

**Treatment of Depression with Acupuncture: A Research Synthesis**  
**In Pursuit of the Question – Can Acupuncture Impact Reproductive Outcomes in Infertile**  
**Women Suffering From Depression**

**A Capstone Project**

**Presented in partial fulfillment of the requirements for the**  
**Doctor of Acupuncture and Oriental Medicine Degree**

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### **Abstract**

The main objective of this research synthesis was to study the effects of acupuncture in the treatment of depression, in order to lay some ground work for the investigation of acupuncture's effect on reproductive outcomes in the treatment of depressed women with infertility. The outcomes of previous reviews and meta-analyses were reviewed, which revealed that most reviews had limited conclusions and required more higher-quality randomized controlled trials. For the research synthesis, twenty-seven studies were retrieved that observed the effects of acupuncture treatment on depression. The articles were reviewed, and data were collected on the details of the participants, treatment interventions, outcome measures and results. The studies consisted of a wide range of study populations, treatment interventions, control interventions, and outcome measures. The outcome of most of the included studies showed that the acupuncture treatment had significantly decreased depression severity. However, many of the studies lacked appropriate controls, were of poor quality, or had small sample sizes. When compared with antidepressants, acupuncture treatment was found to be comparable in effects. When comparing acupuncture to control acupuncture interventions, the results were mixed. Recommendations were provided for future studies on the treatment of depression with acupuncture in infertile women.

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### **Introduction**

Depression is a common condition, and many people who suffer from it look to alternative medicine (Eisenberg et al., 1993). Recent estimates of lifetime prevalence of major depression are around 17% (Kessler et al., 1994). Conventional depression treatments, including antidepressant medications and psychotherapy, can provide significant relief for approximately 50% to 70% of patients who complete treatment. However, about one third of those who start treatment do not complete it (Elkin et al., 1989).

In my clinical practice, I have observed that a significant percentage of women who seek infertility treatment suffer from depression. Several studies (Demyttenaere, Bonte, & Gheldof, 1998; Mao & Wood, 1984; Smeenk et al.; 2001; Thiering, Beaurepaire, Jones, Saunders, & Tennant, 1993) provide evidence that depression can negatively impact reproductive outcomes in women. Therefore, I sought to answer the following question: How effective is acupuncture in treating depression in women who suffer from both depression and infertility, and can treating the depression with acupuncture impact reproductive outcomes? In Chinese medicine, treatments are focused on correcting a pattern of disharmony in the body, which can be the root cause of many symptoms and disease manifestations. Therefore, it is reasonable to hypothesize that the treatment of one disorder will impact the other.

In the exploratory phase of this study, a literature search failed to produce any studies that examined this particular topic. Therefore, the research question explored in this study was a more general one that can be viewed as a first step in answering the more specific question stated above. This more general question is: How effective is acupuncture in the treatment of depression?



## **Research Objectives**

The objective of this research synthesis is to uncover what is known about how effectively acupuncture can treat depression, in order to provide a foundation for future studies that investigate how acupuncture can impact depression and reproductive outcomes in depressed women who suffer from infertility. Specifically, an end goal of this study is to mine the existing literature for effective interventions and research strategies that can shape a study that examines whether the use of acupuncture to treat depression in infertile women impacts both their depressive symptoms as well as infertility symptoms. If the depression decreases in severity or remits following acupuncture treatments, can reproductive outcome improve?

A review and synthesis of the available literature was conducted to explore the following questions relating to the use of acupuncture in the treatment of depression: What is the effect of acupuncture on depression? What are the effects of acupuncture treatments designed specifically to treat depression, compared to “control” acupuncture treatments, including “non-specific”, “sham”, and “placebo” treatments? How does the effectiveness of acupuncture compare to the effectiveness of other modalities used in the treatment of depression, such as antidepressants? What types of acupuncture modalities have been studied for the treatment of depression? What acupuncture points and protocols have been studied for the treatment of depression?

## **Definition of Terms**

- Amitriptyline: a tricyclic antidepressant
- BDI: Beck Depression Inventory, a self-rating scale for severity of depression
- BRMS: Bech-Rafaelson Melancholia Scale
- Bf-S: self-rating scale for evaluating depressive states in longitudinal studies
- CGI: Clinical Global Impressions Scale
- CRSD: Carroll Rating Scale for Depression

- DepHRSD19: modified Hamilton Rating Scale for Depression, with subset of 19 questions specific to depression
- DSM-IV: Diagnostic and Statistical Manual of Mental Disorders from the American Psychiatric Association
- Fluoxetine: an SSRI antidepressant
- GAS: Global Assessment Scale
- GDS-SF: Geriatric Depression Scale – Short Form
- GSC: Grading System Commonly employed in China for the assessment of therapeutic effects (i.e. cured, markedly improved, improved, and failed or deteriorated)
- HADS: Hospital Anxiety and Depression Scale
- HRSD: Hamilton Rating Scale for Depression, a clinician-rated scale for severity of depression
- HRSD17: a commonly used form of the Hamilton Rating Scale for Depression that includes 17 items.
- HRSD19: an alternate version of the Hamilton Rating Scale for Depression that includes 19 items.
- HRSD24: an alternate version of the Hamilton Rating Scale for Depression that includes 24 items.
- MADRS: Montgomery Asberg Depression Rating Scale
- Mianserin: a tetracyclic antidepressant
- MOS-SF-36: Medical Outcomes Study 36-Item Short-Form Health Survey to assess functional improvement
- MYMOP: Measure Yourself Medical Outcome Profile

- Paroxetine: a selective serotonin reuptakes inhibitor
- Prozac: brand name of fluoxetine, a selective serotonin reuptake inhibitors antidepressant
- SCID: structured clinical interview for DSM Axis I disorders
- SDS: Self-rating depression scale measuring severity of depression
- SSRI: selective serotonin reuptake inhibitor
- TEAS: Transcutaneous Electrical Acupoints Stimulation. TEAS is designed to use a low frequency electrical stimulator and can be easily applied to selected acupoints for treatment (Han, 1997).

## **Literature Review**

### **Overview**

This chapter describes the results of the literature review that was conducted for this research synthesis study. A brief description of the literature review process and the resources used in gathering the relevant literature will be provided in the first section. The second section will review the twelve articles included in the literature review. The final section of this chapter will summarize the existing reviews pertaining to the treatment of depression with acupuncture, and how acupuncture's treatment of depression may be a mechanism for its influence on reproductive outcomes in IVF. The final section will also identify gaps and areas for future research.

### **Literature Review Methodology and Resources**

This is a research synthesis study focusing on the treatment of depression using acupuncture, with the end goal of obtaining knowledge to inform future studies investigating acupuncture's treatment of depressed women with infertility. Therefore, the goal of this literature review was to find previous reviews and meta-analyses of the same topic, in order to review previous findings and identify the gaps or limitations that need to be addressed.

A PubMed search was conducted, limited to reviews on the topic of acupuncture's efficacy in the treatment of depression. In total, twenty potentially relevant review articles were found, and twelve were selected for this literature review. Eight review articles were found that reported exclusively on acupuncture, and all of these were included. Six of these reported on depression only (Leo & Ligot, 2007; Mukaino, Park, White, & Ernst, 2005; Smith & Hay, 2004; Smith, Hay, & MacPherson, 2010; Wang et al., 2008; Zhang, Chen, Yip, Ng, & Wong, 2010), while two articles reported on two or more mood disorders (Pilkington, 2010; Samuels, Gropp, Singer, & Oberbaum, 2008). Ten articles were found that surveyed multiple CAM therapies in

the treatment of depression. Although the goal of this review was to focus on acupuncture, two of these were selected for inclusion because one focused specifically on depressive disorders in women (Deligiannidis & Freeman, 2010), and the other was the earliest review found that included a review of acupuncture (Ernst, Rand, & Stevinson, 1998). Finally, two review articles were selected that examined acupuncture's role in infertility, and proposed that acupuncture's effects on depression could be a potential mechanism (Anderson, Haimovici, Ginsburg, Schust, & Wayne, 2007; Huang et al., 2011).

### **Acupuncture's Treatment of Depression May Play a Role in Influencing IVF Outcomes**

Anderson et al. (2007) performed a qualitative review surveying the existing literature to explore the efficacy and potential mechanisms for acupuncture's use in conjunction with IVF. In this review, the explored the impact of depression in IVF patients, reviewed a few articles that demonstrated acupuncture's effectiveness in the treatment of depression, and made recommendations for further study. This was not a comprehensive review, but a selective sampling of articles that made a case for acupuncture's potential benefit in the treatment of depression, and the impact of that benefit on reproductive outcomes.

The authors noted that depressive symptoms are common among patients who undergo IVF, and that the prevalence and severity of depression increase each time a failed IVF treatment occurs (Thiering et al., 1993). Evidence was also cited that supports the assertion that women who experience depression while undergoing IVF have lower pregnancy rates than women who are not depressed (Demyttenaere et al., 1998; Thiering et al. 1993). One small study was described that demonstrated that couples who received counseling during IVF experienced significantly lower anxiety and depression scores, and significantly higher pregnancy rates, than couples who were randomized to a control group (Terzioglu, 2001). Anderson et al. (2007) also referenced a few studies of acupuncture in the treatment of depression, and briefly explored the

mechanistic basis of acupuncture's effects on depression, but concluded that it was not well understood. Examples of proposed mechanisms included modulation of neuropeptide Y levels in the amygdala, production of opioid peptides, enhanced vagal nervous activity, attenuation of the sympathetic nervous system, restoration of hippocampal brain-derived neurotrophic factor levels, and influence on the HPA axis.

Finally, Anderson et al. (2007) concluded that acupuncture may be a safe and effective adjunct therapy for women undergoing IVF, with the caveat that methodological problems in the existing literature significantly limited their conclusions. They suggested more rigorous randomized controlled trials. Other pertinent recommendations included the use of a treatment protocol that is based on TCM principles, and the addition of outcomes measures that are relevant to mechanistic processes, in order to allow for more specialized usage of acupuncture for specific infertility conditions.

Huang et al. (2011) conducted a review of acupuncture treatment for infertility, but the discussion of depression treatment as a potential mechanism was limited to the topic of acupuncture in conjunction with IVF embryo transfer. The analysis was similar to Anderson et al. (2007), but more limited. Some of the same references were made regarding depression's potential impact on IVF outcome, and vice versa (IVF outcome's impact on depression). In this review, stress, anxiety and depression were not differentiated but grouped together for most of the discussion. References were made to studies in which acupuncture promoted stress relief, relaxation, or feelings of optimism. As in Anderson et al. (2007), the authors briefly referenced the same proposed mechanisms of action.

In their concluding statements, Huang et al. (2011) reported that most of the studies reviewed suggested that acupuncture plays a positive role in the management of infertility. They also noted that most of the randomized controlled trials were conducted outside of China, and did

not reflect the “essence of the Chinese medicine perspective”, based on syndrome differentiation and individualized point prescriptions. In their view, the standardized protocols used in the trials might reduce the effect of acupuncture in individual patients. However, they suggested multi-center, high quality trials, as well as further investigation into the mechanisms of acupuncture for the management of infertility.

### **CAM Therapies for Depression in Women**

Deligiannidis & Freeman (2010) conducted a review of complementary and alternative medicine treatments for depressive disorders in women, focusing on aspects of MDD (major depressive disorder) across the reproductive life cycle. They noted that CAM therapies are used more frequently in women than in men. The CAM therapies they recommend incorporating were omega-3 fatty acids, exercise, and folate, because of low risk, benefits for general health, and evidence suggesting an adjunctive role in the treatment of MDD. S-Adenosylmethionine (SAME) and bright light therapy were cited as reasonable options for some individuals, as there is evidence to support monotherapy in MDD. *Hypericum perforatum* (St John’s Wort) was cited as having the most consistent evidence of efficacy in mild to moderate depression, but carries the risk of potential drug-drug interactions.

And finally, the authors concluded that further studies were necessary before acupuncture can be recommended in the treatment of MDD. Only five studies and one meta-analysis were cited in their research of the treatment of MDD with acupuncture. They mentioned the challenges of conducting and interpreting acupuncture research, including the publishing of studies in Asian languages, inconsistency in diagnosis and symptom evaluation, varied treatment techniques, and difficulty of controlling for placebo effect.

### **Treatment of Depression with Acupuncture: Qualitative Reviews**

The earliest publication (found by this researcher) to review acupuncture's treatment of depression was conducted by Ernst et al. in 1998. This was a qualitative review that provides insight into early thoughts and preliminary evidence in this topic. It included a brief summary of the most prevalent complementary therapies for depression at the time. The authors concluded that the scientific data were "extremely limited." They singled out exercise, and the use of *Hypericum perforatum* (St. John's Wort), as the two therapies with the most supporting evidence, and, "to a lesser extent, acupuncture and relaxation therapies" (Ernst et al., 1998).

The authors referenced early studies in acupuncture analgesia (Han & Terenius, 1982) showing that the level of endorphins increased through needling, as well as animal studies (Han, 1986) demonstrating that acupuncture and electro-acupuncture could stimulate synthesis and release of serotonin and noradrenaline-norepinephrine.

Ernst et al. (1998) also briefly discussed eight articles on the treatment of depression with acupuncture, all providing supporting evidence. These included case series, uncontrolled trials, and a few controlled trials. The authors also described three studies on electro-acupuncture, all from the same research group at the Institute of Mental Health in Beijing, China. The first two trials compared electro-acupuncture to the tricyclic antidepressant amitriptyline (Luo, Jia, & Zhan, 1985; Luo, Jia, Wu, & Dai, 1990), and demonstrated that electro-acupuncture produced a significant decrease in depression severity, comparable to amitriptyline, with fewer and less severe adverse effects. The third trial (Luo, Jia, Feng, Zhao, & Tang, 1995) showed preliminary evidence that electro-acupuncture had greater efficacy than "traditional" acupuncture.

Ernst et al. (1998) concluded that the evidence for the treatment of depression with acupuncture was "promising, but not compelling". They noted the lack of control for



nonspecific responses resulting from the “time and attention received” during acupuncture, and recommended replication of electro-acupuncture trials with more rigorously designed RCTs.

Samuels et al. (2008) reviewed the use of acupuncture for psychiatric illnesses, noting that better studies had been conducted for depression than for other disorders such as schizophrenia and substance abuse. The article summarized eight trials regarding efficacy of acupuncture for depression, singling out the study by Luo, Meng, Jia, and Zhao (1998), which found electro-acupuncture to be as effective as amitriptyline, and noted that it is a promising treatment during pregnancy, referencing a study by Manber, Schnyer, Allen, Rush, and Blasey (2004). The article also reviewed epidemiological information regarding the prevalence of depression, the use of antidepressants, and the use of CAM therapies for treatment. TCM theories regarding depression were discussed at a high level, including Five Element theory. The authors recommended large and controlled studies in order for the world of conventional medicine to “take CAM seriously”, and concluded that it was not possible to recommend the routine use of acupuncture.

Pilkington (2010) wrote a review describing many previous meta-analyses and systematic reviews on the topic of acupuncture treatment of depression. Pilkington also presented a brief summary of thirteen trials published since 2007. The most recent one to be mentioned was by Zhang, Yang, and Zhong (2009). Details of individual trials were given, including diagnostic criteria, number of participants, treatment and control interventions, primary outcome measure, and results. However, issues of reliability, quality of methodology, and possibility of bias were not discussed. Also, no synthesis of results was presented and no quantitative analysis was done. A small number of clinical trials that measured acupuncture’s influence on biological parameters associated with depression were also discussed, including magnetic resonance brain imaging, measures of neurotransmitters, plasma levels of neuropeptide Y, and inflammatory markers. The author noted that these types of trials were “few in number and preliminary in nature”, and

concluded that “the limited research on this aspect possibly reflects the fact that the aetiology of depressive and anxiety disorders has not yet been fully explained.” Finally, Pilkington (2010) defended the overall safety of acupuncture, citing several large-scale studies that demonstrated that serious adverse events are rare.

### **Systematic Reviews and Meta-Analyses**

Smith and Hay (2004) retrieved and evaluated seven randomized controlled trials, with a total of 517 participants. Four trials used electro-acupuncture, two used manual acupuncture and one used a combination of electro-acupuncture plus manual acupuncture. The number of points stimulated varied: several of the electro-acupuncture trials used two points, while the manual acupuncture trials tended to use more points. Five trials compared acupuncture with medication, one compared acupuncture treatment with a wait list control group, and only one used a control acupuncture intervention, defined as sham acupuncture. A wide variation in treatment protocols was observed. Six trials used Hamilton Rating Scale for Depression (HRSD), a clinician-rated scale of depression severity, as the primary outcome measure. The authors reported that, due to small sample sizes and poor quality trials, no conclusions could be drawn about the efficacy of acupuncture compared to medication, wait list control or sham acupuncture.

Mukaino et al. (2005) evaluated the results of six trials, including a total of 509 participants. Slightly different inclusion criteria resulted in a different set of trials to analyze than in the Smith and Hay (2004) review. Mukaino et al. (2005) used a modified Jadad score (Jadad et al., 1996) to evaluate the quality of trials. They employed a similar method of comparison as Smith and Hay (2004), looking at results by the comparison group that was used. Similar to the Smith and Hay (2004) review, the authors found that the studies were limited by small sample size and poor quality, and also mentioned that the diversity of the available studies made it difficult to draw conclusions. They concluded that the effects of manual acupuncture

versus sham acupuncture could not be determined, nor could the additive effect of acupuncture when given as an adjunct to antidepressants. However, the results (from four poor quality studies) did suggest that the effect of electro-acupuncture might not be significantly different from that of antidepressants.

Leo and Ligot (2007) evaluated nine RCTs, and also failed to make any conclusions. The methodology of RCTs was assessed using modified Jadad criteria, and five of the nine trials were judged to be of low quality. They also reported the limitations due to small sample sizes, and the heterogeneity of subjects, controls, outcome measures, and modalities with which acupuncture was applied.

Leo and Ligot (2007) also commented that the number of adverse effects associated with acupuncture was not adequately reported, including syncope, localized irritation at the needle insertion site, transient bleeding, anxiety (particularly for those with needle phobias), risk of pneumothorax when improperly administered, and risk of preterm labor when inappropriate points are used.

In 2008, Wang et al. conducted a further meta-analysis of eight trials involving 477 participants. This meta-analysis was limited to trials comparing acupuncture treatment against “sham” acupuncture. Again, the quality of studies was reported as low (by Jadad criteria), except for two Chinese trials that were considered “high quality” (Luo et al., 2003; Fu et al., 2006). A significant difference was reported in the reduction of depression severity but the difference was small in clinical terms, and no difference was found in response or remission rates.

In 2009, Zhang et al. evaluated twenty trials involving 1998 participants suffering from MDD that were judged to be of “relatively high quality” (Jadad score of 3 and above). Trials involving laser acupuncture were excluded. Manual acupuncture was used in ten trials and electro-acupuncture was used in the other ten trials. Zhang et al. (2009) noted that little

information was available on the rationale for the choice of points. In this analysis, acupuncture was found to be equivalent to antidepressants in reducing the symptoms of major depressive disorder and in effecting a clinical response, and appeared to offer advantages over antidepressants in terms of a lower incidence of adverse effects. However, there was insufficient evidence on whether combining acupuncture with antidepressants offered an advantage over antidepressants alone, and no significant difference was found between acupuncture and sham acupuncture.

In the Zhang et al (2009) review, fifteen trials for post-stroke depression (PSD) were also evaluated separately. Acupuncture was found to be superior to antidepressants and waitlist controls in improving both response and symptom severity of PSD.

The most recent quantitative analysis is a Cochrane review (Smith et al., 2010) that is an update on the Smith and Hay (2004) review. A total of thirty trials of acupuncture were selected, including trials in post-stroke depression that were analyzed separately. The authors concluded that there was still insufficient evidence to recommend the use of acupuncture for depression, primarily because of the high risk of bias in the majority of trials.

### **Literature Review Integration**

Twelve review articles and met-analyses were examined in this literature review. Most have been inconclusive, or have conclusion statements indicating that acupuncture is a promising treatment for depression but requires further research, although two of the systematic reviews did conclude that acupuncture seems to have the same efficacy in treating depression as antidepressants. So there is definitely a need to continue to evaluate clinical trials as more are published. The most recent study that was included in the review articles mentioned in this chapter was published in 2009. The following research synthesis study aims to include any

studies conducted after that date, in addition to revisiting prior studies that have already been reviewed.

Most reviews included only randomized controlled trials or had strict criteria on inclusion. The current literature review study was more inclusive, since it does not aim to or perform any type of meta-analysis or quantify the results in a rigorous manner. Small pilot studies, uncontrolled studies, and case series were included in an effort to get a bigger picture of all of the research that has been done, and to review the various treatment approaches and research designs.

Finally, all of the quantitative reviews mentioned in this chapter examined the quality of methodology, using Cochrane Risk of Bias tool, Jadad score or a similar set of criteria. However, not many looked at repeatability of the treatment protocols, or at the level of training of the practitioner who administered the treatments. Smith et al. (2010) did mention training for some but not all studies. The current research synthesis aims to include that information as part of the analysis of studies.

## **Method**

### **Introduction**

The objective of this research synthesis is to gain a better understanding of how effectively acupuncture can treat depression. This is a first step in the investigation of how acupuncture treatment can impact women who are simultaneously suffering from depression and infertility. The information that is gained from investigating acupuncture's treatment effects for depression in the general population can build a foundation for future research studies with more targeted questions. Qualitative method was used to review, analyze and synthesize studies from the currently available literature. Twenty-six articles were collected from the available literature and reviewed for common themes and ideas. This thematic style of analysis was used to identify the variables to be studied and compared.

### **Search Strategy and Criteria for Study Inclusion**

The data sources for this study included research articles that were retrieved from a number of traditional Chinese medicine and Western medicine journals. The articles were found through online searches, using online research databases PubMed, Google Scholar, and EBSCOhost. The search was conducted in the principal investigator's home and at the Yo San University library. The parameters of the online search were as follows: 1) The keywords “\*acup\*” and “depress\*” both needed to appear in the study title. 2) The search was limited to English language and human studies. Of the retrieved articles, a subset of abstracts was examined to find the relevant primary research articles, and the full text was scanned if more details were needed to determine relevance.

The search generated 155 articles from Google Scholar, 51 articles from PubMed, and twenty-six articles from EBSCOhost. There was a great deal of overlap between the three result sets (several articles were found in more than one of the databases). The retrieved list of articles

was scanned to search for relevant primary research articles where acupuncture was a treatment intervention, and change in depression level was an outcome measure.

Out of all of the retrieved articles, twenty-six were selected for inclusion in the research synthesis based on the following criteria: 1) Patients in the studies were diagnosed with depression, 2) Treatment intervention included acupuncture, either used alone or in combination with other therapies, and 3) Outcome assessments included depression remission rate, or measurement of the change in depression level. Articles that studied patients with other medical diagnoses besides depression were included as long as diagnosis of depression was an inclusion criterion for admission to the study. Articles were excluded if the diagnosis of depression was not used as part of the inclusion criteria for participation in the study, even if the article used change in depression level as an outcome measure. Case studies and trials with more subjects were both included. Review articles and meta-analyses were excluded.

### **Instrumentation and Data Collection Procedures**

Data collection tables were used to extract key pieces of information from each article. Summary tables and matrices served to organize all of the data collected, and to compare and summarize the information from all the reviewed articles.

### **Data Analysis**

This section will give a detailed description of the process that was used to extract and analyze data from the collected articles that were used for this research synthesis. When appropriate, data analysis methods were applied that consisted of frequency counts, sums, mean values, median values, and range of values. Appendix A provides a list of the twenty-six research articles that were included, with their assigned study code number(s).

**Quality assessment of research methodology.** Information was collected in Appendix B pertaining to various methodological criteria that contributed to the validity and reliability of

the included studies. The following nine questions assessed the quality of methodology: 1) Were the inclusion and exclusion criteria clearly stated? 2) Was there a control or comparison group (or groups) present? 3) Were subjects randomized into the different groups? 4) Was there a description of the randomization method? 5) Were the participants blinded to treatment assignment? 6) Were providers blinded to treatment assignment? 7) Were the assessors blinded to treatment assignment? 8) Was the description of treatment intervention detailed enough to be repeated by others? 9) Were all outcomes reported?

For all questions except Question 8, the researcher assigned a value as follows: The value 1 was given if the answer was “yes”. The value 0 was given if the answer was “no”, or if it was unclear or not applicable.

For Question 8, the point value assigned by the assessor was 0, 1, or 2. An assignment of 0 points meant that there was not enough detail for the treatment intervention to be repeated by others, a value of 1 point meant that the treatment could be conducted by others in a similar manner as in the study, but some details were missing, and a score of 2 for Question 8 indicated that enough details were provided that the treatment could be repeated exactly as in the study.

The criteria for assigning 0, 1, or 2 to Question 8 depended on the following:

- Were the acupuncture points used for the study described in sufficient detail so that others could determine which exact points to use? For standardized treatments, the exact points should be described. For individualized treatments, the rationale or method for determining the points should be clearly described.
- Were the acupuncture treatment instruments (needles, electro-acupuncture machine, laser device, etc.) clearly described?



- Were the techniques and details of acupuncture administration described in enough detail to be repeatable (angle and depth of insertion, needling method, electro-acupuncture settings, and needle retention time)?
- Were the number of treatments, frequency of treatments, and duration of treatment period clearly described?
- Was the frequency and timing of outcome assessments described?

A summary column in Appendix B sums up the total points from Question 1 through 8, and this sum was called the Quality of Methods “Score”. There were a total of 10 possible points for this score.

**Overview of studies.** A summary and overview of the information collected for each study is given in Appendix C. The following data were compiled for each study: number of subjects, quality of methods score, treatment intervention(s), control/ comparison intervention(s), and primary outcome measure(s).

The characteristics of the study populations from each article were collected in Appendix D. Included were the number of participants, the percentage of participants that were female, the mean age, the age range, the level of depression at baseline, the other diagnoses or special inclusion criteria, and the location of the recruitment pool. Where appropriate, these values were aggregated for the pooled population of participants from all studies.

**Acupuncture treatment protocols and points used.** The specific acupuncture points used in each article were collected into a matrix. The frequency of use for each specific point was totaled, so a list of the most common points could be compiled. The list of points is presented in Appendix E, with details about how many studies used the points as part of standardized treatments or as part of individualized treatments.

Information about how the acupuncture treatment was given in each study was extracted into Appendix F. Variables included the type of acupuncture point stimulation (manual acupuncture, electro-acupuncture, laser, or transcutaneous electrical acupoints stimulation), whether the point protocol was standardized or individualized, the number of points used, and who administered the treatments. Information was also collected about the length of treatment duration, frequency of treatments, and total number of treatments administered. Where appropriate, the values for each variable were counted for frequency, averaged, or otherwise summarized.

**Outcome measures and results.** Each article was reviewed to see which outcome measures were reported pertaining to depression, such as rate of remission or change in severity of depression, according to various assessment instruments. Appendix G listed the outcome measure by study. Each study could have multiple outcome measures. Many of the outcome measures were used by several different studies.

The results for each study were collected and summarized by the type of comparison groups they used. Included were 1) No control group, 2) Acupuncture Control/Comparison Group, 3) Antidepressant comparison group, 4) Other comparison group, and 5) Inactive Control Group (Waitlist, No treatment, etc.). See Appendix H through L.

## Results

### Data Overview

This study was a research synthesis of twenty-seven studies that examined the use of acupuncture to treat depression. The twenty-seven studies were reported in twenty-six articles (one of the articles contained a description of two distinct studies). All of the included articles were published in scientific journals pertaining to western medicine, Chinese medicine, or alternative and complementary and medicine. They were retrieved from the online databases PubMed, EBSCOhost, and Google Scholar. The studies were examined to find common variables, themes and ideas to help shape the data collection instruments that were used to extract data from the articles. In this chapter, the information drawn from the research synthesis process will be used to address the research objectives of the current study, pertaining to the treatment of depression with acupuncture.

### Quality of Methodology

The quality assessment of the research methodology in the twenty-seven studies used for this research synthesis consisted of eight questions, each assigned a value between 0 and 1 (except for Question 8, which had a possible value between 0 and 2). (See Methods section and Appendix B). The mean Quality of Methods Score was 5.9. The range of scores was wide, with one study earning the lowest score of 0 (Williams & Graham, 2006), and one study earning the maximum potential score of 10 (Quah-Smith, Tang, & Russell, 2005). The question that had the highest proportion of “yes” answers (24/27) was Question 9: “Were all outcomes reported?” Closely following was Question 1 (23/27): “Were Inclusion and exclusion criteria clearly stated?” A large percentage (21/27) of the studies had a “yes” for Questions 2 and 3: “Was a control/comparison group present?” and “Were participants randomized into their assigned group?” All studies that had a control group used randomization to divide the participants into

groups. However, only six of these studies described the randomization process (Question 4). The only question with a lower response rate (5/27) was Question 6, which assessed if the provider was blinded to treatment assignment.

### **Summary of Participants**

The mean number of participants in the twenty-seven studies was 63.2, with a range of 6 to 440 participants per study. Summed together, there were a total of 2154 participants in the twenty-seven included studies. Approximately 66% of total study participants were female. The calculation of percentage female excludes two studies (Luo et al., 1998a n=29; Song, Zhou, Fan, Luo, & Halbreich, 2007 n=90), where the female/male ratio was not reported. In four studies (Allen, Schnyer, & Hitt, 1998; Gallagher, Allen, Hitt, Schnyer, & Manber, 2001; Manber et al., 2004; Manber et al., 2010), participants were exclusively female, while the rest included both males and females. The approximate mean age of all study participants was 41.4 years old, and the range was 18 to 80. The calculation of mean age excludes two studies (Allen et al., 1998, n=38), and (Gallagher, 2001, n=38) where mean age was not reported. Another participant characteristic with a wide range of response was the level of depression at baseline. Levels ranged from mild to severe. Some authors reported on the range in level of depression among the study participants at baseline, while others merely reported a mean value. Several of the studies also mentioned that they were focused on a specific study population, such as malignant tumor patients, pregnant women, nursing home elders, or inpatients in a psychological hospital. The highest proportion of studies were conducted in China (12/27), followed by the U.S. (7/27), UK (3/27) and Taiwan (2/27). The remaining countries had one or fewer studies included in the research synthesis.

### Summary of Acupuncture Treatment Protocols and Points Used

The included studies used various treatment protocols, with different acupuncture modalities, different acupuncture points, and different frequencies and duration of treatments. The most frequently used treatment modality was manual acupuncture (13/27), followed by electro-acupuncture (10/27). Other modalities included TEAS (2/27), laser acupuncture (1/27), ear tacks (1/27), and acupressure (1/27). On average, studies used approximately eight points per treatment. The range in number of points used per treatment was between two and twenty. Treatment frequency ranged from once per week to seven times per week. Total number of treatments ranged from eight to forty-five. Treatment duration ranged from 4 weeks to 12 weeks. The treatment point prescriptions varied widely. However, five studies used a very similar treatment protocol, which was electro-acupuncture treatment on two points on the head: Du20 and Yintang. A total of fifty-three acupuncture points were used in the 27 studies. See Table 1 for a summary of the most commonly used points. All points that were used in at least two studies were included in this table.

Table 1

#### *Summary of Most Frequently Used Acupuncture Points*

<b>Most Common Points (listed in order of frequency)</b>	<b>Total number of studies</b>	<b>Total number of studies where the point was used for all participants</b>	<b>Total number of studies where the point was used in a subset of participants</b>
Du20	16	12	4
SP6	13	7	6
Extra: Yintang	13	12	1
H7	11	8	3
P6	11	7	4
LI4	10	4	6
Liv3	10	5	5
ST36	8	4	4

Most Common Points (listed in order of frequency)	Total number of studies	Total number of studies where the point was used for all participants	Total number of studies where the point was used in a subset of participants
ST40	5	3	2
K3	4	1	3
Extra: Sishencong	4	3	1
GB34	3	2	1
SP9	2	1	1
SP10	2	1	1
UB15	2	2	0
K1	2	2	0
K6	2	0	2
Ren14	2	2	0

### Treatment Acupuncture vs. Control Acupuncture

One of the research objectives was to study the effects of acupuncture treatments designed specifically to treat depression, compared to “control” acupuncture treatments, including “non-specific” acupuncture, “sham” acupuncture, and “placebo” acupuncture.

Out of the twenty-seven studies, twelve compared treatment acupuncture with a control acupuncture intervention. Overall, six of the studies (Allen et al., 1998; Fu et al., 2009; Manber et al., 2010; Quah-Smith et al., 2005; Song, Halbreich, Han, Leonard, & Luo, 2009; Vázquez, González-Macías, Berlanga, & Aedo, 2011) showed that the treatment acupuncture group was significantly more effective at reducing depression severity than the control acupuncture group. Five studies (Allen, Schnyer, Chambers, Hitt, Moreno, & Manber, 2006; Andreescu, Glick, Emeremni, Houck, & Mulsant, 2011; Manber et al., 2004; Roschke et al., 2000; Song et al., 2007) did not find a statistically significant difference between the two groups, and one study (Whiting, Leavey, Scammell, Au, & King, 2008) did not analyze for statistical significance.

The studies were categorized based on the type of control acupuncture intervention that was used (see table 1). The categories of control acupuncture interventions included: 1) Non-

specific treatment acupuncture, 2) Sham acupuncture using real acupuncture points, 3) Sham acupuncture using non-acupuncture points, and 4) Sham acupuncture using the same treatment points. Category 2 included studies that used a sham electro-acupuncture device, and Category 4 consisted of a study that used a sham laser device. Table 2 summarizes the comparison groups that were used for analysis of control acupuncture treatments.

Table 2

*Categories of Analysis for Comparison of Treatment Acupuncture vs. Control Acupuncture*

<b>Type of Comparison</b>	<b>Number of studies</b>	<b>Studies that included Type of Comparison (by Study #)</b>
Specific Acupuncture Treatment vs. Non-Specific Treatment Acupuncture	4	1, 2, 11, 12
Treatment Acupuncture vs. Sham Acupuncture Using Real Acupuncture Points	1	22
Treatment Acupuncture vs. Sham Acupuncture Using Non-Acupuncture Points	6	3, 7, 15, 16, 17, 19
Laser Treatment vs. Sham Laser Treatment On Same Treatment Points	1	14

**Specific treatment acupuncture vs. non-specific treatment acupuncture.** Four of the studies (Allen et al., 2006; Allen et al., 1998; Manber et al., 2004; Manber et al., 2010) used active individualized treatment interventions for the control groups that addressed symptoms or diagnoses that the authors deemed to be unrelated to the patients' depression (back pain was given as an example in Allen et al. (1998)). These were compared to individualized depression-specific treatments that were prescribed for the treatment acupuncture group. All four studies had a common author (John JB Allen), who was listed as first author on Study #1 and #2, and

listed as a secondary author in Study #11 and #12. Three of the four studies (Allen et al., 1998; Manber et al., 2004; Manber et al., 2010) showed that the treatment acupuncture group was significantly more effective than the nonspecific acupuncture group in at least one outcome measure. In Allen et al. (2006), the nonspecific acupuncture group was actually more effective than the treatment group in two outcomes, and there was no difference in the third outcome.

In Allen et al. (2006), both the treatment and control acupuncture groups had a significantly greater decrease in HRSD17 score than a waitlist group, but there was no significant difference between the two acupuncture groups. When looking at the response and remission rates, the control group actually had significantly higher rates than both the treatment group and the waitlist group.

In Allen et al. (1998), the treatment acupuncture group was more effective than the nonspecific acupuncture group in all outcome measures, but the nonspecific acupuncture group seemed to be less effective than the waitlist group in some measures. Using the DepHRSD19 score, the treatment group had a significantly greater decrease in score than the control acupuncture group, but no significant difference with the waitlist group. On this measure, the control acupuncture group was less effective than the waitlist group, although the statistical significance of this difference was not reported. Using the BDI measure, the treatment acupuncture group had a greater reduction in score than the control acupuncture group, but could not be compared to the waitlist group because the waitlist group did not complete the BDI. Remission rates according to DepHRSD criteria and DSM-IV criteria were also compared but the differences between groups were not analyzed for significance. By DepHRSD criteria, 50% of the participants in the treatment acupuncture group had remitted, compared to 27% in the nonspecific acupuncture group and 27% in the waitlist group. By DSM-IV criteria, 42% of those



in the acupuncture treatment group remitted, compared to 9% of those in the nonspecific acupuncture group, and 20% of those in the waitlist group.

In Manber et al. (2004), one measure showed a significant improvement in the treatment group compared to the nonspecific acupuncture group, while two measures did not show significant difference between these two groups ( $p > .05$ ), and the statistical significance was not reported for the five remaining measures. The measure showing significant difference was the percentage of participants in full remission at follow-up (85.7% in treatment acupuncture vs. 50.0% in control acupuncture group,  $p = .039$ ). The two measures that did not show a significant difference were change in BDI in the acute phase, and response rate in the acute phase.

In Manber et al. (2010), the treatment acupuncture group was significantly more effective than the control acupuncture group according to two of the outcome measures, but no different according to the third measure. The treatment group had a significantly greater rate of decrease in HRSD17 score ( $p < .05$ ) and a significantly higher response rate ( $p < .05$ ) than the control acupuncture group. Remission rates did not differ between the two groups.

**Treatment acupuncture vs. sham acupuncture using real acupuncture points.** In one study (Whiting, 2008), the control acupuncture intervention consisted of needling valid acupuncture points, but these points were not considered to be specific for depression. In this study, both the treatment acupuncture group and the sham acupuncture group showed a decrease in BDI score. However, the statistical significance of that decrease was not analyzed, and the difference between groups was not analyzed either.

**Treatment acupuncture vs. sham acupuncture using non-acupuncture points.** Six studies (Andreescu et al., 2011; Fu et al., 2009; Roschke et al., 2000; Song et al., 2009; Song et al., 2007; Vasquez, 2011) used a control intervention that consisted of a set of non-acupuncture points that were in the same general body area as the points in the treatment group. Andreescu et

al. (2011) and Roschke et al. (2000) also used a shallower insertion method for the control acupuncture intervention. Four of these six studies (Andreescu et al., 2011; Song et al., 2009; Song et al., 2007; Vasquez, 2011) compared electro-acupuncture treatment with sham electro-acupuncture. In three of these studies (Andreescu et al., 2011; Song et al., 2009; Song et al., 2007), a sham electro-acupuncture device was used that did not deliver current to the needles. In Vasquez et al. (2011), it was not clear from the method description whether or not the sham group received electro-acupuncture current on the needles. One study (Fu et al., 2009) compared a manual acupuncture treatment (plus ear tacks) to a sham treatment using the same methods (manual acupuncture plus ear tacks with the same insertion and manipulation techniques but points that were .5 cm lateral to the treatment points, and ear points were on the back of the ear rather than the front). The remaining study (Roschke, 2000) compared manual acupuncture to “placebo” acupuncture, where nonspecific points in the same general area as the treatment points were needled with a different method than the treatment points (merely pricking the skin superficially, whereas in the treatment acupuncture protocol, the points were needled to a depth of a few millimeters, retained for a few minutes, and then the electrical skin resistance was measured at each acupoint).

Out of the six studies that compared acupuncture treatment to a control using non-acupuncture points, two studies (Fu et al., 2009; Song et al., 2009) found that the sham acupuncture intervention did not show any significant effects in treating depression, and the treatment acupuncture intervention was significantly more effective than the sham in at least one outcome measure. In another three studies (Andreescu et al., 2011; Roschke et al., 2000; Song et al., 2007), the sham acupuncture group showed significant effects in at least one outcome measure, and there was no significant difference between the treatment and sham interventions. In the final study (Vasquez et al., 2011), the sham acupuncture intervention did have significant

effects on depression, but the treatment intervention was significantly more effective than the sham.

#### **Laser acupuncture treatment vs. sham laser treatment on same treatment points.**

One study (Quah-Smith et al., 2005) used a sham laser device for the control intervention, where the device touched the skin at the same points as in the treatment group, but it did not deliver laser energy. In that study, the real laser out-performed the “sham” laser, with a significantly larger decrease in depression severity.

#### **Acupuncture Treatment Compared to Antidepressant Medication**

Another research objective was to compare the effectiveness of acupuncture with other treatment modalities, such as antidepressant therapy. Eleven studies compared acupuncture treatment to antidepressant therapy, with various combinations of interventions used as the treatment and comparison groups. The different categories of comparison and their frequencies of use are summarized in Table 3.

Table 3

#### *Categories of Analysis for Comparison of Acupuncture and Antidepressants*

<b>Type of Comparison</b>	<b>Number of studies*</b>	<b>Studies that included Type of Comparison (by Study #)</b>
Acupuncture Alone vs. Antidepressant Alone	3	6, 7, 20
Acupuncture combined with Antidepressant vs. Antidepressant Alone	4	5, 9a, 15, 25
Acupuncture combined with low-dose Antidepressant vs. Antidepressant combined with Sham Acupuncture	1	26

Acupuncture combined with Placebo vs. Antidepressant Alone	2	9a, 9b
Acupuncture combined with Placebo vs. Antidepressant combined with Sham Acupuncture	2	16, 17

\*The sum of this column = 12 instead of 11, because Study #9a had two different treatment interventions and so it was analyzed in two different categories.

**Acupuncture alone vs. antidepressant alone.** Three studies compared the use of acupuncture treatment directly to antidepressant treatment. All three studies (Feng et al., 2011; Fu et al., 2009; Wang, Ji, & Huo, 2010) used fluoxetine (Fu et al., 2009 used the brand version Prozac). All three studies found that both treatment interventions resulted in significant improvements in depression treatment outcomes. Two of the studies (Feng et al., 2011; Fu et al., 2009) found that the acupuncture group had significantly greater improvements than the fluoxetine group. One study (Wang et al., 2010) found no difference in treatment effect between the two groups at the endpoint, but found that the average effective time in the acupuncture group was significantly shorter.

**Acupuncture combined with antidepressant vs. antidepressant alone.** Four studies looked at the effects of acupuncture combined with antidepressant, compared to the effects of that antidepressant alone. Two of the studies found no significant difference between the two treatment interventions, while the other two found that the combination of acupuncture + antidepressant was more effective than the antidepressant alone in reducing depression severity in at least one outcome measure. In all four studies, both treatment interventions (acupuncture + antidepressant and antidepressant alone) resulted in statistically significant reductions in severity of depression.

The two studies that found no difference in treatment outcome between groups were Duan, Tu, Chen, & Wu (2009) and Luo et al. (1998a). Duan et al. (2009) investigated electro-acupuncture combined with fluoxetine treatment compared with fluoxetine alone. The treatment period was six weeks, during which 25mg of fluoxetine was taken daily by both groups. One group additionally received five electro-acupuncture treatments per week during the 6-week period. Luo et al. (1998a) compared electro-acupuncture combined with amitriptyline to amitriptyline alone. The first group took 150 mg/day of amitriptyline and had six electro-acupuncture treatments per week over a 6-week period. The second group took amitriptyline alone, and the dosage was 175 mg/day on average.

Roschke et al. (2000) and Zhang, Shi, Liu, Gong, Liu, & Liu, (2007) both found a significant difference between treatment groups in at least one treatment outcome. Roschke et al. (2000) compared manual acupuncture combined with Mianserin to Mianserin alone over a four-week treatment period. For the combined treatment group, each patient received a standardized manual acupuncture treatment three times per week, plus 90-120 mg/day of Mianserin. The other group only received 90-120 mg/day of Mianserin. The authors found that the combination treatment group had a significantly greater improvement in two outcome measures than the Mianserin alone group: GAS ( $p = .052$ ) and CGI item 2 ( $p = .048$ ). However, no significant differences were found between the two groups for the other three treatment outcomes (CGI item 1, BRMS, and Bf-S).

Zhang et al. (2007) compared electro-acupuncture + Paroxetine to Paroxetine alone over a six week treatment period. For the combined treatment group, each patient received a standardized electro-acupuncture treatment six times per week, plus 10-40 mg/day of Paroxetine. The other group only received 10-40 mg/day of Paroxetine. The treatment outcome was HRSD17 score. There was no difference between groups before treatment started, but at all

subsequent time points during the treatment course (Weeks 1, 2, 4, and 6), the EA + Paroxetine group had a significantly lower HRSD17 score compared to the Paroxetine only group ( $p < .05$ ). Also, the combined treatment group showed a significant decrease in score ( $p < .01$ ) at the end of Week 1, as compared to the Paroxetine only group, which did not show a significant decrease from baseline until the end of Week 2. Finally, the effective rate and markedly effective rate were evaluated at the end of the treatment period. The combined treatment group had a significantly higher markedly effective rate (72.7% vs. 40.0%,  $p < .05$ ), but there was no significant difference in the effective rate (90.9% vs. 75.0%,  $p > .05$ ).

**Acupuncture combined with low-dose antidepressant vs. antidepressant combined with sham acupuncture.** One study (Zhang et al., 2009) compared Acupuncture + low-dose Antidepressant to Antidepressant + Sham Acupuncture. In this study, the “verum acupuncture” group received a manual acupuncture treatment five times per week, along with 10mg/day fluoxetine plus placebo throughout the 6-week treatment period. The manual acupuncture treatment consisted of a standardized set of 15 points. The “sham acupuncture” group received a “sham” manual acupuncture treatment five times per week for six weeks, along with 20 mg/day fluoxetine for the first two weeks, and 30 mg/day fluoxetine for the final four weeks. The “sham” acupuncture treatment consisted of a standardized set of 15 non-acupoints that were near the treatment points, but off meridian lines, and were needled with shallow insertion and minimal manipulation compared to the “verum” acupuncture method. Both groups had a significant improvement in HRSD score, but there was no significant difference between groups. Likewise, the response rate was not significantly different between groups.

**Acupuncture combined with placebo vs. antidepressant alone.** Two studies compared the use of acupuncture treatment plus placebo pill to treatment with antidepressant alone. Both studies found that both treatment interventions significantly decreased depression severity. One

study found no significant difference between groups, while the other study found significant differences between groups for a subset of outcome measures. The two studies (Luo et al., 1998a; Luo et al., 1998b) were conducted by the same investigator, had very similar treatment interventions, and were described in the same article (Luo et al., 1998). In both studies, the acupuncture + placebo group received a daily placebo pill, along with a standard electro-acupuncture treatment 6 times per week, for six weeks. The treatment given was electro-stimulation to two points on the head (Du20 and Yintang). In Luo et al. (1998a), the Antidepressant alone group received an average dose of 175 mg/day of amitriptyline. In Luo et al. (1998b), the Antidepressant alone group received an average dose of 161 mg/day.

In both studies, the overall HRSD24 score decreased significantly in both groups ( $p < .01$ ), but no difference was found between groups. Similarly, in both studies, there was no difference in the change in CGI score between groups. Luo et al., (1998b) looked at GSC ratings, which showed that the rate for the cured together with the markedly improved was not statistically different between groups.

Luo et al. (1998b) examined some other outcomes that showed a significant difference between groups. The HRSD24 score change for the sub-group of patients with reactive depression ( $n=48$ ) was reported. Among these patients, the acupuncture + placebo group had a greater score reduction of HRSD than that of the amitriptyline group ( $p < .05$ ). Luo et al. (1998b) also examined factor analysis on HRSD, which showed that the acupuncture + placebo group had a larger therapeutic effect for anxiety somatization and cognitive process disturbance than amitriptyline ( $p < 0.05$ ). Finally, the ASBERG rating scale showed that the side effects were significantly fewer in the EA treatment group than in the amitriptyline group ( $p < .001$ ).

**Acupuncture combined with placebo vs. antidepressant combined with sham acupuncture.** Two studies (Song et al., 2009; Song et al., 2007) compared the use of

acupuncture treatment plus placebo pill to treatment with antidepressant alone. Both of these studies compared electro-acupuncture + placebo to sham electro-acupuncture + fluoxetine. Both studies found significant reductions in depression severity in both treatment groups, but did not report any significant difference between the two groups.

In Song et al. (2009), the Acupuncture + Placebo group received electro-acupuncture on two points on the head, Du20 and Yintang, three times per week for six weeks, plus a daily placebo pill. The other group received 20 mg/day fluoxetine plus the sham acupuncture treatment 3 times per week, consisting of non-acupoints near the treatment points, with no current applied to the needles. Significant decreases in HRSD score were found in both groups compared to baseline ( $p < .01$ ), but the article (Song et al., 2009) did not state whether there was a significant difference between groups. There was a decrease in CGI score for both groups, but the authors did not state if the decrease was statistically significant, nor was it clear if there was any significant difference between groups.

In Song et al. (2007), the Acupuncture + Placebo group received electro-acupuncture on two points on the head, Du20 and Yintang, five times per week for six weeks, plus a daily placebo pill. The other group received 20 mg/day fluoxetine plus the sham acupuncture treatment five times per week, consisting of non-acupoints near the treatment points, with no current applied to the needles. There was significant reduction in the severity of depression in both groups according to HRSD19 scores ( $p < .01$ ), but there was no significant difference between the two groups.



## **Discussion**

### **Summary of Findings**

Twenty-seven studies pertaining to the treatment of depression with acupuncture were reviewed for this research synthesis. There was a lot of variation in study populations, treatment interventions, comparison groups, and outcome measures. The main treatment modalities used were acupuncture with manual stimulation, and electro-acupuncture. Most studies found that acupuncture treatment resulted in significant decrease in severity of depression over the course of treatment. In studies that compared acupuncture treatment to control acupuncture intervention, 50% of the studies found the treatment acupuncture to be significantly more effective, while the other 50% found no difference between the two. In studies that compared acupuncture treatment to antidepressant treatment, most found that the two treatment methods were comparable. Of the studies that compared acupuncture to antidepressant, one study showed a faster treatment effect in the acupuncture group, and one study demonstrated that adding acupuncture in combination with fluoxetine enabled the patients to get the same treatment effect with a lower dosage of fluoxetine.

### **Implications for Theory and Practice**

This research synthesis explored the strengths and limitations of the available research studies in the literature that measured the effectiveness of acupuncture in the treatment of depression. It provides a foundation on which future studies on this topic can be built. It can also serve as a reference for designing research studies using acupuncture specifically to treat infertility patients who suffer from depression.

This research synthesis identified acupuncture points and protocols that were effective in research studies for the treatment of depression. Chinese medicine practitioners can benefit from the knowledge gained in the review of these studies. Although Chinese medicine treatment plans

tend to be individualized and based upon a patient's unique constitution and presentation, being aware of successful documented protocols and techniques can provide added information to guide treatment planning. Chinese medicine practitioners may also use the knowledge gained to educate their patients with evidence-based information.

The findings of this study indicate that acupuncture may be a viable alternative to antidepressant medication for the treatment of depression in some people. Patients who are resistant to antidepressant medication or experience side effects from the medications may both benefit from acupuncture treatment. Other healthcare practitioners can use their knowledge of the existing evidence base for the treatment of depression with acupuncture to help them make appropriate referrals. Another group who can benefit from this knowledge are people who suffer from depression and have not found conventional treatments to be effective, or are searching for alternative or complementary treatments.

### **Limitations of the Current Study**

The inherent limitation of a research synthesis is the lack of control of the researcher over the variables of interest in the articles being studied. The small number of articles that were available for analysis was also a limiting factor. Additionally, several of the included studies were small-scale studies, pilot studies, uncontrolled studies, or case series. Among the selected articles, there was significant heterogeneity in the study populations, treatment interventions, control interventions, and outcome measurements. This could have compromised the validity of study comparisons and aggregated data. Finally, there was only one researcher who screened the articles for inclusion, collected and coded the data, and synthesized the information. Therefore, there is potential that the reliability of the data was compromised due to single rater limitations.

### **Recommendations for Future Research**

The original research question that I sought to answer was: How effective is acupuncture in treating depression in women who suffer from both depression and infertility, and can treating the depression with acupuncture impact reproductive outcomes?

Due to the lack of relevant research on this topic, this research synthesis was focused on a more general and preliminary research objective, which was to examine what is known about the treatment of depression with acupuncture. The studied articles revealed a large evidence base supporting the effectiveness of acupuncture for depression. There were some conflicting results, and more research is still necessary. However, from my assessment, there was more than enough evidence to recommend that future studies be conducted that examine the effects of acupuncture for the treatment of depression specifically in infertile women.

One idea for a first step would be to take the treatment protocol that was found to be the most effective for depression in a general population and use this for a new study on depressed infertile women. It would be interesting to see if this subset of depressed patients would benefit from a protocol that was designed with a broader, mixed population in mind. Furthermore, it would also be interesting to measure reproductive outcomes or fertility-related measures.

Another approach would be to find studies where the guiding TCM principles of the intervention are especially relevant for infertile women, and to use those specific treatment interventions as a starting point for studies on depression in infertile women. An obvious example is the treatment principle of regulating the liver for patients with liver qi stagnation. Liver qi stagnation was the most frequently mentioned diagnosis among the articles included for this literature synthesis review, and it was focused on exclusively in one study (Fu et al., 2009). It is also known to be a very common diagnosis in women that impacts the female reproductive system.

New treatment approaches for the interaction of depression and infertility in women can also be drawn from classical texts or clinical experience of practitioners who are experienced in the treatment of infertility. These could include timing the treatments around a woman's menstrual cycle. If a treatment approach or specific intervention is found to effectively treat depression in women who suffer from infertility, the next (or parallel) step would be to include measurements of treatment outcomes specific to infertility. Depending on the diagnosis or the potential cause of the infertility, outcome measures for observation could include: antral follicle counts, measurement of ovarian reserve markers such as FSH, AMH and inhibin B, and observation of physical signs and symptoms relating to fertility such as cervical mucus, BBT charts, and details of the menstrual cycle.

A study could also be conducted that examines how acupuncture specific for depression can affect IVF outcomes in women who are depressed. Some appropriate outcome measures would include number of eggs retrieved, pregnancy rate, and live birth rate. Many studies have measured the effectiveness of acupuncture in conjunction with IVF (Paulus, 2002; Westergaard et al., 2006), and have even theorized that acupuncture's general effects on stress and depression may contribute to its effectiveness in improving IVF outcome (Balk, Catov, Horn, Gececi, & Wakim, 2010). However, to the best of my knowledge, none have specifically studied depressed women, and none have included a treatment protocol that specifically targets depression.

## **Conclusion**

The main objective of this research synthesis was to study the effects of acupuncture in the treatment of depression, in order to lay some ground work for the investigation of acupuncture's effect on reproductive outcomes in the treatment of depressed women with infertility. With a couple exceptions, almost all of the included studies found that the acupuncture treatment interventions had a significant effect on decreasing depression levels,

even though there was a great deal of variation in the treatment interventions, study populations and outcome measures. However, caution needs to be used when interpreting this data, as many of the trials were of poor quality or small in sample size. When compared with antidepressant medications, most studies found acupuncture to have a comparable effect. Some of these studies also found significantly less side effects associated with acupuncture treatment than with antidepressants. When comparing acupuncture to control acupuncture interventions, the results were mixed, with treatment group demonstrating a significantly greater effect than the control group in about half of cases. The control interventions should be examined to see if they may have unanticipated treatment effects. In summary, the studies included in this research synthesis provide a great deal of evidence in support of the continued investigation of the role of acupuncture in the treatment of depression.

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**Appendix A: Articles Used for Research Synthesis**

Study #	Author(s)	Year	Article Title	Journal
1	Allen, Schnyer, & Hitt	1998	The efficacy of acupuncture in the treatment of major depression in women.	<i>Psychological Science</i>
2	Allen, Schnyer, Chambers, Hitt, Moreno, & Manber	2006	Acupuncture for depression: a randomized controlled trial.	<i>The Journal of Clinical Psychiatry</i>
3	Andresescu, Glick, Emeremni, Houck, & Mulsant	2011	Acupuncture for the treatment of major depressive disorder: a randomized controlled trial.	<i>The Journal of Clinical Psychiatry</i>
4	Chang, Fang, & Yang	2010	Effectiveness of transcutaneous electrical acupoint stimulation for improving depressive mood status among nursing home elders in Taiwan: a pilot study.	<i>Geriatric Nursing</i>
5	Duan, Tu, Chen, & Wu	2009	Efficacy evaluation for depression with somatic symptoms treated by electroacupuncture combined with fluoxetine.	<i>Journal of Traditional Chinese Medicine</i>
6	Feng, Wang, Li, Zhang, Wang, Li, Cao, Ye, & Zhang	2011	Clinical research of acupuncture on malignant tumor patients for improving depression and sleep quality.	<i>Journal of Traditional Chinese Medicine</i>
7	Fu, Fan, Zhu, He, Wang, Zhuang, Liu, Tang, Li, Meng, Zhang, & Yan	2009	Depressive neurosis treated by acupuncture for regulating the liver - A report of 176 cases.	<i>Journal of Traditional Chinese Medicine</i>
8	Gallagher, Allen, Hitt, Schnyer, & Manber	2001	Six-month depression relapse rates among women treated with acupuncture.	<i>Complementary Therapies in Medicine</i>
9a	Luo, Meng, Jia, & Zhao	1998	Clinical research on the therapeutic effect of the electro-acupuncture treatment in patients with depression.	<i>Psychiatry and Clinical Neurosciences</i>
9b	Luo, Meng, Jia, & Zhao	1998	Clinical research on the therapeutic effect of the electro-acupuncture treatment in patients with depression.	<i>Psychiatry and Clinical Neurosciences</i>
10	MacPherson, Thorpe, Thomas, & Geddes	2004	Acupuncture for depression: first steps toward a clinical evaluation.	<i>Journal of Alternative and Complementary Medicine</i>
11	Manber, Schnyer, Allen, Rush, & Blasey	2004	Acupuncture: a promising treatment for depression during pregnancy.	<i>Journal of Affective disorders</i>
12	Manber, Schnyer, Lyell, Chambers, Caughey, Druzin, Carlyle, Celio, Gress, Huang, Kalista, Martin-Okada, & Allen	2010	Acupuncture for depression during pregnancy: a randomized controlled trial.	<i>Obstetrics and Gynecology</i>
13	Pohl & Nordin	2002	Clinical and biochemical observations during treatment of depression with electroacupuncture: a pilot study.	<i>Human Psychopharmacology</i>
14	Quah-Smith, Tang, & Russell	2005	Laser acupuncture for mild to moderate depression in a primary care setting--a randomised controlled trial.	<i>Acupuncture in medicine : Journal of the British Medical Acupuncture Society</i>

15	Röschke, Wolf, Müller, Wagner, Mann, Grözinger, & Bech	2000	The benefit from whole body acupuncture in major depression.	<i>Journal of Affective Disorders</i>
16	Song, Halbreich, Han, Leonard, & Luo	2009	Imbalance between pro- and anti-inflammatory cytokines, and between Th1 and Th2 cytokines in depressed patients: The effect of electroacupuncture or fluoxetine treatment.	<i>Pharmacopsychiatry</i>
17	Song, Zhou, Fan, Luo, & Halbreich	2007	Effects of electroacupuncture and fluoxetine on the density of GTP-binding-proteins in platelet membrane in patients with major depressive disorder.	<i>Journal of Affective Disorders</i>
18	Tsay, Cho, & Chen	2004	Acupressure and Transcutaneous Electrical Acupoint Stimulation in improving fatigue, sleep quality and depression in hemodialysis patients.	<i>The American Journal of Chinese Medicine</i>
19	Vázquez, González-Macías, Berlanga, & Aedo	2011	Effect of acupuncture treatment on depression: Correlation between psychological outcomes and salivary cortisol levels.	<i>Salud Mental</i>
20	Wang, Ji, & Huo	2010	Clinical study on treatment of post-stroke depression by scalp acupuncture plus body acupuncture.	<i>Journal of Acupuncture and Tuina Science</i>
21	Wang, X., Zhang, Wang, Y.L., & Wang, T.	2005	Acupuncture treatment of depression by pattern identification.	<i>Journal of Acupuncture and Tuina Science</i>
22	Whiting, Leavey, Scammell, Au, & King	2008	Using acupuncture to treat depression: a feasibility study.	<i>Complementary Therapies in Medicine</i>
23	Williams & Graham	2006	Acupuncture for older adults with depression – a pilot study to assess acceptability and feasibility.	<i>International Journal of Geriatric Psychiatry</i>
24	Yeung, Ameral, Chuzi, Fava, & Mischoulon	2011	A pilot study of acupuncture augmentation therapy in antidepressant partial and non-responders with major depressive disorder.	<i>Journal of Affective Disorders</i>
25	Zhang, Shi, Liu, S., Gong, Liu, J.Q., & Liu, J.S.	2007	Clinical observation on treatment of depression by electro-acupuncture combined with paroxetine.	<i>Chinese Journal of Integrative Medicine</i>
26	Zhang, Yang, & Zhong	2009	Combination of acupuncture and fluoxetine for depression: a randomized, double-blind, sham-controlled trial.	<i>Journal of Alternative and Complementary Medicine</i>

**Appendix B: Quality of Methodology**

Study#	Inclusion/exclusion criteria clearly stated?	Control/comparison group(s) present?	Assignment to groups randomized?	Randomization method described?	Were all parties blinded?			Treatment interventions repeatable? (0,1,2)*	All outcomes reported?	Total Score
					Participants	Provider	Assessor			
1	1	1	1	1	1	1	1	1	1	9
2	1	1	1	0	1	1	1	0	1	7
3	1	1	1	0	1	0	1	2	1	8
4	1	1	1	1	0	0	0	1	0	5
5	1	1	1	0	0	0	0	1	1	5
6	1	1	1	0	0	0	0	2	1	6
7	1	1	1	0	1	0	1	2	1	8
8	1	0	0	0	0	0	0	0	1	2
9	1	1	1	0	1	1	1	2	1	9
10	1	0	0	0	0	0	0	0	1	2
11	1	1	1	0	1	1	0	1	1	7
12	1	1	1	1	1	1	1	1	1	9
13	0	0	0	0	0	0	0	1	1	2
14	1	1	1	1	1	1	1	2	1	10
15	1	1	1	0	1	0	1	2	1	8
16	1	1	1	0	1	0	0	1	1	6
17	1	1	1	0	1	0	1	1	1	7
18	1	1	1	0	0	0	0	2	1	6
19	1	1	1	0	1	0	1	2	1	8
20	0	1	1	0	1	0	0	1	0	4
21	0	0	0	0	0	0	0	1	1	2
22	1	1	1	1	1	0	1	1	1	8
23	0	0	0	0	0	0	0	0	0	0
24	1	0	0	0	0	0	0	2	1	4
25	1	1	1	0	0	0	0	0	1	4
26	1	1	1	1	1	0	1	2	1	9

\*In the column "Treatment interventions repeatable?" the value can be 0, 1, or 2. (0 = not repeatable, 1 = somewhat repeatable, 2 = repeatable)

In all other columns:

1=Yes

0=No, N/A, not stated, or unclear



### Appendix C: Overview of Articles

Study #	N	Quality of Methods "Score"	Treatment Intervention	Control/Comparison Interventions	Primary Outcome Measure(s)*
1	151	9	MA	1- Non-specific acupuncture 2- Waitlist	HRSD17, BDI
2	38	7	MA	1- Non-specific acupuncture 2- Waitlist	BDI, DepHRSD19
3	53	8	EA	1- Sham acupuncture	HRSD, MOS-SF-36
4	20	5	TEAS	1- 15 min social visits	GDS-SF
5	95	5	EA + fluoxetine	1- Fluoxetine	HRSD
6	80	6	MA	1- Fluoxetine	HRSD
7	440	8	MA + ear tacks	1- Sham acupuncture 2- Prozac	SDS
8	38	2	MA	<i>None</i>	DepHRSD, SCID
9a	29	9	1- EA+amitriptyline 2- EA + placebo pill	1- Amitriptyline	HRSD, CGI
9b	241	2	EA + placebo pill	1- Amitriptyline	HRSD, CGI, GSC
10	10	7	MA	<i>None</i>	BDI, HADS
11	61	9	MA	1- Non-specific acupuncture 2- 20 minute massage	BDI, HRSD17, SCID
12	150	2	MA	1- Non-specific acupuncture 2- 20 minute massage	HRSD17
13	6	10	EA	<i>None</i>	HRSD, MADRS
14	30	8	Laser	1- Sham laser	BDI
15	70	6	MA+ Mianserin	1- Sham acupuncture + Mianserin 2- Mianserin	BRMS, Bf-S, CGI, GAS
16	95	7	EA + placebo pill	1- Sham acupuncture + Placebo pill 2- Sham acupuncture + Fluoxetine	HRSD, CGI
17	90	6	EA	1- Sham acupuncture 2- Fluoxetine	HRSD19
18	108	8	1- TEAS 2- acupressure	1- Routine unit care	BDI
19	42	4	EA	1- Sham acupuncture	CRSD
20	60	2	MA	1- Fluoxetine	HRSD
21	63	8	MA	<i>None</i>	Researcher defined levels of improvement
22	19	0	MA	1- Sham acupuncture	BDI
23	13	4	MA	<i>None</i>	HRSD, MYMOP
24	30	4	EA	<i>None</i>	HRSD17
25	42	9	EA+Paroxetine	1- Paroxetine	HRSD
26	80	9	MA + low-dose Fluoxetine + placebo	1- Fluoxetine	HRSD17

\* Full name and descriptions of the outcome measures can be found in the Definition of Terms section of the Introduction.

EA = electroacupuncture (needle acupuncture with electro-stimulation on one or more needles)

MA = manual acupuncture (needle acupuncture with no electro-stimulation)

TEAS = transcutaneous electro-acupuncture stimulation

HRSD: Hamilton Rating Scale for depression. Also referred to as HDRS, HAMD, HAM-D

HRSD17: a common version of the HRSD that uses 17 items

DepHRSD: a variation of the HRSD that uses 19 items and a subset of depression symptoms

SCID: structured clinical interview for DSM disorders

CGI: Clinical Global Impressions Scale

BDI: Beck Depression Inventory

CRSD: Carroll Rating Scale for Depression

BRMS: Bech-Rafaelson Melancholia Scale

Bf-S: self-rating scale for evaluating depressive states in longitudinal studies

GAS: global assessment scale

**Appendix D: Summary of Study Participants**

Study #	N	Percent Female	Mean Age	Age Range	Level of Depression at Baseline	Other diagnoses/ special inclusion criteria	Recruitment Pool Location
1	151	69%	41	18-65	Mild to moderate	--	Arizona
2	38	100%	Unclear	18-45	Mild to moderate	--	Arizona
3	53	28%	46	18-80	HRSD 18.1	--	Pennsylvania
4	20	45%	84	65+	Mild to moderate	Nursing home residents	Taiwan
5	95	62%	38	18-60	Mild to moderate	in- and outpatients from Department of Neurology and Department of Psychology	China
6	80	34%	64	18-75	HRSD17=20.82	Malignant tumor patients	China
7	440	66%	41	Unclear	SDS=67.33 HRSD >or equal 20	Liver Qi Stagnation patients	China
8	38	100%		18-45	Mild to Moderate	--	Arizona
9a	29	Unclear	37	Unclear	HRSD=28.1	Inpatients at Institute of Mental Health (bipolar included)	China
9b	241	55%	32	Unclear	HRSD=36.5	Inpatients in psychiatric hospitals (bipolar included)	China
10	10	60%	51	30-77	Minimal to severe, mean BDI=24.7	--	UK
11	61	100%	33		HRSD17=21	Pregnant	California
12	150	100%	33	18+	HRSD17 = 20.7, BDI = 30	Pregnant	California
13	6	83%	44	Unclear	HRSD 19.5	--	Sweden
14	30	77%	39	21-49	Mild to Moderate	--	Australia
15	70	69%	48	21-68	severe depression, mean HRSD = 28	Inpatients	Germany
16	95	59%	32	Unclear	HRSD=22.5	Outpatients from Mental Health Institute	China
17	90	Unclear	33	Unclear	Moderate, HRSD24=25.3	Outpatients from Institute of Mental Health	China
18	108	66%	58	Unclear	(Moderate) BDI=20.1	Dialysis Center patients with fatigue and sleep disturbance	Taiwan
19	42	83%	44	18+	Carroll Scale 28.8	--	University Primary care center
20	60	40%	65	Unclear	HRSD 22.3	Post-stroke patients	China
21	63	65%	37	16-62	Unclear	--	China
22	19	74%	40	18+	BDI 28.8	--	UK
23	13	92%	74	Unclear	Unclear	--	UK
24	30	47%	48	18+	HRSD17>14, mean HRSD17=18.5	Partial or non-responders to antidepressants (including natural remedies)	Massachusetts
25	42	50%	37	18-65	HRSD17=28.8	Inpatients in Psychology department	China
26	80	66%	36	Unclear	HRSD 21.3	--	China

## Appendix E: Acupuncture Points Used

Acupuncture Point	Number of studies Total (S*, I**)	List of studies (by code) where the point was used for all patients in the treatment group*	List of studies (by code) where the point was used for a subset of patients**
LU1	1 (1,0)	15	--
LU7	1 (0,1)	--	10
LU9	1 (0,1)	--	25
LI4	10 (4,6)	7, 22, 24, 26	5, 10, 14, 20, 21, 25
LI11	1 (0,1)	--	20
ST36	8 (4,4)	4, 13, 18, 24	5, 10, 21, 25
ST40	5 (3,2)	6, 15, 22	20, 25
SP3	1 (0,1)	--	21
SP4	1 (0,1)	--	10
SP5	1 (1,0)	15	--
SP6	13 (7,6)	4, 6, 15, 18, 19, 22, 24	5, 10, 14, 20, 21, 25
SP9	2 (1,1)	6	10
SP10	2 (1,1)	6	21
H7	11 (8,3)	4, 6, 14, 15, 19, 22, 24, 26	5, 21, 25
UB15	2 (2,0)	15, 19	--
UB17	1 (1,0)	15	--
UB18	1 (1,0)	15	--
UB23	1 (1,0)	19	--
UB57	1 (1,0)	13	--
K1	2 (2,0)	4, 18	--
K3	4 (1,3)	4	5, 10, 21
K6	2 (0,2)	--	5, 10
K7	1 (0,1)	--	10
K10	1 (0,1)	--	14
P6	11 (7,4)	4, 6, 13, 15, 19, 21, 26	5, 10, 22, 25
SJ5	1 (0,1)	--	25
SJ6	1 (0,1)	--	21
GB13	1 (0,1)	--	20
GB21	1 (0,1)	--	10
GB34	3 (2,1)	4, 18	21
GB43	1 (0,1)	--	5
Liv2	1 (0,1)	--	5
Liv3	10 (5,5)	4, 7, 22, 24, 26	5, 10, 20, 21, 25
Liv4	1 (1,0)	13	--
Liv8	1 (1,0)	14	--
Liv14	1 (1,0)	14	--
Ren4	1 (0,1)	--	21
Ren12	1 (0,1)	--	10
Ren14	2 (2,0)	14, 21	--
Ren15	1 (1,0)	14	--
Ren17	1 (0,1)	--	20
Du14	1 (0,1)	--	20
Du20	16 (12,4)	3, 5, 6, 7, 9, 13, 16, 17, 21, 24, 25, 26	10, 14, 20, 22
Du26	1 (1,0)	26	--
Extra: Sishencong	4 (3,1)	6, 21, 26	20
Extra: Yintang	13 (12,1)	3, 5, 6, 7, 9, 13, 16, 17, 20, 24, 25, 26	10
Extra: Taiyang	1 (1,0)	19	--
Ear: Heart	1 (1,0)	7	--
Ear: Liver	1 (1,0)	7	--
Scalp Area 1	1 (0,1)	--	20
Scalp Area 2	1 (0,1)	--	20
Scalp Area 3	1 (0,1)	--	20
Scalp Area 4	1 (0,1)	--	20

\*S = number of studies where the point was used as part of the standardized treatment protocol, where every participant in the treatment group received the point

\*\*I = number of studies where the point was optional, or used as part of individualized treatments that were give to a subset of the participants in the treatment group.

Scalp Area 1: Anterior Temporal Line

Scalp Area 2: Anterior Oblique Line of Vertex-temporal

Scalp Area 3: Lower-lateral Line of Occiput

Scalp Area 4: Lateral Line 1 of Vertex

Note: The following six studies used completely individualized treatments and did not mention any

specific acupuncture points: 1, 2, 8, 11, 12, 23

## Appendix F: Acupuncture Treatment Protocols

Study #	Type of Acupuncture in Treatment Group	Standardized or Individualized	Number of points used	Total number of treatments	Frequency of Treatments	Treatment duration	Who administered acupuncture?
1	MA	I	10-16	12	2/wk for 4 wks, then 1/wk for 4 wks	8 wks	several NCCAOM board certified, in practice for at least 5 years
2	MA	I	Unclear	12	2/wk for 4 wks, then 1/wk for 4 wks	8 wks	4 trained and board certified acupuncturists
3	EA	S	2	12	2/wk	6 wks	1 licensed acupuncturist NCCAOM certified with 5 yrs experience
4	TEAS	S	16	22*	5/wk	1 month	2 trained registered nurses who had received 18 wks training in TCM
5	EA + Fluoxetine	S/I	6	30	5/wk	6 wks	Unclear
6	MA	S	18	30	1/day	30 days	Unclear
7	MA + ear tacks	S	8	26	2/wk	3 months	Unclear
8	MA	I	Unclear	12**	2/wk for 4 wks, then 1/wk for 4 wks	8 wks	4 trained and board certified acupuncturists
9	EA	S	2	36	6/wk	6 wks	Unclear
10	MA and/or other modalities***	I	Unclear	1-10 (avg 7)	1-2/wk	10 wks	L.Ac. with minimum 10 yrs experience
11	MA	I	Unclear	12	2/wk for 4 wks, then 1/wk for 4 wks	8 wks	Unclear
12	MA	I	7-12	12	2/wk for 4 wks, then 1/wk for 4 wks	8 wks	L.Ac. w/less than 2 yrs experience (point prescription designed by senior L.Ac w/ min 5 years experience)
13	EA	S	6	18-20	5/wk for 2 wks, then 3/wk for 2 wks, then 1-2/wk for 2 wks	6 wks	Unclear
14	MA	S/I	6+	12	2/wk for 4wks 1/wk for 4 wks	8 wks	Medical acupuncturist w/ full time medical acupuncture practice
15	MA	S	18	12	3/wks	4 wks	2 clinicians experienced in traditional Chinese acupuncture
16	EA	S	2	18	3/wk	6 wks	Unclear
17	EA	S	2	30	5/wk	6 wks	Unclear
18	1- TEAS 2- Acupressure	S	8	12	3/wk	4 wks	Investigators and research assistants trained for 2 months by Chinese medicine physician
19	EA	S	7	12	2/wk	6 wks	Medical doctor, acupuncture specialist
20	MA	S/I	9-13	20-22	5/wk	30 days	Unclear
21	MA + optional moxa	S/I	14-15	13-45 (avg 26)	2-3/wk	Unclear	Study authors (training unclear)
22	MA	S/I	10-13	Up to 12 (avg 10)	Unclear	Unclear	Accredited TCM healthcare practitioner with 10 yrs clinical experience
23	MA	I	6-12	12	1/wk	12 wks	Qualified acupuncturist registered with British acupuncture council
24	EA	S	12	8 (n=18) or 16 (n=2)	1/wk (n=18) or 2/wk (n=2)	8 wks	Accredited medical acupuncturists
25	EA	S/I	2-20	36	6/wk	6 wks	Unclear
26	MA	S	15	30	5/wk	6 wks	Two licensed and experienced acupuncturists; 3 months of formal research training; in continuous practice for 3 years and 5 years, respectively

\*estimated based on 4.35 weeks/month

\*\*This is pooled data for follow-up from 3 groups that all received 12 specific acupuncture treatments within a 16 week period: 1) Group 1 received 12 nonspecific acupuncture treatments in the first 8 week period before receiving 12 specific acupuncture treatments in the second 8 week period. 2) Group 2 was waitlisted for 8 weeks before receiving 12 specific treatments. 3) Group 3 received 12 specific treatments in the first 8 week period.

\*\*\*Other modalities included acupressure, massage, flower remedies, relaxation exercises, and lifestyle advice. On patient received only acupressure and no acupuncture.

MA = manual acupuncture

EA = electroacupuncture

S = Standardized treatment: all participants in treatment group received the same point protocol

I = Individualized treatments: each participant received a completely individualized acupuncture treatment

S/I: some mixture of standardized and individual treatments. Examples: 1) all participants received 6 standard acupuncture points, but additional points were added according to symptoms. 2) Participants received one of four point prescriptions, dependent upon their TCM diagnosis.

### Appendix G: Outcome Measures by Study Number

#### *Depression Outcome measures by Study #*

Study #	Outcome Measures
1	HRSD17, BDI
2	Remission Rate <sup>1</sup> , BDI, DepHRSD19, SCID, IDS, BHS
3	HRSD, Response Rate <sup>2</sup> , MOS-SF-36
4	GDS-SF
5	HRSD, % effective <sup>3</sup>
6	HRSD
7	SDS
8	DepHRSD, SCID, Remission rate <sup>4</sup> , Relapse Rate <sup>5</sup>
9a	HRSD, CGI
9b	HRSD, CGI
10	BDI, HADS
11	BDI, HRSD17, SCID
12	HRSD17, depression remission rate <sup>6</sup> , response rate <sup>7</sup>
13	HRSD, MADRS
14	BDI, Caseness <sup>8</sup>
15	BRMS, Bf-S, CGI, GAS
16	HRSD, CGI
17	HRSD19
18	BDI
19	Carroll Rating Scale for Depression
20	HRSD
21	Researcher derived Symptoms Reduction scale
22	BDI
23	HRSD, MYMOP
24	HRSD17, treatment response <sup>9</sup>
25	HRSD
26	HRSD17, therapeutic response rate <sup>10</sup>

1 **Remission rate** = absence of both core symptoms of depression (depressed mood and anhedonia)

2 **Response Rate** = HRSD score 50% or greater improvement plus HRSD less than or equal to 10

3 **% effective** = the percentage of patients whose HRSD score has reduced by at least 25% from baseline. The score-reducing rate >75% was considered to be clinically controlled, 50%–75% markedly relieved, 25%–49% improved, and <25% failed.

4 **Remission rate**: full remission was defined as the absence of both core symptoms of depression (depressed mood, anhedonia) as determined by the SCID.

5 **Relapse rate**: defined as once again meeting DSM-IV criteria for major depression.

6 **Depression remission rate**: the absence of the core symptoms of depression (depressed mood and anhedonia) and Hamilton Rating Scale for Depression score of 7 or less

7 **Response rate**: 1) at least 50% reduction in the Hamilton Rating Scale for Depression score from baseline, 2) Hamilton Rating Scale for Depression between 7 and 14, and 3) failure to meet full criteria for the DSM-IV.

8 **Caseness**: BDI < 11

9 **Treatment response**: 50% or greater improvement in HRSD17 score

10 **Therapeutic response rate**: at least 50% decrease in HRSD scores at final assessment relative to baseline

**Appendix H: Results for Studies with No Control Group**

<b>Study #</b>	<b>Treatment Intervention</b>	<b>Control/Comparison Interventions</b>	<b>Primary Outcome Measure(s)</b>	<b>Results</b>
8	MA	<i>None</i>	DepHRSD, SCID	38% of participants (10/26) met the criteria for depression in the 6 month follow-up period. Among women who were in full remission after treatment, 24% (4/17) had fully relapsed within six months. Of those who had not achieved full remission, 67% (6/9) met criteria for major depressive episode at some point during the follow-up period.
10	MA	<i>None</i>	BDI, HADS	BDI and HADS: Significant reduction in severity of depression SF-36: trend toward improvement but no significant change
13	EA	<i>None</i>	HRSD, MADRS	HRSD: Reduction in severity of depression did not reach statistical significance. MADRS: Reduction in severity of depression did not reach statistical significance. CPRS-S-A: Significant reduction in severity
21	MA	<i>None</i>	Researcher defined levels of improvement	"Clinical cure": 21. "Remarkable effect": 18 , "Improvement": 20, "Failure": 4 (Statistical significance was not analyzed)
23	MA	<i>None</i>	HRSD, MYMOP	HRSD: Score significantly improved (p=.001) after treatment and at 1 month follow-up.
24	EA	<i>None</i>	HRSD17	HRSD17: significant decrease in severity (p<.001)



### Appendix I: Results for Studies with Acupuncture as The Control Group

Study #	Treatment Intervention	Control/Comparison Interventions	Primary Outcome Measure(s)	Results
1	MA	1- Non-specific acupuncture 2- Waitlist	HRSD17, BDI	For BDI and HRSD17, treatment group had greater reduction in severity of depression than waitlist group, but there was no significant difference between treatment and control acupuncture. Response and remission rates were higher in the control acupuncture group than in both the treatment group and waitlist group.
2	MA	1- Non-specific acupuncture 2- Waitlist	BDI, DepHRSD19	DepHRSD19: Treatment group had greater reduction in severity of depression than control acupuncture group, but no significant difference with waitlist group. BDI: Treatment group had greater reduction in severity of depression than control acupuncture group. (BDI was not completed in waitlist group).
3	EA	1- Sham acupuncture	HRSD, MOS-SF-36	HRSD: decrease in both groups, with no significant difference between the two. No serious adverse events in either group.
7	MA + ear tacks	1- Sham acupuncture 2- Prozac	SDS	SDS: After 1, 2, and 3 months of treatment, Treatment group had significantly greater reduction in severity of depression than Prozac group and non-acupuncture point group. No side effects were found in either acupuncture group.
11	MA	1- Non-specific acupuncture 2- 20 minute massage	BDI, HRSD17, SCID	HRSD17: significant reduction in treatment group but unclear if significant compared to other groups BDI: Treatment group had significant reduction in severity of depression compared to massage group in the first month, but no significant difference compared to nonspecific acupuncture group. Follow-up at postpartum: all 3 had significant reduction in severity.
12	MA	1- Non-specific acupuncture 2- 20 minute massage	HRSD17	HRSD17: greater rate of decrease in symptom severity ( $p < .05$ ) compared with the combined controls or control acupuncture alone, but no significant difference than massage group. Adverse events did not differ between groups. Significantly more side effects occurred in acupuncture groups as compared to massage group (tiredness, irritability, sleep disturbance, headache, nausea, aggravation of depression)
14	Laser	1- Sham laser	BDI	BDI: Significant reduction in treatment group as compared to control acupuncture group Follow-up: Treatment group was not statistically different from control group at 4 weeks follow-up, but did show significant decrease in severity of depression at 12 weeks follow-up.
15	MA+ Mianserin	1- Sham acupuncture + Mianserin 2- Mianserin	BRMS, Bf-S, CGI, GAS	All groups had a reduction in severity of depression. No significant differences were seen between groups except that in CGI-2 (improvement in psychopathology), there was a significant improvement in both acupuncture groups as compared to Mianserin alone.
16	EA + placebo pill	1- Sham acupuncture + Placebo pill 2- Sham acupuncture + Fluoxetine	HRSD, CGI	HRSD: EA group and Fluoxetine group both showed significant ( $p < .01$ ) decrease in severity of depression as compared to baseline, but Control+Placebo did not. EA had a lower severity of depression post-treatment than Control+Placebo group ( $p < .05$ ), while baseline values did not differ. CGI: No groups showed significant change as compared to baseline. However, EA had a significant decrease as compared to the Control+Placebo group.
17	EA	1- Sham acupuncture 2- Fluoxetine	HRSD19	HRSD24: Significant decrease in all three groups, but groups did not differ.

19	EA	1- Sham acupuncture	CRSD	Carroll: There was a significant decrease in severity in both Treatment group ( $p < .001$ ) and Control acupuncture ( $p = .005$ ). The reduction in the Treatment group was significantly larger than in the Control group ( $p = .03$ ). SCL-90 Depression: Treatment group showed a significant decrease in depression but Control group did not.
22	MA	1- Sham acupuncture	BDI	BDI: Both groups showed decrease in BDI score but statistical significance was not analyzed.

### Appendix J: Results for Studies Comparing Acupuncture Treatment With Antidepressant

Study #	Treatment Intervention	Control/Comparison Interventions	Primary Outcome Measure(s)	Results
5	EA + fluoxetine	1- Fluoxetine	HRSD	HRSD: significant reduction in both groups with no difference between the two. Faster effective rate in EA group than in fluoxetine group, with less adverse effects.
6	MA	1- Fluoxetine	HRSD	SDS: "The results indicated that acupuncture and Fluoxetine Hydrochloride capsule were both effective in relieving depression mood of patients suffering from malignant tumor; and the effectiveness of acupuncture was obviously higher." HRSD: "acupuncture and Fluoxetine Hydrochloride capsule were both effective in relieving depression mood of patients suffering from malignant tumor; and the effectiveness of acupuncture was obviously higher."
7	MA + ear tacks	1- Sham acupuncture 2- Prozac	SDS	SDS: After 1, 2, and 3 months of treatment, Treatment group had significantly greater reduction in severity of depression than Prozac group and non-acupuncture point group. No side effects were found in either acupuncture group.
9a	1- EA+amitriptyline 2- EA + placebo pill	1- Amitriptyline	HRSD, CGI	HRSD: All 3 groups reduced significantly, but no difference between the 3 groups. CGI: changes almost similar in each of treatment groups?
9b	EA + placebo pill	1- Amitriptyline	HRSD, CGI, GSC	HRSD: Both reduced significantly but no difference between the 2 groups overall. EA was significantly more effective for reactive depression than was amitriptyline. CGI: No difference between the 2 groups
15	MA+ Mianserin	1- Sham acupuncture + Mianserin 2- Mianserin	BRMS, Bf-S, CGI, GAS	All groups had a reduction in severity of depression. No significant differences were seen between groups except that in CGI-2 (improvement in psychopathology), there was a significant improvement in both acupuncture groups as compared to Mianserin alone.
16	EA + placebo pill	1- Sham acupuncture + Placebo pill 2- Sham acupuncture + Fluoxetine	HRSD, CGI	HRSD: EA group and Fluoxetine group both showed significant ( $p < .01$ ) decrease in severity of depression as compared to baseline, but Control+Placebo did not. EA had a lower severity of depression post-treatment than Control+Placebo group ( $p < .05$ ), while baseline values did not differ. CGI: No groups showed significant change as compared to baseline. However, EA had a significant decrease as compared to the Control+Placebo group.
17	EA	1- Sham acupuncture 2- Fluoxetine	HRSD19	HRSD24: Significant decrease in all three groups, but groups did not differ.
20	MA	1- Fluoxetine	HRSD	HRSD: Significant reduction in severity of depression in both treatment groups ( $p < .05$ ) but no significant difference between the two groups.
25	EA+Paroxetine	1- Paroxetine	HRSD	HRSD scores determined at the end of the 1st, 2nd, 4th, and 6th week of the treatment course were significantly lower in the observation group than those in the control group ( $p < 0.05$ ). The significant improvement rate evaluated at the end of the 6-week treatment was remarkably higher in the observation group than that in the control group (72.7% vs. 40.0%) No significant difference in adverse effects between groups
26	MA + low-dose Fluoxetine	1- Fluoxetine	HRSD17	HRSD17: significant decrease in depression severity across all participants ( $z=1.80$ , $p < 0.001$ ) but no significant difference between groups.

**Appendix K: Results for Studies Comparing Acupuncture to Other comparison group**

Study #	Treatment Intervention	Control/Comparison Interventions	Primary Outcome Measure(s)	Results
11	MA	1- Non-specific acupuncture 2- 20 minute massage	BDI, HRSD17, SCID	HRSD17: significant reduction in treatment group but unclear if significant compared to other groups BDI: Treatment group had significant reduction in severity of depression compared to massage group in the first month, but no significant difference compared to nonspecific acupuncture group. Follow-up at postpartum: all 3 had significant reduction in severity.
12	MA	1- Non-specific acupuncture 2- 20 minute massage	HRSD17	HRSD17: greater rate of decrease in symptom severity ( $P < .05$ ) compared with the combined controls or control acupuncture alone, but no significant difference than massage group. Adverse events did not differ between groups. Significantly more side effects occurred in acupuncture groups as compared to massage group (tiredness, irritability, sleep disturbance, headache, nausea, aggravation of depression)

**Appendix L: Results for Studies Comparing Acupuncture to Inactive Control Group**

Study #	Treatment Intervention	Control/Comparison Interventions	Primary Outcome Measure(s)	Results
1	MA	1- Non-specific acupuncture 2- Waitlist	HRSD17, BDI	For BDI and HRSD17, treatment group had greater reduction in severity of depression than waitlist group, but there was no significant difference between treatment and control acupuncture. Response and remission rates were higher in the control acupuncture group than in both the treatment group and waitlist group.
2	MA	1- Non-specific acupuncture 2- Waitlist	BDI, DepHRSD19	DepHRSD19: Treatment group had greater reduction in severity of depression than control acupuncture group, but no significant difference with waitlist group. BDI: Treatment group had greater reduction in severity of depression than control acupuncture group. (BDI was not completed in waitlist group).
4	TEAS	1- 15 min social visits	GDS-SF	GDS-SF: Treatment group showed a statistically significant improvement in depressive mood status, but changes in the depressive mood status of Social Visit group were not significant.
18	1- TEAS 2- acupressure	1- Routine unit care	BDI	BDI: Significant reduction ( $p=.01$ ) in severity of depression in TEAS and Acupressure group but not the Routine care group. TEAS and Acupressure reduction in severity were significant compared to Routine care group ( $p < .01$ ), but did not differ compared to each other.