scales; and an improvement in depression defined as remission vs no remission. In seven trials including 517 participants, there was no evidence that medication was better than acupuncture in reducing the severity of depression (WMD 0.53, 95%CI -1.42 to 2.47), or in improving depression, defined as remission versus no remission (RR1.2, 95%CI 0.94 to 1.51). However, scientific study design was poor and the number of people studied was small.

**Manber, R. Acupuncture: a promising treatment for depression during pregnancy. Journal of Affective Disorders 83 (2004) 89-95.**

Compared active acupuncture to active control acupuncture and massage in depression relief for pregnant women. While the study size was very small, it found active acupuncture to decrease depressive symptoms at rates similar to medications and therapy. The researchers call for further investigation since their numbers were small and the blind was inadequate.

## **Chromium Picolate**

While the research supported Chromium Picolate is not as strong as many other treatments, there is some evidence that it might be helpful for people who experience depression with strong cravings for carbohydrates.

### **Research**

**DOCHERTY, JOHN P. MD; SACK, DAVID A. MD; ROFFMAN, MARK PhD; FINCH, MANLEY; KOMOROWSKI, JAMES R. MS. A Double-Blind, Placebo-Controlled, Exploratory Trial of Chromium Picolate in Atypical Depression: Effect on Carbohydrate Craving. Journal of Psychiatric Practice. 11(5):302-314, September 2005.**

There was no significant difference between the CrPic and placebo groups on the primary efficacy measures, with both groups showing significant improvement from baseline on total HAM-D-29 scores during the course of treatment ( $p < 0.0001$ ). The data suggested the slight possibility of being more effective with depressed people with high carbohydrate craving.

## Homeopathy

While there is not enough high quality research to determine whether homeopathy has a specific effect on depression, there are many published cases of people whose depression was greatly improved on homeopathic treatments. Since they are not compared with a control group, we can't be sure that the improvement was just due to placebo or their positive relationship with the homeopathic practitioner. There are no serious side-effects to homeopathic treatment for depression, and it is almost surely better than no treatment.

### Research

**Pilkington, K. Homeopathy for depression: a systematic review of the research evidence. *Homeopathy*, 94 (3), pp. 153-163, July 2005.**

After a comprehensive review of medical databases, found no controlled trials with sufficient statistical power. Most of the research is in the form of observational studies without a control group. These studies uniformly report high levels of effectiveness, but it cannot be known if this is due to the specific treatment.

## Melatonin for Depression

It is clear that people suffering from depression may have a delayed melatonin cycle. It is unclear whether this should be understood as a cause or an effect of depression. There is some evidence that they also have lower levels of melatonin in their blood, but other studies do not show this pattern.

Research on melatonin as a treatment for depression is sorely lacking in both design strength and numbers of subjects. While most studies show a small positive effect on depression, at least one study reports a significant negative effect.

## Research

**Pacchierotti, C. et al. Melatonin in Psychiatric Disorders: A Review on the Melatonin Involvement in Psychiatry. *Frontiers in Neuroendocrinology*. Volume 22, Issue 1, January 2001, Pages 18-32.**

Reviews the complicated relationship between melatonin and mood. Finds insufficient evidence to theorize a relationship or recommend it as a treatment.

**Carman, J. et al. Negative effects of melatonin on depression. *Am J Psychiatry* 1976; 133:1181-1186.**

In a double-blind crossover study with only 6 depressed patients, melatonin was found to have a negative impact on mood. There was no placebo control.

**Dalton, E. et al. Use of slow-release melatonin in treatment-resistant depression. *J Psychiatry Neurosci*. 2000 January; 25(1): 48-52.**

In a four week trial of only 9 depressed patients who had not responded to drugs, SR-melatonin was administered. It did not significantly improve depressed symptoms, and there was no placebo control.

**Lewy, A. et al. Melatonin treatment of winter depression: a pilot study. *Psychiatry Research*. Volume 77, Issue 1, 16 January 1998, Pages 57-61.**

In a placebo-controlled trial of only 5 depressed patients, low doses of melatonin in the afternoon showed significant antidepressive effects.

**Mendlewicz, J. et al. Abnormal 24 hour pattern of melatonin secretion in depression. *Lancet*. 1979 Dec 22-29;2(8156-8157):1362.**

Reviewed evidence that people suffering from depression have low levels of melatonin and an abnormal pattern of the chemical's secretion.

**Nair NP, Hariharasubramanian N, Pilapil C. Circadian rhythm of plasma melatonin in endogenous depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 1984;8(4-6):715-8.**

Tested the melatonin levels in the blood of young, old and depressed men over a 24-hour period. Found that depressed men have lower levels of melatonin, that it has an earlier peak and a later fall-off than controls.

**Crasson, M. et al. Serum melatonin and urinary 6-sulfatoxymelatonin in major depression. *Psychoneuroendocrinology*. Volume 29, Issue 1, January 2004, Pages 1-12.**

Tested melatonin levels in 14 depressed subjects and 14 matched controls. Found that total melatonin levels did not differ significantly, but confirmed that depressed subject have a delayed melatonin cycle.

# SAMe for Depression

SAMe (pronounced 'sammy') is a relatively new supplement being used for depression. It is a naturally occurring coenzyme that is produced and utilized mostly in the liver. There is not enough evidence yet to say whether SAMe outperforms placebo in treating depression because the studies that have been done have not had large enough numbers of participants.

There is some evidence that a Vitamin B12 deficiency would lead to a deficiency in SAMe and that people who have not had sufficient amounts of B12 would respond well to SAMe. B12 has been shown to have active antidepressant properties.

## Research

**Papakostas, G. (2009). Evidence for S-adenosyl-L-methionine (SAM-e) for the treatment of major depressive disorder. *The Journal Of Clinical Psychiatry*, 70 Suppl 518-22.**

Found that SAMe taken orally does not beat placebo, but intravenous or intramuscular injections do. However, was unclear if those were compared to intravenously or intramuscularly administered placebos.

**Hardy, M. et al. (2002). S-Adenosyl-L-Methionine for Treatment of Depression, Osteoarthritis, and Liver Disease. U.S. Department of Health and Human Services; Rockville, MD.**

Meta-analysis of SAMe vs. placebo showed that no trial has yet reached statistical significance. Each of the studies is limited by the small number of subjects included. The studies ranged in size from about six patients in the SAMe and placebo groups respectively, to nine patients in each group. The risk ranged from about 25 percent to 75 percent across the two outcomes and across studies in the SAMe group. If we assume that the risk ratio is 0.4, which is about the average risk ratio observed, then the risk in the placebo group ranges from 10 percent to 30 percent. The power to detect differences in risk between the two groups for this range (25 percent versus 10 percent; 50 percent versus 20 percent; and 75 percent versus 30 percent) is extremely low for comparison groups of sizes six and nine. In fact, the power does not exceed 30 percent in any case. Even if the risk ratio is as low as the minimum observed (0.12) and assuming the sample sizes in that study (seven and five in each group respectively), the power is only 34 percent. Therefore, these studies are so limited in statistical power that no definitive conclusion can be drawn.

## Selenium for Depression

There is evidence that many people suffer from a selenium deficiency (especially heavy drinkers) and that supplementing selenium leads to noticeable improvements in mood. Few controlled studies for the use of selenium in treating depression have been done, but the results look promising.

If someone believes their diet may be low in selenium, supplementation could improve their mood.

### Research

**Mokhber N; et al. Effect of supplementation with selenium on postpartum depression: a randomized double-blind placebo-controlled trial. The Journal Of Maternal-Fetal & Neonatal Medicine: The Official Journal Of The European Association Of Perinatal Medicine, The Federation Of Asia And Oceania Perinatal Societies, The International Society Of Perinatal Obstetricians [J Matern Fetal Neonatal Med] 2011 Jan; Vol. 24 (1), pp. 104-8.**

Randomized placebo-control trial found that selenium supplements had a specific positive effect on postpartum depression.

**Benton, D. Cook, R. The impact of selenium supplementation on mood. Biol-Psychiatry. 1991 Jun 1; 29(11): 1092-8.**

In a double-blind crossover placebo-controlled study of 50 subjects, it was found that selenium supplements improve overall mood, especially for those whose diets were lower in selenium. Seemed to indicate a subclinical deficiency that was affecting mood.

**Jorm, A. Effectiveness of complementary and self-help treatments for depression. Med Journal Australia 2002; 176: S84-S96.**

Reviewed evidence for selenium as a depression treatment and found that there have been no controlled trials to date.

**Sher, L. Role of thyroid hormones in the effects of selenium on mood, behavior, and cognitive function. Medical Hypotheses. Volume 57, Issue 4, October 2001, Pages 480-483.**

Suggests that people who are experiencing depression, hypothyroidism and susceptibility to viral infections should be tested for selenium deficiency.

**Rayman, M. The importance of selenium to human health. Lancet. Volume 356, Issue 9225, 15 July 2000, Pages 233-241.**

Discusses the importance of selenium for proper thyroid function and reviews that deficiencies have a negative impact on mood.

## St. John's Wort for Depression

The extract of the St. John's Wort flower is commonly used for treating depression. It is particularly popular in Europe. After numerous controlled trials, the research is still inconsistent and many positive studies were poorly designed. If it does have active antidepressant properties, they are associated with the chemical hyperforin, and a clinical-grade extract is considered to have not less than 5% hyperforin. There is some evidence that lower doses of hyperforin could be effective when combined with Passiflora.

While there is little evidence against St. John's Wort, there are many treatments with more support.

### Research

**Fiebich BL; Knörle R; Appel K; Kammler T; Weiss G. Pharmacological studies in an herbal drug combination of St. John's Wort (*Hypericum perforatum*) and passion flower (*Passiflora incarnata*): in vitro and in vivo evidence of synergy between *Hypericum* and *Passiflora* in antidepressant pharmacological models. *Fitoterapia [Fitoterapia]* 2011 Apr; Vol. 82 (3), pp. 474-80.**

Used synaptic uptake of serotonin (a highly problematic measure) and the forced swimming test (in mice) to demonstrate that *Passiflora* extract can enhance effects of hyperforin.

**Laakmann G, Schule C, Baghai T, Kieser M. St. John's wort in mild to moderate depression: the relevance of hyperforin for the clinical efficacy. *Pharmacopsychiatry*. 1998;31:S54-S59.**

In a randomized, double-blind, placebo-controlled, multicenter study, the clinical efficacy and safety of two different extracts of St. John's wort were investigated in 147 male and female outpatients suffering from mild or moderate depression according to DSM-IV criteria. The therapeutic effect of St. John's Wort in mild to moderate depression was found to depend on its hyperforin content. Extracts of 5% hyperforin outperformed placebo at a significant level, while those of 0.5% hyperforin did not.

**KIM, H. STRELTZER, J. GOEBERT, D. St. John's Wort for Depression: A Meta-Analysis of Well-Defined Clinical Trials. *Journal of Nervous & Mental Disease*. 187(9):532-538, September 1999.**

Studies concluding that St. John's wort (*Hypericum perforatum*) is an effective antidepressant can be challenged due to questionable methodology. Attempts to correct this by a meta-analysis utilizing only well-defined clinical trials. Controlled, double-blind studies using strictly defined depression criteria were analyzed by the rate of change of depression and by the number of "treatment responders." Rates of side effects and dropouts were also analyzed. *Hypericum* was 1.5 times more likely to result in an antidepressant response than placebo and was equivalent to tricyclic

antidepressants (TCAs). The meta-analysis also showed that there was a higher dropout rate in the TCA group and that the TCAs were nearly twice as likely to cause side effects, including those more severe than hypericum. Hypericum perforatum was more effective than placebo and similar in effectiveness to low-dose TCAs in the short-term treatment of mild to moderately severe depression. However, design problems in existing studies prevent definitively concluding that St. John's wort is an effective anti-depressant.

**Shelton RC, Keller MB, Gelenberg A, et al. Effectiveness of St. John's wort in major depression: a randomized controlled trial. JAMA. 2001;285(15):1978-86.**

Found no specific antidepressant effects for St. Johns Wort beyond placebo.

## **Vagus Nerve Stimulation**

Vagus Nerve Stimulation is a surgical procedure in which an electrical device is implanted in the patient's chest and wired to major nerves. The nerves then receive shocks of electricity at controlled doses.

There has been a great deal of research on Vagus Nerve Stimulation for depression over the past 8 years. Sadly, the quality of research is very poor. There have been no studies comparing VNS to a placebo that in any way replicates the experience of having the procedure done. In fact, some authors admit that the treatment's efficacy could be mostly or all placebo response.

The experience of having major surgery is likely to lead to a high level of expectancy on the part of the patient. The meaning and expectation as part of the ordeal of surgery might be entirely responsible for the therapeutic effects. In other words, the only way to know if this treatment has any specific effects would be to do the surgery on a group of people but not turn their devices on.

Until there is better research, this should not be considered a treatment that is worth the risk of major surgery.

### **Research**

**George, M. et al. Vagus nerve stimulation therapy: A research update. Neurology. 2002;59:S56-S61.**

Reviews several trials of VNS on people suffering from depression. Finds strong positive evidence; however, none of the trials used a structurally equivalent placebo.

**Sackeim, H. et al. Vagus Nerve Stimulation (VNS™) for Treatment-Resistant Depression: Efficacy, Side Effects, and Predictors of Outcome. Neuropsychopharmacology. 2001-VOL.25, NO. 5.**

Trial of VNS for depression without a placebo control. The authors admit that most or all of the treatment effects could be placebo.

**Nahas, Z. et al. Two-Year Outcome of Vagus Nerve Stimulation (VNS) for Treatment of Major Depressive Episodes. J. Clin. Psychiatry. 2005; 66: 1097-1104.**

Trial of VNS for depression without a placebo control.

## **Substances One May Want to Avoid**

### **Alcohol and Marijuana**

While the evidence on alcohol's relationship to mood is somewhat complicated, certain things are clear. Although it is not well understood whether moderate drinkers or abstainers are less likely to experience depression, heavy drinking is known to have a highly negative effect on mood.

Using alcohol to try escape from painful feelings has a net negative effect on mood, even for moderate drinkers. Also, moderate drinkers who are experiencing depression are more responsive to treatments when they abstain.

The research paints a similar, although not as dark, picture for marijuana use. While recreational use has not been shown to increase depression, people who use marijuana to cope with problems have higher rates of depression and there is some evidence that they develop Post Traumatic symptoms more easily and have more suicidal thoughts.

#### **Research**

##### **- Alcohol**

**Brown SA, Schuckit MA. Changes in depression among abstinent alcoholics. J Stud Alcohol 1988; 49: 412-417.**

Heavy drinkers experienced a dramatic decrease in depressive symptoms upon abstaining from alcohol.

**Worthington J, Fava M, Agustin C, Alpert J, Nierenberg AA, Pava JA, Rosenbaum JF. Consumption of alcohol, nicotine, and caffeine among depressed outpatients. Relationship with response to treatment. Psychosomatics. 1996 Nov-Dec;37(6):518-22.**

Found that even moderate levels of alcohol consumptions interfered with depression treatment.

**S . Gilman. A longitudinal study of the order of onset of alcohol dependence and major depression. Drug and Alcohol Dependence , Volume 63 , Issue 3 , Pages 277 - 286**

This study followed more than 14,000 consumers of community mental health services and found that when someone begins to drink heavily, they are likely to meet criteria for Major Depression within the next year. The converse is also true.

**Jürgen Rehm, Robin Room, Kathryn Graham, Maristela Monteiro, Gerhard Gmel & Christopher T. Sempos. The relationship of average volume of alcohol consumption and patterns of drinking to burden of disease: an overview. Addiction. Volume 98 Issue 9, Pages 1209 - 1228**

Found that alcohol consumption correlated to several serious health problems from Major Depression to various forms of cancer.

**David W. Oslin, M.D., Ira R. Katz, M.D., Ph.D., William S. Edell, Ph.D., and Thomas R. Ten Have, Ph.D. Effects of Alcohol Consumption on the Treatment of Depression Among Elderly Patients. Am J Geriatr Psychiatry 8:215-220, August 2000**

Found that decreasing alcohol use, even for moderate drinkers, lead to an improvement in mood for elderly people with depression.

**Davidson KM. Diagnosis of depression in alcohol dependence: changes in prevalence with drinking status. Br J Psychiatry 1995; 166: 199-204.**

Eighty-two alcohol-dependent in-patients were tested and during the episode of drinking which led to admission, a diagnosis of major depression was found in the majority of patients (67%). Once detoxification from alcohol took place, only the minority (13%) met criteria for major depression. This suggest that alcohol use might cause depression that remits upon abstinence.

#### **- Marijuana**

**Vlahov, D. et al. Increased Use of Cigarettes, Alcohol, and Marijuana among Manhattan, New York, Residents after the September 11th Terrorist Attacks. American Journal of Epidemiology. 155(11):988-996, June 1, 2002.**

Found that New Yorkers who increased their use of marijuana, tobacco or alcohol in after September 11 had increased chances of developing Post Traumatic Symptoms. Marijuana increased both PTS symptoms and depression more than the other substances. This could have been due to a selection bias.

**GREEN B. RITTER C. Marijuana use and depression. Journal of health and social behavior. 2000, vol. 41, no1, pp. 40-49 (1 p.3/4)**

In a large drug use survey of men born between 1944-1954, found that marijuana users who use the drug to cope with problems are more depressed than those who do not use to cope with problems.

**Musty, R. Kaback, L. Relationships between motivation and depression in chronic marijuana users. Life Sciences. Volume 56, Issues 23-24, 5 May 1995, Pages 2151-2158.**

Compared heavy and moderate marijuana users on several motivation and depression scales. Found that heavy users' lack of motivation is correlated with their level of depression. This is correlational and does not imply causation.

**Bovasso, G. Cannabis Abuse as a Risk Factor for Depressive Symptoms. Am J Psychiatry 158:2033-2037, December 2001.**

People with a diagnosis of cannabis abuse at baseline were four times more likely than those with no cannabis abuse diagnosis to have depressive symptoms at the follow-up assessment, after adjusting for age, gender, antisocial symptoms, and other baseline covariates. In particular, these participants were more likely to have experienced suicidal ideation and anhedonia during the follow-up period.

## **Caffeine and Sugar**

Sugar and caffeine both create drug effects in the body and can cause physical addiction. Sugar affects the opiate system which has a powerful impact on mood. There is not enough evidence to say for sure whether they contribute to depression, but care is warranted.

At least one study has shown a significant link between sugar consumption and depression. People suffering from depression report increases in anxiety with caffeine use; however, some substances that contain caffeine such as coffee and chocolate have been found to correlate with lower levels of depression. However, it is unclear whether increased coffee protects against depression or whether depression leads to decreased coffee consumption.

### **Research**

**Peet, M. International variations in the outcome of schizophrenia and the prevalence of depression in relation to national dietary practices: an ecological analysis. The British Journal of Psychiatry (2004) 184: 404-408**

The diets in New Zealand, Canada, Germany, France, USA, USSR, Taiwan and Japan were correlated with their rates of depression. The most consistent finding was that a greater consumption of refined sugar is associated with a greater prevalence of depression. Conversely, high intake of starchy roots was associated with a reduced prevalence of depression.

**Carlo Colantuoni, Pedro Rada, Joseph McCarthy, Caroline Patten, Nicole M. Avena, Andrew Chadeayne, and Bartley G. Hoebel. Evidence That Intermittent, Excessive Sugar Intake Causes Endogenous Opioid Dependence *Obes Res.* 2002;10:478-488.**

Intermittent excessive intake of sugar led to physical addiction in rats, marked by strong withdrawal symptoms. Withdrawal symptoms could be triggered after high sugar doses by either fasting or an opioid blocker, Naloxone.

**Lee MA, Flegel P, Greden JF, Cameron OG. Anxiogenic effects of caffeine on panic and depressed patients. *Am J Psychiatry.* 1988 May;145(5):632-5.**

Found that people who have been diagnosed with depression report that caffeine makes them feel anxious at a level higher than people who are not feeling depressed.

**Michel Lucas, PhD, RD, et al. Coffee, Caffeine and Risk of Depression Among Women. *Arch Intern Med.* 2011;171(17):1571-1578.**

Huge study of women over 10 years found a negative correlation between depression risk and coffee consumption.

## **Fried Foods**

While there is not a large body primary evidence linking fried foods to depression, the connection is inevitable given what we know about nutritional treatments. For example, there is strong evidence that antioxidants such as vitamin E are depleted in people suffering from depression and that increasing antioxidants is an effective treatment. We also know that a major part of what antioxidants do is to combat the effects of oxidized fats. Since the main source of oxidized fats in our diet is fried food, it seems to follow that one would do well to not only increase antioxidants but also to decrease fried foods.

### **Research**

**Tsuboi H, Shimoi K, Kinae N, Oguni I, Hori R, Kobayashi F. Depressive symptoms are independently correlated with lipid peroxidation in a female population: comparison with vitamins and carotenoids. *J Psychosom Res.* 2004; 56(1): 53-8**

Oxidated fats, such as any fat or oil that has been used for frying, increases chances for depression. Antioxidants neutralize these oxidated fats.

# Dairy

While there is not a lot of evidence, at least one study found a link between dairy consumption and depression risk.

## Research

**Peet, M. International variations in the outcome of schizophrenia and the prevalence of depression in relation to national dietary practices: an ecological analysis. *The British Journal of Psychiatry* (2004) 184: 404-408**

The diets in New Zealand, Canada, Germany, France, USA, USSR, Taiwan and Japan were correlated with their rates of depression. It was found that a high intake of dairy products was associated with an increased prevalence of depression.