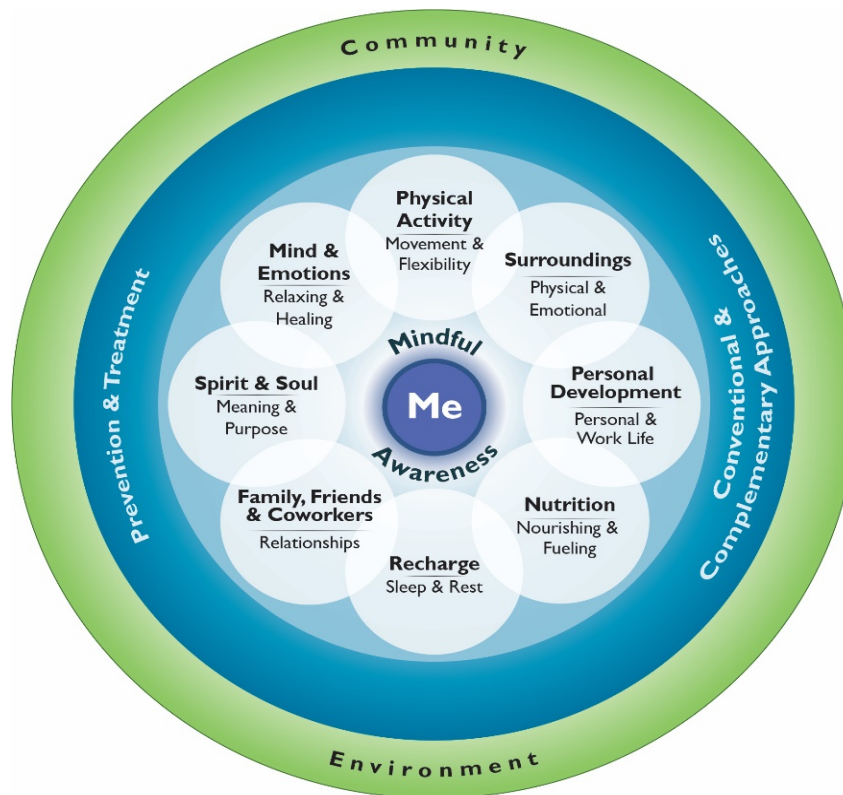


Integrative Approach to Depression, Part III

This document reviews self-care approaches for depression. Part 1 introduced a patient, Frank. Part 2 reviews options and related research for the eight areas of self-care, as featured in the Circle of Health. To see all of this applied to a patient, you may review a [Personal Health Inventory](#) and a Personal Health Plan found at the end of this document.



Psychotherapy

The American Psychiatric Association (APA) considers psychotherapy to be a first-line therapeutic option for patients with mild to moderate major depressive disorder. It can be used alone or, in cases of severe major depressive disorder, as combination therapy with other modalities. A [2018 Cochrane review](#) concluded, "Moderate-quality evidence shows that psychotherapy added to usual care (with antidepressants) is beneficial for depressive symptoms and for response and remission rates over the short term for patients with treatment-resistant depression. Medium- and long-term effects seem similarly beneficial...."¹

Using it in combination with medications appears to have superior efficacy to use of medications alone in all levels of depression severity. The [APA](#) has a number of patient-friendly, informative videos and documents on psychotherapy.

Factors to consider in choosing any of the psychotherapy modalities include the following:

- Availability of trained clinicians
- Patient preference
- Psychosocial context
- Prior beneficial response to psychotherapy
- The presence or absence of significant psychosocial stressors or interpersonal difficulties
- Intrapsychic conflict
- Presence of Axis II disorders (e.g., personality disorders)
- Stage, chronicity, and severity of major depressive episodes

Several psychotherapies are described below, with a discussion of the state of the evidence supporting (or not supporting) their use. The list is by no means comprehensive, and some approaches are much more widely available than others. Check to see what is available in your facility/community.

Clinicians are encouraged to know the various forms of psychotherapy available to people with depression so that you can be an effective matchmaker between a given individual and a given therapy (or therapist). The “fit” between patient and therapist may be as important as the therapy itself.

Cognitive Behavioral Therapy (CBT)

CBT is the most-studied psychotherapy used for depression.² The clinician guides the patient in identifying and replacing negative patterns of thinking with more positive and realistic approaches. CBT includes education about the relationship between thoughts, behaviors, and emotions. Patients are taught behaviors that serve as more productive responses to challenging circumstances or feelings. CBT is considered a short-term therapy; the length is usually 10-20 sessions. For more information, refer to the [National Alliance on Mental Illness \(NAMI\)](#) website.

CBT decreases the risk of relapse if continued when a person is doing well.³ CBT can be as effective as medications in the acute treatment of depressed outpatients.⁴

Interpersonal Therapy (IPT)

Developed in the 1970s, IPT is based on the idea that many psychological symptoms arise through interpersonal distress. Treatment usually is offered for 12-16 weeks and focuses on exploring relationships and how they influence—and are influenced by—one’s behavior and mood.

IPT’s efficacy has been shown in RCTs.^{5,6} IPT can be as effective as medications in the acute treatment of depressed outpatients.⁴ The degree to which patient and therapist can resolve the

interpersonal crisis on which IPT focuses (e.g. a role transition) appears to correlate with symptomatic improvement.⁷

For more information, refer to the [International Society for Interpersonal Psychotherapy](#) website.

Psychodynamic Therapy (PT)

PT is defined differently in various studies. It is also known as insight-oriented therapy. It focuses on gaining insight into unconscious processes and how they manifest in the way a person behaves.⁸ Recent meta-analyses suggest that both short-term and long-term psychodynamic psychotherapy are effective for depressed patients.^{9,10}

For more information, go to the [Good Therapy](#) website.

Problem-Solving Therapy (PST)

PST is a brief intervention, done in four to eight sessions. A therapist reviews the problems a person is experiencing in his or her life and then focuses on solving one or more of those problems to demonstrate more effective problem-solving techniques. PST has shown modest improvement in study participants with mild depressive symptoms; most studies have been done with geriatric populations. Twelve sessions of problem-solving therapy were superior to supportive psychotherapy for this population with major depressive disorder and executive dysfunction.¹¹

For more information, refer to the [University of Auckland Problem Solving Therapy website](#).

Marital Therapy (MT)

MT, or couple's therapy, involves working with both the depressed individual and their significant other. MT showed comparable efficacy to individual psychotherapy for the treatment of depression in a 2006 meta-analysis.¹² Several reviews have found that MT therapy is effective for treating depressive symptoms and reducing risk for relapse.^{13,14} Some individual studies have suggested that the efficacy of MT may depend on whether or not marital problems are present.¹⁵ Lower dropout rate and greater improvement in subjective symptoms of depression, at no greater cost, were found for a couples therapy group in comparison to medications alone.¹⁶

Patients with major depressive disorder admitted to inpatient units were more likely to improve if family therapy was part of their treatment. They had significant reductions in interviewer-rated depression and suicidal ideation.¹⁷

Acceptance and Commitment Therapy (ACT)

This is another approach that incorporates mindful awareness to prevent depression relapse. It is classed in this document as a "conventional therapy" because it is rapidly gaining popularity. Research has shown that ACT has powerful positive effects on depression, as well as many other illnesses.¹⁸ ACT invokes mindfulness techniques, acceptance, and commitment/behavior-change strategies to enhance a person's psychological flexibility. A person learns to focus effectively in the present moment to address any given situation that arises. People are encouraged to "make healthy contact" with thoughts, memories, feelings, and sensations they have avoided in the past.

To learn more, refer to the [Association for Contextual Behavioral Science](#) (ACBS) website.

Pharmaceuticals

According to current APA guidelines, medication is recommended as one of the initial treatment choices for patients with mild to moderate major depressive disorder and should be offered for those with severe major depressive disorder.¹⁹ Effectiveness of antidepressant medications is generally comparable between classes and within classes of medications. Therefore, there are several elements to take into consideration in choosing the initial medication. These include medication response in prior episodes, expected side effects, safety or tolerability of these side effects for the individual patient, pharmacological properties of the medication including other drug interactions, cost, and patient preference. Many studies demonstrate efficacy for various pharmacological and psychological therapies as first-line treatments; however, the degree to which they are effective is, in many studies, disappointing. This is especially true in the treatment of depression in its mild to moderate forms.²⁰ Specific guidance for pharmacotherapy for depression is beyond the scope of this document, but numerous large-scale reviews can be helpful.¹⁹

Clinicians often find it challenging to know how to make individualized medication choices; for more information on personalizing medication remedies, consider the following websites:

- A [2018 article](#) in The Lancet compared 21 different medications for depression.²¹
- [Up to Date](#) (subscription service offered by many organizations)
- Agency for Healthcare Research and Quality. "[Antidepressants](#)"

One recent study of note found that pharmaceutical treatments prevent the progression of microglial (nervous system immune cell) activation that otherwise will progress in people with depression.²² SSRIs seem to induce a "juvenile-like neuroplasticity" in the adult brain.²³

Other Conventional Approaches

Electroconvulsive Therapy (ECT)

ECT has the highest response and remission rates of any form of treatment for depression, with an improvement up to 70%–90% of those treated.²⁴ ECT should be contemplated in patients who fail to respond to medication and/or psychotherapy interventions.²⁵ It may be first-line treatment in patients with severe major depression when a fast antidepressant response is desired and when any of the following elements are present: suicide risk, catatonia, psychotic features, severe illness, or food refusal with nutritional compromise.²⁶

Transcranial Magnetic Stimulation (TMS)

TMS aims to produce electrical stimulation of superficial cortical neurons at left dorsolateral prefrontal cortex through the use of a magnetic coil that generates rapidly alternating magnetic fields. These fields are similar in strength to those used for MRIs.²⁷ TMS has been approved by the FDA to treat depression in patients who have not had an acceptable response to at least one antidepressant trial in the current episode of illness. Most, but not all, meta-analyses have found small to moderate benefits of TMS in depression. Efficacy is either less than or similar to that of ECT.²⁸ TMS is well tolerated; the most common side effects are transient scalp discomfort and headaches.²⁹

Vagus Nerve Stimulation (VNS)

VNS involves implanting a device that sends electrical pulses to the brain. It has been found useful in chronic depression, but not in the acute phase.³⁰ In 2005, based on clinical trial data, the FDA approved the use of VNS as an adjunctive therapy for treatment-resistant depression in adult patients who have failed four or more medications. VNS can safely be combined with ECT for patients with acute relapse. The cost is very high, around above \$40,000 for a day of surgery plus adjustments.³¹

Complementary And Integrative Health Approaches

A 2015 review noted that 10%-30% of people with depression and 20%-50% of those with bipolar disorder used CIH.³² It is important to ask patients about use, and it is important, regardless of your standpoint regarding the use of complementary approaches, to be able to discuss them with people in your care. In 2016, the Canadian Network for Mood and Anxiety Therapies (CANMAT) created guidelines regarding CIH for depression, noting, "For major depressive disorder (MDD) of mild to moderate severity, exercise, light therapy, St. John's wort, omega-3 fatty acids, SAM-e, and yoga are recommended as first- or second-line treatments. Adjunctive exercise and adjunctive St. John's wort are second-line recommendations for moderate to severe MDD."³³

Dietary Supplements³⁴

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

Nonbotanical Supplements

Folate

People with depression have lower folate levels and lower dietary intake of folate than the general population.³⁵ Known to be linked to serotonin metabolism,³⁶ mostly due to its role in methylation reactions that form the rate-limiting step in the production of neurotransmitters like serotonin.³⁷ Trials identified in a 2004 Cochrane review did not find evidence of adverse effects for folate. It is not clear from the few trials that exist whether or not folate is beneficial as a treatment for depression.³⁸

Inositol

Sometimes referred to as vitamin B8 (though not actually a vitamin in the strict sense), inositol is a sugar found especially commonly in the brain. It is involved in multiple cell signaling mechanisms. A meta-analysis identified two depression studies where inositol had marginally more responders in depression than placebo ($p = 0.06$).³⁸, but recent meta-analyses have not found benefit.³⁹ Inositol caused minimal gastrointestinal upset compared with placebo ($p = 0.06$)³⁸. Other side effects are rare.

Magnesium

Magnesium's first use dates back 100 years ago, when magnesium sulfate injected hypodermically was found to be helpful in patients with agitated depression.⁴⁰ A 2018 meta-

analysis did not find a link between serum magnesium levels and depression.⁴¹ Magnesium's mechanism of action is unknown, but it may be related to the glutamatergic mechanism, since magnesium acts as physiological NMDA receptor antagonist.⁴² A 2018 review notes that research remains inconclusive in terms of magnesium's efficacy.⁴³ Oral magnesium supplementation may prevent depression and might be used as an adjunctive therapy, but further research is needed.⁴⁴

Omega-3 Fatty Acids

People with depression have been found to have a deficiency of omega-3 fatty acids or an imbalance in the ratio of omega-6 and omega-3 fatty acids.⁴⁵ Synaptic membrane fluidity is significantly determined by cholesterol and dietary polyunsaturated fat levels, and other physiological functions are heavily reliant on them as well.⁴⁶ Therefore, optimal proportion of these elements is postulated to have an impact in depression.⁴⁷ US (APA) and Canadian guidelines support use of omega-3s for depression, noting that while efficacy may seem modest in research to date, harms are minimal.^{33,48}

A 2017 network meta-analysis found that omega-3 therapy was not as effective as SSRI therapy, but that when the two were combined, the effect was better than either intervention alone.⁴⁹ A 2015 Cochrane review concluded, "At present, we do not have sufficient high quality evidence to determine the effects of n-3PUFAs as a treatment for MDD. Our primary analyses suggest a small-to-modest, non-clinically beneficial effect of n-3PUFAs on depressive symptomatology compared to placebo; however the estimate is imprecise, and we judged the quality of the evidence on which this result is based to be low/very low."⁵⁰

Two other meta-analysis concluded that omega-3 supplementation demonstrated significant clinical benefit, noting that eicosapentaenoic acid (EPA) content was particularly important.^{51,52} In rat models, diets rich in omega-3 led to increased hippocampal neurogenesis.⁴⁷ An elevated ratio of omega-6 to omega-3 fatty acids predicted depression development following interferon-alpha treatment.⁵³ A low omega-3 index in late pregnancy was associated with a higher depression score three months postpartum.⁵⁴

Probiotics

Taking probiotics daily may modulate immune function and mood. For mood benefits, *Bifidobacterium infantis* has been found especially useful.^{55,56} One billion colony forming units (CFUs) is a good starting point, and taking a variety of different species may be best. It is recommended that probiotics be taken for at least two weeks and up to two months.

For more information, refer to "[Promoting a Healthy Microbiome with Food and Probiotics.](#)"

S-Adenosyl Methionine (SAME)

Pronounced "Sammy," S-adenosyl methionine is an amino acid derivative that is found in virtually all body tissues and fluids. It plays a role in over 100 biochemical reactions, most of which involve the transfer of methyl groups. SAME is important for the synthesis and metabolism of proteins, nucleic acids, neurotransmitters, hormones, and many other compounds. Severely depressed patients often have low levels of SAME in the spinal fluid, and SAME supplementation can normalize them.⁵⁷ Deficiencies of B12 and folate are linked to low levels of SAME in the nervous system. SAME's mechanism of action is unclear, but higher

SAMe levels have been linked to increased serotonin turnover and elevated dopamine and norepinephrine levels. SAMe is often used for treatment of both depression and pain. Some people refer to it as the supplement equivalent of duloxetine (Cymbalta). A 2016 Cochrane review that included eight trials noted a paucity of high-quality evidence but noted that SAMe often shows similar effects to SSRIs.⁵⁸ Other reviews note that it “holds promise.”

SAMe is thought to have a more rapid onset than many antidepressants, so some clinicians may use it as a stopgap while waiting for drug therapies to take effect.⁵⁹ It can significantly improve remission rates in depressed patients who do not respond to medications.⁶⁰ SAMe tends to be quite safe.⁶⁰ Side effects can occur with high doses, such as nausea, vomiting, diarrhea, constipation, nervousness, dry mouth, and headache, but these tend to be minimal in comparison with side effects from antidepressants. Mania and hypomania are rarely reported. Dosing ranges from 400 mg to 1,600 mg daily divided into two doses. SAMe’s biggest drawback is that it can be quite expensive to purchase over the counter.

Tryptophan and 5-Hydroxytryptophan (5-HTP)

A Cochrane review found that in two of 108 trials, tryptophan and 5-HTP were better than placebo at alleviating depression.⁵⁹ There is a possible association between these substances and the potentially fatal eosinophilia-myalgia syndrome.⁶¹ Most authorities agree this was largely attributable to contamination of a specific batch of supplements made by one company. Tryptophan intake in the diet is inversely associated with depression risk.⁶² Most Americans get more than enough in their diets.

Zinc and Other Minerals

Research suggests potential benefits of zinc supplementation for depression, either as a stand-alone therapy or as an adjunct to drug therapy. A 2018 review suggested that levels of zinc, iron, copper, and selenium intake are inversely related to depression risk.⁶³ Zinc-sensing cell receptors may be partly linked to zinc’s efficacy.⁶⁴

A 2017 systematic review and meta-analysis noted the following about various nutrients and their effects on depression³⁹: “Our meta-analyses of 10 articles on n-3 PUFAs and four on zinc support their efficacy. For folic acid, our meta-analysis does not support efficacy.... For the remaining substances, only a few RCTs were available. The preliminary data on inositol was negative, while one RCT for vitamin D demonstrated positive results. For vitamin B12 one and for SAMe two RCTs and a few open trials are available reporting positive and mixed results.”

Botanicals⁶⁵

Roughly 10 years ago, there was a 50% increase in the number of studies of botanicals for depression,⁶⁶ including a number of epigenetic studies.⁶⁷ Surveys indicate that 44%-54% of depressed patients have used herbal remedies in the past 12 months.⁶⁸ Most research focuses on the use of botanicals for mild to moderate depression. Botanicals differ from medications, most notably because they are polyvalent. That is, they contain multiple chemicals that may contribute to therapeutic benefit that may work in synergy to bring about a therapeutic effect. This is thought to lead to a lower rate of side effects but also to difficulty in standardization. Since depressive disorders tend to be associated with comorbid anxiety and other psychiatric disorders, the use of polypharmacy in psychiatry is increasing; antipsychotics are often used

along with antidepressants. Using multiple plant-based compounds (either from one remedy or a combination) may have similar benefits. A 2018 review featuring 110 herbal remedies found that only 1%-2% of studies were clinical. Most herbals, like antidepressants, affected monoamine neurotransmitters (i.e. serotonin, norepinephrine, dopamine).⁶⁹

Ginkgo (*Ginkgo biloba*)

Ginkgo is useful in treating older patients (ages 51-78) with depression related to organic brain dysfunction, especially when they have proved unresponsive to standard drug treatment.⁷⁰ Dosing used in depression studies was 40 mg to 80 mg three times daily of a 50:1 extract standardized to contain 24% ginkgo-flavone glycosides. Due to potential anticoagulation effects, ginkgo should not be used by anyone during the periods before or after surgery or labor and delivery, and it should be used with caution in people with bleeding problems. It may interact with blood thinners, calcium channel blockers, aminoglycoside antibiotics, anticonvulsants, and neuroleptics.

Roseroot (*Rhodiola rosea*)

Roseroot significantly improved HAMD scores as well as insomnia, somatization, and emotional instability subscale outcome measures at doses of 340 mg daily of standardized extracts.⁷¹ A review of two RCTs and multiple open-label studies found a possible anti-depressant effect.⁷²

Saffron (*Crocus sativus*)

A 2018 review concluded that saffron has similar anti-depressant effects to SSRIs but with fewer side effects.⁷³ Saffron demonstrated significant improvement for depression over placebo on Hamilton Depression Rating (HAMD) scores.⁷⁴ Equivalent therapeutic response was demonstrated for saffron, imipramine 100 mg daily, and fluoxetine at 20 mg bid on the HAMD. Petals and stamens are used in doses of 30 mg daily.

St. John's Wort (*Hypericum perforatum*)

St. John's wort is one of the main supplements used for treating depression. It is typically dosed at 300 mg three times a day standardized to between 3% and 6% hyperforin and not less than 6% flavonoids for depression. Outcomes in studies include reduction in Hamilton Rating Scale for Depression (HAMD) scores,⁶⁸ lower relapse rate (18%), and longer time to relapse compared to placebo groups after 26 weeks of treatment.⁷⁵ A 2017 network meta-analysis found that St. John's wort was similar to SSRIs in terms of response rates, remission rates, and degree of change on the HAM-D scale.⁴⁹ It was found to have superior effects relative to exercise or omega-3s. Of note, it also had fewer adverse effects than SSRIs (relative risk 1.19). Another 2017 meta-analysis concluded that St. John's wort was comparable with SSRIs for people with mild to moderate depression.⁷⁶ St. John's wort is not just an herbal SSRI; it seems to affect multiple different biochemical pathways.

If anyone ever asks what botanical has the most interactions with medications, it is St. John's wort. It alters the cytochrome P-450 3A4 detoxification pathway. Caution should be used with taking St. John's wort with antiretrovirals, warfarin, cyclosporine, or oral contraceptives, among other medications. Because it is known to be a mild MAO-I, similar dietary and medication interaction precautions should be taken as with an MAO-I drug.

Turmeric (*Curcuma longa*)

Turmeric, a spice that is commonly used in many Asian foods, contains curcumin and other anti-inflammatories that seem to have multiple benefits for inflammation. A 2017 meta-analysis conclude that “Curcumin appears to be safe, well-tolerated, and efficacious among depressed patients.” More robust randomized controlled trials with larger sample sizes and follow-up studies carried out over a longer duration should be planned to ascertain its benefits.”⁷⁷

Nonconventional Botanicals

Chinese Herbal Medicine (CHM)

A systematic review looking at studies that used a variety of different Chinese formulations for depression concluded that CHM was superior to placebo and as effective as antidepressants in terms of effects on HAMD scores; there were fewer adverse events as well.⁷⁸

Psychedelics

The potential of psychedelics to treat depression and other mental health disorders is the subject of a great deal of current research. They seem to affect inflammation, and it is theorized they may also reset a number of brain networks by destabilizing and “resetting” them.⁷⁹

A 2019 review concluded that using a shotgun approach to taking supplements (simultaneously taking a large array of them with hopes of combined benefit) is not effective.⁸⁰

Aromatherapy

Aromatherapy effected mood in several small studies. A small nonrandomized pilot trial found that adjunctive aromatherapy allowed for reductions in dose of antidepressants compared with usual therapy.⁸¹ Short-term, but not persistent, mood benefits were found for aromatherapy with citrus oil combined with massage in patients with cancer who were suffering from depression.⁸² It was not clear in the latter study how much each element, that is massage or oils, contributed to the positive effect.

Body-Based Therapies: Massage

Massage therapy, defined as intentional and systematic hand motion practiced on soft tissues of the body, has been found to decrease stress and muscle tension, increase pain threshold, and stimulate positive emotions.⁸³ Classical European “Swedish” massage has been the most researched for depression. Rationale for investigating the role of massage in depression stems from findings that massage leads to changes in electroencephalogram (EEG) patterns. A symmetrical or left frontal pattern is found, which is associated with positive affect. Massage also stimulates facial expressions and increases vagal activity, which has been shown to reduce depressed affect.⁸⁴ A multicenter RCT found aromatherapy massage to be associated with clinically important benefit for depression symptoms for up to two weeks in patients with cancer.⁸²

A recent meta-analysis including 17 studies containing 786 persons concluded that massage therapy is significantly associated with alleviation of depressive symptoms.⁸⁵ Given this information, massage should be seen as an effective ancillary treatment that likely promotes remission maintenance.. There is no evidence to support its being used alone as a first-line therapy.

For more general information, refer to the Massage Therapy Tool featured in the [Passport to Whole Health](#), Chapter 16.”

Whole Systems

Chinese Medicine and Acupuncture

In Chinese medicine (CM), one of the proposed etiologies of mental disorders is internal damage caused by the deregulation of the seven emotions: anger, worry, contemplation (thinking), sorrow (grief), fear, and shock.⁸⁶

In acupuncture, points are stimulated by needles, electricity-augmented needles, and lasers. There are also needleless approaches. Many mechanisms of action have been proposed for acupuncture, and it is thought to influence mood through the modulation of the neuroendocrine and immune systems, regulating levels of 5-HT, norepinephrine, dopamine, endorphins, and/or glucocorticoids and stimulating responses in the hypothalamus and hippocampus.⁸⁷

Conclusions of various reviews of acupuncture trials are mixed, but favorable overall. A [2018 Cochrane review](#) concluded that “Acupuncture may result in a moderate reduction in the severity of depression when compared with treatment as usual or no treatment. Use of acupuncture may lead to a small reduction in the severity of depression when compared with control acupuncture. Effects of acupuncture versus medication and psychological therapy are uncertain, owing to the very low quality of evidence.”⁸⁸ A 2013 trial found that acupuncture in combination with the drug paroxetine led to a higher treatment response rate but no changes in remission rate.⁸⁹ 2010 Cochrane review found insufficient evidence to recommend using acupuncture for depression, based on 30 studies identified as meeting inclusion criteria (n=2,812).⁹⁰ It was noted that a subgroup of 94 participants in three studies who had depression as a comorbidity did have a reduction of depression⁹⁰ in comparison with the use of SSRIs. A meta-analysis of 35 RCTs conducted by Zhang and colleagues identified that acupuncture is a safe and effective treatment for major depressive disorder and post-stroke depression.⁹¹ A meta-analysis of eight RCTs by Wang and colleagues concluded that acupuncture can significantly reduce the severity of depression.⁹² Another study found that a combination of acupuncture plus low-dose fluoxetine was as effective for depression as the recommended dose of fluoxetine, with the lower dose being beneficial for people with intolerable side effects.⁹³ Increasing numbers of studies focus on whether or not acupuncture can decrease medication side effects; for example, a Cochrane review found that stimulation of the P6 acupuncture point was more effective than antiemetic medication for managing medication-related nausea and vomiting.⁹⁴

A 2011 “systematic review of systematic reviews” looked at eight reviews that included 71 primary studies. Five of the reviews arrived at positive conclusions and three did not.⁹⁵ The positive studies were all done in China. The reviewers concluded that the effectiveness of acupuncture as a treatment for depression remains unproven. Adverse events are rare and include soreness, pain, bruising, and mild bleeding at the needle site.⁸⁶

The mixed results for studies of acupuncture for treating depression are likely due to four factors:

1. The particular challenge of inadequate placebo interventions
2. Variation in definitions/diagnostic criteria of depression; most studies have been done with diagnostic criteria that differ from DSM-IV TR/V
3. Considerable disparities in the way that acupuncture is routinely practiced, especially in the West
4. Most of the evidence available is published in Chinese-language journals

Given the above information, acupuncture seems to have a growing body of evidence of positive clinical use as monotherapy, as augmentation for treatment of symptoms of depression, and for treatment of side effects of medication. Not having a well-trained acupuncturist available might perhaps be the main obstacle to recommending this intervention. Most therapists will note that multiple sessions are needed to treat chronic conditions. For example, a patient may be seen for 30-60 minutes a week for three months or more.

Homeopathy

Evidence for the effectiveness of homeopathy in depression is limited, due to a lack of clinical trials of high quality or insufficient numbers of participants.⁹⁶ Over 50 single case reports/studies mostly serve to indicate the range of remedies employed in patients whose symptoms include depression. Homeopathic medicines rarely provoke adverse effects and when this occurs, they are relatively rare, mild, and transient. Still, it is difficult to justify using homeopathy based on the current state of the research.

Follow-Up with Frank

Frank has seen his new counselor four times now and is feeling much happier. He learned the skill of paying attention and noticing the early signs and signals of feeling heavy. That gave him an opportunity to take action before he became sad and depressed.

Frank's family loved the idea of helping him connect more to his grandkids. They set up a Zoom account for him and scheduled a time every day (alternating between the families) for the whole family to check in on each other. He also learned how to get on the older kids' Facebook pages. He loved this.

Keeping a food diary helped him see that he often used food to feel better, particularly sweets. If it was after 5 pm he might have an alcoholic drink or two to 'calm his nerves.' He noticed that eating sweets or drinking alcohol made him feel better for a little while, but then he started feeling worse. And feeling worse would then result in him eating or drinking even more. He decided that when he found himself having those cravings, he would get up and walk, and he succeeded in walking around the block 3 times a week for 15 minutes. He has increased it to 30 minutes at a time, 4 times a week. When he returned, if he still wanted the food or drink, he could have it, but more than half of the time he found he no longer wanted it.

He was surprised to find that his sleep was improved as well and found even more benefit with the relaxation techniques he learned to use before bed or if he awakens in the middle of the night. He tried doing light therapy when the days began getting shorter, and it has helped him a great deal, especially with reducing daytime fatigue.

Frank decided to do some volunteer work at a local nonprofit and will start in two months when he feels more comfortable with his new routines. Frank's most recent PHQ-9 score was a "5," which is on the borderline between minimal and mild depression and an improvement since the last score.

Personal Health Plan for Frank S

Note: This plan is more elaborate, as might be discussed during a longer visit or a consultation. Health plans evolve over time, and they may be just one specific goal. People can work with their team members to keep updating the plan, and with each success, new goals can be set in new areas.

Meaning, Aspiration, Purpose (MAP):

My purpose is to bring the love and joy of my relationship with my grandchildren into my everyday life in more regular ways.

My Goals:

Develop a plan to "dial up the joy" and improve my mood.

1. Starting at the beginning of next month, I will walk for at least 15 minutes 3 times a week. I will try to do it with a friend or family member. After 2 weeks, I will check in with the nurse at my clinic
2. I will start a mind-body practice. I will work with a counselor to help me find one. Tomorrow, I will call to set up an appointment
3. If I am not feeling better in 2 months, I will check in with my primary care team and decide on next steps
4. I will call my children and grandchildren at least once every 2 weeks, on Sunday. We will set up a regular virtual visit

My Strengths:

1. I feel great about my surroundings. I like my flower garden
2. I love my family and enjoy my grandkids
3. I feel good about my professional care

Mindful Awareness:

- I will practice paying more attention to the signs and signals from my body that my mood is going downhill. Check in with my body and mind several times a day, noting how I am feeling

Areas of Self-Care:

- Physical Activity
 - I will start with walking, and then maybe try some tai chi later on. There is a class being taught online I could take
 - I will keep going with my gardening
- Surroundings

- I will have my family send pictures of the grandchildren to place around the house and see their faces frequently
- We will schedule regular calls, at least once every 2 weeks
- Personal Development
 - Explore opportunities for continued learning or volunteer work
 - Consider a financial adviser
- Nutrition
 - Keep a food, drink, and mood diary and notice if there is a connection between eating and mood
- Recharge
 - Develop a sleep hygiene routine that includes relaxation techniques. Will review the handout, "[Improving and Maintaining Healthy Sleep Habits](#)"
- Family, Friends, and Co-Workers
 - Talk to my son and daughter and their spouses about wanting to find more regular avenues to connect, even if we are social distancing
- Spirit and Soul
 - Look for ways to increase connections with my grandchildren, which fuel my spiritual well-being

Professional Care

- My Support Team
 - Medical: Primary care team, counselor (will help him find one, may be able to work with integrated mental health provider in his clinic)
 - Children and grandchildren
 - Best friend, Rick
- Prevention/Screening
 - Up-to-date
- Treatment (e.g., conventional and complementary approaches, medications, and supplements)
 - Medications: continue taking my citalopram
- Skill building and education
 - Nutrition: Consider a dietitian down the road
 - Relaxation and breathing techniques
 - Aerobic exercise class

Community

- Volunteer work
- Consider a community support group for people with depression.

Next Steps

- Telephone visit with primary care team nurse in one week to discuss progress and other needs
- Schedule integrative health coaching sessions to work on self-care portion of the plan

Resources

Patient Education Programs

- [Behavioral Health Lab](#)
- [Translating Initiatives for Depression into Effective Solutions](#) (TIDES)
- [VISN 2 Center for Integrated Healthcare](#)
- [University of Massachusetts Center for Integrated Primary Care](#)

Author(s)

This handout was adapted for the University of Wisconsin Integrative Health Program by Adam Rindfleisch from the original written for the Veterans Health Administration (VHA) by Mario Salguero, MD, PhD and updated by Adam Rindfleisch, MPhil, MD (2014, 2019).

This overview was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

11/24/2020

References

1. Ijaz S, Davies P, Williams CJ, Kessler D, Lewis G, Wiles N. Psychological therapies for treatment-resistant depression in adults. *Cochrane Database Syst Rev*. 2018;5:Cd010558.
2. Anthes E. Depression: a change of mind. *Nature*. 2014;515(7526):185-187.
3. Paykel ES, Scott J, Teasdale JD, et al. Prevention of relapse in residual depression by cognitive therapy: a controlled trial. *Arch Gen Psychiatry*. 1999;56(9):829-835.
4. Hollon SD, Jarrett RB, Nierenberg AA, Thase ME, Trivedi M, Rush AJ. Psychotherapy and medication in the treatment of adult and geriatric depression: which monotherapy or combined treatment? *J Clin Psychiatry*. 2005;66(4):455-468.
5. de Mello MF, de Jesus Mari J, Bacaltchuk J, Verdelli H, Neugebauer R. A systematic review of research findings on the efficacy of interpersonal therapy for depressive disorders. *Eur Arch Psychiatry Clin Neurosci*. 2005;255(2):75-82.
6. Weissman MM. Cognitive therapy and interpersonal psychotherapy: 30 years later. *Am J Psychiatry*. 2007;164(5):693-696.
7. Markowitz JC, Bleiberg KL, Christos P, Levitan E. Solving interpersonal problems correlates with symptom improvement in interpersonal psychotherapy: preliminary findings. *J Nerv Ment Dis*. 2006;194(1):15-20.
8. Haggerty J. Psychodynamic Therapy. Psych Central website. Available at: <http://psychcentral.com/lib/psychodynamic-therapy/000119>. Accessed August 14, 2014.
9. Driessen E, Cuijpers P, de Maat SC, Abbass AA, de Jonghe F, Dekker JJ. The efficacy of short-term psychodynamic psychotherapy for depression: a meta-analysis. *Clin Psychol Rev*. 2010;30(1):25-36.
10. Leichsenring F, Rabung S. Effectiveness of long-term psychodynamic psychotherapy: a meta-analysis. *JAMA*. 2008;300(13):1551-1565.



11. Alexopoulos GS, Raue PJ, Kiosses DN, et al. Problem-solving therapy and supportive therapy in older adults with major depression and executive dysfunction: effect on disability. *Arch Gen Psychiatry*. 2011;68(1):33-41.
12. Barbato A, D'Avanzo B. Marital therapy for depression. *Cochrane Database Syst Rev*. 2006(2):CD004188.
13. Hahlweg K, Markman HJ. Effectiveness of behavioral marital therapy: empirical status of behavioral techniques in preventing and alleviating marital distress. *J Consult Clin Psychol*. 1988;56(3):440-447.
14. Jacobson NS, Martin B. Behavioral marriage therapy: current status. *Psychol Bull*. 1976;83(4):540-556.
15. Jacobson NS, Addis ME. Research on couples and couple therapy: what do we know? Where are we going? *J Consult Clin Psychol*. 1993;61(1):85-93.
16. Leff J, Vearnals S, Brewin CR, et al. The London Depression Intervention Trial. Randomised controlled trial of antidepressants v. couple therapy in the treatment and maintenance of people with depression living with a partner: clinical outcome and costs. *Br J Psychiatry*. 2000;177:95-100.
17. Miller IW, Keitner GI, Ryan CE, Solomon DA, Cardemil EV, Beevers CG. Treatment matching in the posthospital care of depressed patients. *Am J Psychiatry*. 2005;162(11):2131-2138.
18. Montgomery KL, Kim JS, Franklin C. Acceptance and commitment therapy for psychological and physiological illnesses: a systematic review for social workers. *Health Soc Work*. 2011;36(3):169-181.
19. Gelenberg AJ. A review of the current guidelines for depression treatment. *J Clin Psychiatry*. 2010;71(7):e15.
20. Fournier JC, DeRubeis RJ, Hollon SD, et al. Antidepressant drug effects and depression severity: a patient-level meta-analysis. *JAMA*. 2010;303(1):47-53.
21. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet*. 2018;391(10128):1357-1366.
22. Setiawan E, Attwells S, Wilson AA, et al. Association of translocator protein total distribution volume with duration of untreated major depressive disorder: a cross-sectional study. *Lancet Psychiatry*. 2018;5(4):339-347.
23. Kraus C, Castren E, Kasper S, Lanzenberger R. Serotonin and neuroplasticity - Links between molecular, functional and structural pathophysiology in depression. *Neurosci Biobehav Rev*. 2017;77:317-326.
24. Kellner CH, Knapp RG, Petrides G, et al. Continuation electroconvulsive therapy vs pharmacotherapy for relapse prevention in major depression: a multisite study from the Consortium for Research in Electroconvulsive Therapy (CORE). *Arch Gen Psychiatry*. 2006;63(12):1337-1344.
25. Husain SS, Kevan IM, Linnell R, Scott AI. Electroconvulsive therapy in depressive illness that has not responded to drug treatment. *J Affect Disord*. 2004;83(2-3):121-126.
26. Husain MM, Rush AJ, Fink M, et al. Speed of response and remission in major depressive disorder with acute electroconvulsive therapy (ECT): a Consortium for Research in ECT (CORE) report. *J Clin Psychiatry*. 2004;65(4):485-491.
27. O'Reardon JP, Solvason HB, Janicak PG, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biol Psychiatry*. 2007;62(11):1208-1216.
28. CADTH Rapid Response Reports. In: *Transcranial Magnetic Stimulation for the Treatment of Adults with PTSD, GAD, or Depression: A Review of Clinical Effectiveness and Guidelines*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health Copyright (c) 2014 Canadian Agency for Drugs and Technologies in Health.; 2014.
29. Lam RW, Chan P, Wilkins-Ho M, Yatham LN. Repetitive transcranial magnetic stimulation for treatment-resistant depression: a systematic review and metaanalysis. *Can J Psychiatry*. 2008;53(9):621-631.
30. Rush AJ, Marangell LB, Sackeim HA, et al. Vagus nerve stimulation for treatment-resistant depression: a randomized, controlled acute phase trial. *Biol Psychiatry*. 2005;58(5):347-354.



31. Cusin C, Dougherty DD. Somatic therapies for treatment-resistant depression: ECT, TMS, VNS, DBS. *Biol Mood Anxiety Disord.* 2012;2(1):14.
32. Solomon D, Adams J. The use of complementary and alternative medicine in adults with depressive disorders. A critical integrative review. *J Affect Disord.* 2015;179:101-113.
33. Ravindran AV, Lam RW, Filteau MJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. V. Complementary and alternative medicine treatments. *J Affect Disord.* 2009;117 Suppl 1:S54-64.
34. Schneider C, Wissink T. Depression. In: Rakel D, ed. *Integrative Medicine.* 3rd ed. Philadelphia, PA: Saunders; 2019.
35. Bender A, Hagan KE, Kingston N. The association of folate and depression: A meta-analysis. *J Psychiatr Res.* 2017;95:9-18.
36. Botez MI, Young SN, Bachevalier J, Gauthier S. Effect of folic acid and vitamin B12 deficiencies on 5-hydroxyindoleacetic acid in human cerebrospinal fluid. *Ann Neurol.* 1982;12(5):479-484.
37. Kaufman S. Some metabolic relationships between bipterin and folate: implications for the "methyl trap hypothesis". *Neurochem Res.* 1991;16(9):1031-1036.
38. Taylor MJ, Carney SM, Goodwin GM, Geddes JR. Folate for depressive disorders: systematic review and meta-analysis of randomized controlled trials. *J Psychopharmacol.* 2004;18(2):251-256.
39. Schefft C, Kilarski LL, Bschor T, Kohler S. Efficacy of adding nutritional supplements in unipolar depression: A systematic review and meta-analysis. *Eur Neuropsychopharmacol.* 2017;27(11):1090-1109.
40. Serefko A, Szopa A, Wlaz P, et al. Magnesium in depression. *Pharmacol Rep.* 2013;65(3):547-554.
41. You HJ, Cho SE, Kang SG, Cho SJ, Na KS. Decreased serum magnesium levels in depression: a systematic review and meta-analysis. *Nord J Psychiatry.* 2018;72(7):534-541.
42. Murck H. Ketamine, magnesium and major depression--from pharmacology to pathophysiology and back. *J Psychiatr Res.* 2013;47(7):955-965.
43. Wang J, Um P, Dickerman BA, Liu J. Zinc, magnesium, selenium and depression: a review of the evidence, potential mechanisms and implications. *Nutrients.* 2018;10(5).
44. Derom ML, Sayon-Orea C, Martinez-Ortega JM, Martinez-Gonzalez MA. Magnesium and depression: a systematic review. *Nutr Neurosci.* 2013;16(5):191-206.
45. Bruinsma KA, Taren DL. Dieting, essential fatty acid intake, and depression. *Nutr Rev.* 2000;58(4):98-108.
46. Messamore E, Almeida DM, Jandacek RJ, McNamara RK. Polyunsaturated fatty acids and recurrent mood disorders: Phenomenology, mechanisms, and clinical application. *Prog Lipid Res.* 2017;66:1-13.
47. Kang JX, Gleason ED. Omega-3 Fatty acids and hippocampal neurogenesis in depression. *CNS Neurol Disord Drug Targets.* 2013;12(4):460-465.
48. Freeman MP, Fava M, Lake J, Trivedi MH, Wisner KL, Mischoulon D. Complementary and alternative medicine in major depressive disorder: the American Psychiatric Association Task Force report. *J Clin Psychiatry.* 2010;71(6):669-681.
49. Asher GN, Gartlehner G, Gaynes BN, et al. Comparative benefits and harms of complementary and alternative medicine therapies for initial treatment of major depressive disorder: systematic review and meta-analysis. *J Altern Complement Med.* 2017;23(12):907-919.
50. Appleton KM, Sallis HM, Perry R, Ness AR, Churchill R. Omega-3 fatty acids for depression in adults. *Cochrane Database Syst Rev.* 2015(11):Cd004692.
51. Grosso G, Pajak A, Marventano S, et al. Role of omega-3 fatty acids in the treatment of depressive disorders: a comprehensive meta-analysis of randomized clinical trials. *PLoS One.* 2014;9(5):e96905.
52. Mocking RJ, Harmsen I, Assies J, Koeter MW, Ruhe HG, Schene AH. Meta-analysis and meta-regression of omega-3 polyunsaturated fatty acid supplementation for major depressive disorder. *Transl Psychiatry.* 2016;6:e756.

53. Lotrich FE, Sears B, McNamara RK. Elevated ratio of arachidonic acid to long-chain omega-3 fatty acids predicts depression development following interferon-alpha treatment: relationship with interleukin-6. *Brain Behav Immun*. 2013;31:48-53.
54. Markhus MW, Skotheim S, Graff IE, et al. Low omega-3 index in pregnancy is a possible biological risk factor for postpartum depression. *PLoS One*. 2013;8(7):e67617.
55. Desbonnet L, Garrett L, Clarke G, Kiely B, Cryan JF, Dinan TG. Effects of the probiotic *Bifidobacterium infantis* in the maternal separation model of depression. *Neuroscience*. 2010;170(4):1179-1188.
56. Diaz Heijtz R, Wang S, Anuar F, et al. Normal gut microbiota modulates brain development and behavior. *Proc Natl Acad Sci U S A*. 2011;108(7):3047-3052.
57. Nelson JC. S-adenosyl methionine (SAMe) augmentation in major depressive disorder. *Am J Psychiatry*. 2010;167(8):889-891.
58. Galizia I, Oldani L, Macritchie K, et al. S-adenosyl methionine (SAMe) for depression in adults. *Cochrane Database Syst Rev*. 2016;10:CD011286.
59. Papakostas GI, Mischoulon D, Shyu I, Alpert JE, Fava M. S-adenosyl methionine (SAMe) augmentation of serotonin reuptake inhibitors for antidepressant nonresponders with major depressive disorder: a double-blind, randomized clinical trial. *Am J Psychiatry*. 2010;167(8):942-948.
60. Review NMCD. SAMe.
<http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=786&ds>. Accessed March 14, 2014.
61. Shaw K, Turner J, Del Mar C. Tryptophan and 5-hydroxytryptophan for depression. *Cochrane Database Syst Rev*. 2002(1):CD003198.
62. Lieberman HR, Agarwal S, Fulgoni VL, 3rd. Tryptophan intake in the US adult population is not related to liver or kidney function but is associated with depression and sleep outcomes. *J Nutr*. 2016;146(12):2609s-2615s.
63. Li Z, Wang W, Xin X, Song X, Zhang D. Association of total zinc, iron, copper and selenium intakes with depression in the US adults. *J Affect Disord*. 2018;228:68-74.
64. Doboszewska U, Wlaz P, Nowak G, Radziwon-Zaleska M, Cui R, Mlyniec K. Zinc in the monoaminergic theory of depression: its relationship to neural plasticity. *Neural Plast*. 2017;2017:3682752.
65. Natural Medicines Comprehensive Database.
<http://naturaldatabase.therapeuticresearch.com/home.aspx?cs=&s=ND>. Accessed June 8, 2014.
66. Garcia-Garcia P, Lopez-Munoz F, Rubio G, Martin-Agueda B, Alamo C. Phytotherapy and psychiatry: bibliometric study of the scientific literature from the last 20 years. *Phytomedicine*. 2008;15(8):566-576.
67. Ulrich-Merzenich G, Zeitler H, Jobst D, Panek D, Vetter H, Wagner H. Application of the "-Omic-" technologies in phytomedicine. *Phytomedicine*. 2007;14(1):70-82.
68. Elkins G, Rajab MH, Marcus J. Complementary and alternative medicine use by psychiatric inpatients. *Psychol Rep*. 2005;96(1):163-166.
69. Martins J, S B. Phytochemistry and pharmacology of anti-depressant medicinal plants: A review. *Biomed Pharmacother*. 2018;104:343-365.
70. Varteresian T, Lavretsky H. Natural products and supplements for geriatric depression and cognitive disorders: an evaluation of the research. *Curr Psychiatry Rep*. 2014;16(8):456.
71. Darbinyan V, Aslanyan G, Amroyan E, Gabrielyan E, Malmstrom C, Panossian A. Clinical trial of *Rhodiola rosea* L. extract SHR-5 in the treatment of mild to moderate depression. *Nord J Psychiatry*. 2007;61(5):343-348.
72. Amsterdam JD, Panossian AG. *Rhodiola rosea* L. as a putative botanical antidepressant. *Phytomedicine*. 2016;23(7):770-783.
73. Shafiee M, Arekhi S, Omranzadeh A, Sahebkar A. Saffron in the treatment of depression, anxiety and other mental disorders: Current evidence and potential mechanisms of action. *J Affect Disord*. 2018;227:330-337.

74. Hausenblas HA, Saha D, Dubyak PJ, Anton SD. Saffron (*Crocus sativus* L.) and major depressive disorder: a meta-analysis of randomized clinical trials. *J Integr Med*. 2013;11(6):377-383.
75. St. John's Wort. Natural Medicines Comprehensive Database website. Available at: <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=329&fs=ND&searchid=48583572>. Accessed October 3, 2014.
76. Ng QX, Venkatanarayanan N, Ho CY. Clinical use of *Hypericum perforatum* (St John's wort) in depression: a meta-analysis. *J Affect Disord*. 2017;210:211-221.
77. Ng QX, Koh SSH, Chan HW, Ho CYX. Clinical use of curcumin in depression: a meta-analysis. *J Am Med Dir Assoc*. 2017;18(6):503-508.
78. Yeung WF, Chung KF, Ng KY, Yu YM, Ziea ET, Ng BF. A systematic review on the efficacy, safety and types of Chinese herbal medicine for depression. *J Psychiatr Res*. 2014;57:165-175.
79. Nichols DE, Johnson MW, Nichols CD. Psychedelics as medicines: an emerging new paradigm. *Clin Pharmacol Ther*. 2017;101(2):209-219.
80. Sarris J, Byrne GJ, Stough C, et al. Nutraceuticals for major depressive disorder- more is not merrier: An 8-week double-blind, randomised, controlled trial. *J Affect Disord*. 2019;245:1007-1015.
81. Komori T, Fujiwara R, Tanida M, Nomura J, Yokoyama MM. Effects of citrus fragrance on immune function and depressive states. *Neuroimmunomodulation*. 1995;2(3):174-180.
82. Wilkinson SM, Love SB, Westcombe AM, et al. Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer: a multicenter randomized controlled trial. *J Clin Oncol*. 2007;25(5):532-539.
83. Moyer CA, Rounds J, Hannum JW. A meta-analysis of massage therapy research. *Psychol Bull*. 2004;130(1):3-18.
84. Field TM. Massage therapy effects. *Am Psychol*. 1998;53(12):1270-1281.
85. Hou WH, Chiang PT, Hsu TY, Chiu SY, Yen YC. Treatment effects of massage therapy in depressed people: a meta-analysis. *J Clin Psychiatry*. 2010;71(7):894-901.
86. Hong H. *Acupuncture : theories and evidence*. 2013.
87. Wu J, Yeung AS, Schnyer R, Wang Y, Mischoulon D. Acupuncture for depression: a review of clinical applications. *Can J Psychiatry*. 2012;57(7):397-405.
88. Smith CA, Armour M, Lee MS, Wang LQ, Hay PJ. Acupuncture for depression. *Cochrane Database Syst Rev*. 2018;3:Cd004046.
89. Qu SS, Huang Y, Zhang ZJ, et al. A 6-week randomized controlled trial with 4-week follow-up of acupuncture combined with paroxetine in patients with major depressive disorder. *J Psychiatr Res*. 2013;47(6):726-732.
90. Smith CA, Hay PP, Macpherson H. Acupuncture for depression. *Cochrane Database Syst Rev*. 2010(1):Cd004046.
91. Zhang ZJ, Chen HY, Yip KC, Ng R, Wong VT. The effectiveness and safety of acupuncture therapy in depressive disorders: systematic review and meta-analysis. *J Affect Disord*. 2010;124(1-2):9-21.
92. Wang H, Qi H, Wang BS, et al. Is acupuncture beneficial in depression: a meta-analysis of 8 randomized controlled trials? *J Affect Disord*. 2008;111(2-3):125-134.
93. Zhang WJ, Yang XB, Zhong BL. Combination of acupuncture and fluoxetine for depression: a randomized, double-blind, sham-controlled trial. *J Altern Complement Med*. 2009;15(8):837-844.
94. Ezzo J, Streitberger K, Schneider A. Cochrane systematic reviews examine P6 acupuncture-point stimulation for nausea and vomiting. *J Altern Complement Med*. 2006;12(5):489-495.
95. Ernst E, Lee MS, Choi TY. Acupuncture for depression?: A systematic review of systematic reviews. *Eval Health Prof*. 2011;34(4):403-412.
96. Pilkington K, Kirkwood G, Rampes H, Fisher P, Richardson J. Homeopathy for depression: a systematic review of the research evidence. *Homeopathy*. 2005;94(3):153-163.