



NATIONAL DEFENSE RESEARCH INSTITUTE

# Acupuncture for Major Depressive Disorder

A Systematic Review

Melony E. Sorbero, Kerry A. Reynolds, Benjamin Colaiaco, Susan L. Lovejoy,  
Coreen Farris, Christine Anne Vaughan, Jennifer Sloan, Ryan Kandrack,  
Eric Apaydin, Patricia M. Herman

For more information on this publication, visit [www.rand.org/t/RR1135](http://www.rand.org/t/RR1135)

Published by the RAND Corporation, Santa Monica, Calif.

© Copyright 2015 RAND Corporation

**RAND**® is a registered trademark.

#### Limited Print and Electronic Distribution Rights

This document and trademark(s) contained herein are protected by law. This representation of RAND intellectual property is provided for noncommercial use only. Unauthorized posting of this publication online is prohibited. Permission is given to duplicate this document for personal use only, as long as it is unaltered and complete. Permission is required from RAND to reproduce, or reuse in another form, any of its research documents for commercial use. For information on reprint and linking permissions, please visit [www.rand.org/pubs/permissions.html](http://www.rand.org/pubs/permissions.html).

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.

RAND's publications do not necessarily reflect the opinions of its research clients and sponsors.

#### Support RAND

Make a tax-deductible charitable contribution at  
[www.rand.org/giving/contribute](http://www.rand.org/giving/contribute)

[www.rand.org](http://www.rand.org)

## Preface

---

Major depressive disorder (MDD) is a common condition with a significant burden in terms of reduced quality of life, lower productivity, increased prevalence of other conditions, and increased health care costs. Complementary and alternative medicine approaches to MDD treatment are becoming more common, and a number of military treatment facilities offer these services, including acupuncture.

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury is interested in determining the efficacy and comparative effectiveness of integrative medicine approaches for psychological health conditions. This report describes a systematic review and qualitative synthesis of the relevant literature on the use of acupuncture in treating MDD, conducted during a two-year project on integrative medicine approaches for psychological health conditions. Key questions guiding this work focused on the efficacy and effectiveness of acupuncture for improving MDD symptoms and quality of life, as well as describing the occurrence of adverse events related to acupuncture among MDD populations. This report should be of interest to health care providers and clinical policymakers interested in the treatment of MDD or the use of acupuncture.

A version of this report was provided to the committee for review in May 2015; we reproduce that version here, with minor editorial updates. None of the authors has any conflict of interest to declare.

This research was sponsored by the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury and conducted within the Forces and Resources Policy Center of the RAND National Defense Research Institute, a federally funded research and development center sponsored by the Office of the Secretary of Defense, the Joint Staff, the Unified Combatant Commands, the Navy, the Marine Corps, the defense agencies, and the defense Intelligence Community. For more information on the RAND Forces and Resources Policy Center, see <http://www.rand.org/nsrd/ndri/centers/frp.html> or contact the director (contact information is provided on the web page).



## Abstract

---

Major depressive disorder (MDD) is a prevalent condition associated with significant burden in terms of reduced quality of life, lower productivity, increased prevalence of other conditions, and increased health care costs. We conducted a systematic review and qualitative summary of randomized controlled trials (RCTs) that assessed the effectiveness and safety of acupuncture for treating MDD.

We searched the databases PubMed, CINAHL, PsycINFO, Web of Science, Embase, CDSR, CENTRAL, clinicaltrials.gov, DARE, and PILOTS for English-language RCTs published through January 2015. Two independent reviewers screened the identified literature against inclusion and exclusion criteria, abstracted study-level data, and assessed the risk of bias and methodological quality of included studies. The quality of the evidence was assessed using the GRADE approach.

Eighteen studies met inclusion criteria. Eleven assessed acupuncture as monotherapy and seven as adjunct depression treatment. Intervention approaches and comparators varied. Evidence on the effectiveness and comparative effectiveness of acupuncture to treat MDD for the outcomes depression improvement (measured as scale score differences) and the number of responders is very weak. Acupuncture may be superior to waitlist (low quality of evidence), but findings for effect estimates compared with other comparators are inconclusive. Few studies reported on patients achieving remission. The effect of acupuncture on relapse rates could not be determined. Too few studies assessed quality of life to estimate treatment effects. Reported adverse events were typically mild in nature, but the assessment lacked rigor and studies were not designed to detect rare events.



# Table of Contents

---

Preface.....	iii
Abstract.....	v
Figures.....	xi
Tables.....	xiii
Summary.....	xv
Acknowledgments.....	xxi
Abbreviations.....	xxiii
Chapter One: Introduction.....	1
Key Questions.....	2
Chapter Two: Methods.....	5
Search Strategy.....	5
Eligibility Criteria.....	5
Inclusion Screening.....	6
Data Extraction.....	6
Risk of Bias.....	7
Data Synthesis.....	8
Quality of Evidence.....	8
Protocol Deviations.....	9
Chapter Three: Results.....	11
Results of Literature Searches.....	11
Description of Included Studies.....	12
Key Question.....	12
Design.....	13
Setting.....	13
Participants.....	14
Interventions and Providers.....	14
Comparators.....	14
Outcome Measures.....	14
Risk of Bias.....	15
KQ 1: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD?.....	19
Acupuncture Versus Waitlist Control.....	19
Acupuncture Versus Sham Acupuncture Using Nonpenetrating Needles.....	20
Depression-Specific Acupuncture Versus Acupuncture Targeting Acupoints Not Specific to Depression.....	20
Acupuncture Versus Attention Control.....	23

Acupuncture Versus Antidepressants.....	24
KQ 1a: Among Publications That Address Monotherapy Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events? .....	25
KQ 2: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD? .....	26
Acupuncture Plus Antidepressant Versus Antidepressants Alone .....	26
Acupuncture Plus Usual Care Versus Sham Acupuncture Plus Usual Care .....	28
Acupuncture Plus Antidepressants Versus Sham Acupuncture Using Nonpenetrating Needles Plus Antidepressants .....	28
Acupuncture Plus Antidepressants Versus Sham Acupuncture at Nonspecific Points Plus Antidepressants .....	29
KQ 2a: Among Publications That Address Adjunctive Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events? .....	29
KQ 3: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD? .....	30
KQ 4: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD? .....	30
KQ 5: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD? .....	31
KQ 6: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD?.....	31
Chapter Four: Discussion.....	33
Summary of Findings .....	33
KQ 1: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD?.....	33
KQ 1a: Among Publications That Address Monotherapy Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events? .....	34
KQ 2: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD? .....	35
KQ 2a: Among Publications That Address Adjunctive Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events? .....	36
KQ 3: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD? .....	36



KQ 4: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD? .....	36
KQ 5: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD? .....	36
KQ 6: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD? .....	37
Other Reviews in This Area .....	47
Strengths and Limitations .....	47
Implications for Future Research and Practice .....	48
Appendix A: PubMed Search Strategy .....	49
Appendix B: Excluded Full-Text Articles .....	51
Appendix C: Evidence Tables of Included Studies .....	77
References .....	105



## Figures

---

Figure 3.1. Publication Review and Inclusion .....	11
--	----



## Tables

---

Table 3.1. Evidence Base for Key Questions .....	12
Table 3.2. Study Quality/Risk of Bias for Each Monotherapy Acupuncture Randomized Controlled Trial.....	17
Table 3.3. Study Quality/Risk of Bias for Each Adjunctive Acupuncture Randomized Controlled Trial.....	18
Table 4.1. Summary of Findings and Quality of Evidence.....	38
Table C.1. Monotherapy Acupuncture Studies.....	77
Table C.2. Adjunctive Acupuncture Studies.....	95



# Summary

---

## Introduction

Major depressive disorder (MDD) is a prevalent condition associated with significant burden in terms of reduced quality of life, lower productivity, increased prevalence of other conditions, and increased health care costs. Several evidence-based treatments for MDD exist, but these interventions vary in their effectiveness, safety, and acceptability to different patient populations (Tylee and Jones, 2005). Individuals with depression sometimes use complementary and alternative medicine therapies, including acupuncture. Monotherapy acupuncture refers to its use instead of or as an alternative to conventional therapies, such as antidepressants and psychotherapy. Acupuncture may also be used adjunctively with conventional therapies as a complementary medicine. When used as adjunctive therapy, patients may obtain acupuncture separately from other treatments for depression with no communication between health care providers, or acupuncture may be part of integrative health care when its use is planned and coordinated with conventional therapies. This systematic review summarizes the evidence from randomized controlled trials (RCTs) testing the efficacy and safety of acupuncture to treat adults with MDD. Specifically, this systematic review aimed to answer the following primary key questions (KQs) and subquestions:

- KQ 1: Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in reducing depressive symptoms in adults with MDD?
  - KQ 1a: Among publications that address monotherapy acupuncture as a treatment for adults with MDD, how common and severe are adverse events?
- KQ 2: Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in reducing depressive symptoms in adults with MDD?
  - KQ 2a: Among publications that address adjunctive acupuncture for adults with MDD, how common and severe are adverse events?
- KQ 3: Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in decreasing relapse rates in adults with MDD?<sup>1</sup>

---

<sup>1</sup> A *relapse* occurs when a patient previously in remission experiences another episode of MDD less than a year after the previous episode; a *recurrence* occurs when a patient experiences a subsequent episode of major depression at least a year after the previous episode. Here, we use the term *relapse* to include both relapses and recurrences.

- KQ 4: Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in decreasing relapse rates in adults with MDD?

In addition, the review aimed to answer the following secondary questions:

- KQ 5: Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in improving health-related quality of life in adults with MDD?
- KQ 6: Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in improving health-related quality of life in adults with MDD?

## Methods

We conducted a systematic search of databases—PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, Web of Science, Embase, CENTRAL (Cochrane Central Register of Controlled Trials), clinicaltrials.gov, DARE (Database of Abstracts of Reviews of Effects), and PILOTS (Published International Literature on Traumatic Stress)—for English-language studies published through January 2015 to identify RCTs testing the effectiveness and safety of acupuncture either as monotherapy or as adjunctive therapy to treat adults with MDD. In addition, we screened bibliographies of prior systematic reviews and included studies.

Two independent reviewers used pre-established eligibility criteria to screen identified studies, abstract study-level information, and assess the quality of included studies. Outcomes of interest included depressive symptoms, response to treatment, remission, relapse, health-related quality of life, and adverse events. Study details were documented in detailed evidence tables and summarized in a narrative synthesis. The quality of evidence was assessed using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach.

## Results

We identified 18 RCTs that examined acupuncture in the treatment of MDD. Eleven of these studies focused on acupuncture as a monotherapy, and seven examined its use as an adjunctive therapy to antidepressants or treatment as usual. Assessment of the literature is complicated by a variety of factors, including variation in comparators (e.g., sham acupuncture with nonpenetrating needles, acupuncture at nonacupoints, waitlist). We found that the methodological quality of the studies was generally poor, with limited blinding, high attrition, and limited use of intention-to-treat analysis. Study samples were small and ranged from 20 to 160 participants.



## *Key Question 1*

We identified 11 RCTs assessing treatment effects of acupuncture as monotherapy on depressive symptoms in patients diagnosed with MDD. Studies used a variety of acupuncture schedules. Eight studies compared acupuncture at acupoints specifically targeting depression with nonspecific acupuncture.

There was low quality of evidence that acupuncture is superior to waitlist in reducing depression scale scores, but the size of the treatment effect could not be determined and only two RCTs contributed to the finding.

There is very low quality of evidence that acupuncture is not statistically significantly different from sham acupuncture using nonpenetrating needles in reducing depression scale scores, but this result is based on one small RCT only and the true effect may be substantially different.

Eight RCTs assessed the effect of depression-specific acupuncture on depression scale scores compared with acupuncture targeting acupoints not specific to depression. The direction of effects varied, sometimes favoring depression-specific acupuncture, sometimes the nonspecific acupuncture, and some studies showed no statistically significant difference between study arms. The quality of the evidence is very low, and it is not possible to determine with confidence whether depression-specific acupuncture is superior to control acupuncture targeting nonspecific points.

There was low quality evidence that acupuncture is not statistically significantly different from massage in reducing depression scale scores, but the statistical power to detect differences between study arms was unclear and the result is based on one fair and one poor quality RCT.

Four fair and poor quality RCTs compared acupuncture and antidepressants. Differences in depression scale scores varied somewhat across arms. Two studies reported no statistically significant differences between study arms, but none of the RCTs reported a statistical power calculation to determine whether the studies were sufficiently powered to detect differences; hence, it is difficult to draw conclusions from the very low quality of evidence.

Results for an alternative measure of depression improvement, the number of patients showing a treatment response (usually defined as a 50-percent reduction in depression scale scores), showed inconclusive findings. Effect estimates for the rate of treatment responders comparing acupuncture with waitlist, sham acupuncture using nonpenetrating needles or using nonspecific acupoints, massage, or antidepressants were hampered by inconsistent results across individual studies, or results were based on only one or two RCTs reporting on the outcome. Hence, all results were graded as very low quality evidence.

Four studies reported on the outcome remission. Acupuncture arms reported a higher remission rate than waitlist in two RCTs, but the one study that tested the statistical significance of the results did not find results different from chance. Acupuncture versus sham acupuncture with nonpenetrating needles reported a higher, but not statistically significantly different,

remission rate in the sham acupuncture group, but the result is based on a single RCT. Remission rates varied comparing depression-specific acupuncture and control acupuncture using nonspecific acupoints and sometimes favored the targeted acupuncture, sometimes the nonspecific arm across four RCTs. Two RCTs comparing acupuncture and massage showed inconsistent results. All evidence statements for the outcome remission were determined to be very low quality of evidence due to the methodological quality, inconsistency in or lack of replication, or the imprecision and lack of statistical power to detect a difference between alternative interventions.

### *Key Question 1a*

Six RCTs of monotherapy acupuncture reported on adverse events, five of which systematically assessed adverse events by using a structured instrument or by systematically asking participants about side effects. Three studies compared the rate of adverse events between acupuncture and control groups.

Among the monotherapy studies that reported on adverse events, there were few events and most were mild, such as pain, bruises, or discomfort at acupuncture sites. Severe adverse events either occurred in the comparator group or were deemed unrelated to the acupuncture intervention. Two RCTs reported no statistically significant differences between arms in the rate of adverse events; one study reported that milder side effects were more common among those receiving acupuncture than massage.

### *Key Question 2*

Seven RCTs assessed acupuncture as an adjunctive therapy. Five studies compared acupuncture adjunctive to antidepressants with antidepressants alone. One study compared acupuncture plus usual care with sham acupuncture at nonacupoints plus usual care, and one study compared acupuncture plus usual care with sham acupuncture using nonpenetrating needles plus usual care.

The combination of acupuncture and antidepressants tended to show lower depression scale scores or reported a greater reduction in scores than antidepressant arms alone, but the size of the effect varied and the difference was only statistically significant in three of five studies.

The RCT comparing acupuncture with minimal pricking at nonacupoints showed no difference between arms; both arms also received treatment as usual. The RCT comparing acupuncture with sham acupuncture using nonpenetrating needles also showed no statistically significant differences; both arms received treatment as usual. One RCT reported a comparison with nonspecific acupoints and found no statistically significant differences. A comparison of acupuncture plus antidepressants with sham acupuncture using nonpenetrating needles plus antidepressants showed a statistically significant difference between arms in favor of true acupuncture, but the result is based on one, poor quality RCT and the quality of evidence is very low.

Three RCTs that compared acupuncture plus antidepressants with antidepressants alone reported the rate of treatment responders. All three favored the combination groups, but only one RCT reported a statistically significant difference. All three studies contributing to this result were of poor quality; hence, our confidence in the finding is limited. One RCT comparing acupuncture plus antidepressants with sham acupuncture using nonpenetrating needles plus antidepressants found a higher response rate in the true acupuncture group, but the difference was not statistically significant and the study was a poor quality RCT.

Effects on remission rates showed no differences between acupuncture plus antidepressants with antidepressants alone, acupuncture plus treatment as usual with sham acupuncture using nonpenetrating needles plus treatment as usual, or acupuncture plus antidepressants with sham acupuncture using nonpenetrating needles plus antidepressants. The rate of patients achieving remission was low and the quality of the evidence was very low for all findings because of the methodological quality and the inconsistency and imprecision of the effect estimates.

### *Key Question 2a*

Five studies reported on the occurrence of adverse events during the course of the study, but only two studies systematically assessed adverse events for adjunctive acupuncture with a structured instrument and compared the frequency of events between groups.

For participants who received acupuncture, most recorded adverse events were mild in nature, such as discomfort and mild bleeding or bruising at the needling site. Among participants in both acupuncture and sham acupuncture interventions, more-severe adverse events were occasionally reported, such as heart attack (cranial electroacupuncture plus body acupuncture plus fluoxetine group), but, in general, studies were too small to adequately assess rare adverse events. Both RCTs with systematic assessments compared acupuncture and antidepressants with antidepressants alone and found no significant differences between any of the groups in the rate of adverse events.

### *Key Question 3*

We identified no RCTs of acupuncture as monotherapy that examined depression relapse rates; the review is not able to answer this question.

### *Key Question 4*

We identified no RCTs of acupuncture as adjunctive therapy that examined depression relapse rates; the review is not able to answer this question.

### *Key Question 5*

There was only one, poor quality study that examined the effect of monotherapy acupuncture on health-related quality of life. The study did not find a statistically significant difference in

quality of life between the electroacupuncture group and the control group, which used nonspecific acupoints, but the finding is based on very low quality of evidence.

### *Key Question 6*

We identified no RCTs of acupuncture as adjunctive therapy that examined health-related quality of life; the review is not able to answer this question.

## **Conclusions**

This review systematically documents the available evidence for the effectiveness and safety of acupuncture in treating MDD. Evidence on the effectiveness and comparative effectiveness of acupuncture to treat depression for the outcomes depression improvement (measured as scale score differences) and the number of responders is very weak. Acupuncture may be superior to waitlist (low quality of evidence). The limited evidence suggests a higher rate of responders with adjunctive acupuncture plus antidepressants than with antidepressants alone, but the studies were of poor quality (low quality of evidence). Findings for effect estimates of acupuncture compared with other comparators are inconclusive. Few studies reported on patients achieving remission. The effect of acupuncture on relapse rates could not be determined. Too few studies assessed quality of life to estimate treatment effects. Reported adverse events were typically mild in nature, but the assessment lacked rigor and studies were not designed to detect rare events.

## Acknowledgments

---

We gratefully acknowledge the assistance of Jody Larkin, the research librarian who conducted the literature searches, as well as Reema Singh and Barbara Hennessey, who provided administrative support, technical support, and other assistance in conducting the literature review and preparing the technical report. We are grateful to Kristie Gore for her support and guidance throughout the project. Thank you also to our project officers and points of contact at the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, Mark Bates, Chris Crowe, Marina Khusid, Katherine McGraw, and Angela Steele, for their support of our work. In addition, we thank Susanne Hempel and David Sniezek for reviewing the report and for their helpful suggestions. Any errors of fact or interpretation in this report remain the responsibility of the authors.



## Abbreviations

---

BDI	Beck Depression Inventory
BRMS	Bech-Rafaelsen Melancholia Scale
CENTRAL	Cochrane Central Register of Controlled Trials
CGI	Clinical Global Impression
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
DARE	Database of Abstracts of Reviews of Effects
DoD	U.S. Department of Defense
DSM	<i>Diagnostic and Statistical Manual of Mental Disorders</i>
EA	electroacupuncture
EPDS	Edinburgh Postnatal Depression Scale
GAS	Global Assessment Scale
GDS-SF	Geriatric Depression Scale – Short Form
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
HRSD	Hamilton Rating Scale for Depression
Hz	hertz
ICD	International Classification of Diseases
ITT	intention-to-treat
KQ	key question
MDD	major depressive disorder
MMPI	Minnesota Multiphasic Personality Inventory
NCCAOM	National Certification Commission for Acupuncture and Oriental Medicine
PILOTS	Published International Literature on Traumatic Stress
RCT	randomized controlled trial
SCL	Symptom Checklist
SCID	Structured Clinical Interview for DSM Disorders
SDS	Self-Rating Depression Scale
SERS	Åsbergs’s Side Effects Rating Scale

SSRIs	selective serotonin reuptake inhibitors
TCM	Traditional Chinese Medicine
TESS	treatment-emergent signs and symptoms
VA	U.S. Department of Veterans Affairs



## Chapter One: Introduction

---

Major depressive disorder (MDD) is a prevalent condition associated with significant burden in terms of reduced quality of life, lower productivity, increased prevalence of other conditions, and increased health care costs. In the general population of the United States, epidemiological studies of MDD estimate lifetime prevalence between 13 and 16 percent and 12-month prevalence between 5 and 7 percent among adults (Hasin et al., 2005; Kessler, Berglund, et al., 2003). Depression screening suggests that military service members and veterans with a history of combat exposure have higher rates of MDD than the general population (Hoge et al., 2004; Schell and Marshall, 2008; Vaughan et al., 2011; Wells et al., 2010). The prevalence is also higher among women and those who are socioeconomically disadvantaged (e.g., lower education, lower income level) (Hasin et al., 2005; Kessler, Berglund, et al., 2003). Although the majority (80 percent) of individuals who develop MDD will experience remission within a year of onset of the major depressive episode (Coryell et al., 1994; Spijker et al., 2002), the probability of experiencing a recurrent episode is high, with approximately 80 percent of depressed individuals experiencing another episode in the future (Judd, 1997). MDD is associated with significant medical, social, and economic consequences, including increased risk of a variety of physical conditions, relationship problems, lost productivity, and increased health care costs (Donohue and Pincus, 2007; Kessler, 2012). Despite its prevalence and burden, MDD remains underdiagnosed and undertreated, particularly among military and veteran populations (Management of Major Depressive Disorder Working Group, 2009).

Several evidence-based treatments for MDD exist and are highlighted as front-line treatments in the U.S. Department of Veterans Affairs (VA) and U.S. Department of Defense (DoD) *Clinical Practice Guidelines for Management of Major Depressive Disorder* (Management of Major Depressive Disorder Working Group, 2009). However, these interventions vary in their effectiveness, safety, and acceptability to different patient populations, and many Americans who would benefit from treatment do not receive depression-related care (Tylee and Jones, 2005). This is true among military personnel and veterans, and the literature has documented a wide variety of barriers to depression treatment—for example, stigma associated with mental health treatment and lack of access to mental health providers (Ben-Zeev et al., 2012; Vogt, 2011; Zinzow et al., 2012).

Individuals with depression sometimes use complementary and alternative medicine therapies, including acupuncture (Kessler, Soukup, et al., 2001). Monotherapy acupuncture refers to its use instead of or as an alternative to conventional therapies, such as antidepressants and psychotherapy. Acupuncture may also be used adjunctively to conventional therapies as a complementary medicine. When used as adjunctive therapy, patients may obtain acupuncture separately from other treatments for depression with no communication between health care

providers, or acupuncture may be part of integrative health care when its use is planned and coordinated with conventional therapies.

Needle acupuncture generally involves inserting and manipulating thin solid needles into specific documented acupuncture points on the body in order to create a therapeutic impact on bodily functions, organs, and systems. Acupuncture is thought to provide a safe, simple, and inexpensive alternative or complement to traditional treatments for MDD. A 2010 Cochrane review and other recent reviews concluded that there was insufficient evidence to recommend the use of acupuncture in treating depression and that more high-quality trials are needed to determine the efficacy of acupuncture for MDD (Freeman et al., 2010; Nahas and Sheikh, 2011; Smith, Hay, and MacPherson, 2010). Frequent reassessments of the literature are warranted due to the rapidly emerging literature on the use of acupuncture for treating MDD.

The current *VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder* states that acupuncture should not be recommended for MDD because there is insufficient evidence of its efficacy (Management of Major Depressive Disorder Working Group, 2009). This review seeks to examine the current state of the evidence regarding the efficacy and effectiveness of acupuncture for MDD to inform a decision about whether the guideline should be modified.

## Key Questions

We conducted a systematic review to identify randomized controlled trials (RCTs) testing the efficacy and safety of acupuncture to treat individuals with MDD. Specifically, this systematic review aimed to answer the following primary key questions (KQs) and subquestions:

- KQ 1: Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in reducing depressive symptoms in adults with MDD?
  - KQ 1a: Among publications that address monotherapy acupuncture as a treatment for adults with MDD, how common and severe are adverse events?
- KQ 2: Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in reducing depressive symptoms in adults with MDD?
  - KQ 2a: Among publications that address adjunctive acupuncture for adults with MDD, how common and severe are adverse events?

- KQ 3: Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in decreasing relapse rates in adults with MDD?<sup>2</sup>
- KQ 4: Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in decreasing relapse rates in adults with MDD?

In addition, the review aimed to answer the following secondary questions:

- KQ 5: Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in improving health-related quality of life in adults with MDD?
- KQ 6: Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in improving health-related quality of life in adults with MDD?

---

<sup>2</sup> A *relapse* occurs when a patient previously in remission experiences another episode of MDD less than a year after the previous episode; a *recurrence* occurs when a patient experiences a subsequent episode of major depression at least a year after the previous episode. Here, we use the term *relapse* to include both relapses and recurrences.



## Chapter Two: Methods

---

### Search Strategy

We searched the databases PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, Web of Science, Embase, CENTRAL (Cochrane Central Register of Controlled Trials), DARE (Database of Abstracts of Reviews of Effects), and PILOTS (Published International Literature on Traumatic Stress) for studies published through January 2015. Studies are limited to those published in English because of resource constraints and concerns raised in the scientific literature regarding acupuncture trials published in other languages (Vickers et al., 1998). In addition to this search, we screened studies included in prior systematic reviews related to this topic. We searched Clinicaltrials.gov and contacted authors of all relevant, completed trials for which published data were not available to invite the submission of in-press publications.

Search strings were developed in conjunction with a reference librarian for RAND's Knowledge Services department and were informed by search results of existing reviews. The PubMed search string is described in Appendix A.

### Eligibility Criteria

The inclusion and exclusion criteria we applied to retrieved publications were developed using the framework of participants, interventions, comparators, outcomes, timing, settings, and study design, or PICOTSS.

- *Participants*: Studies were limited to adults, male and female, 18 years of age or older. Participants must be diagnosed with MDD at the time of study enrollment. To be eligible for inclusion, studies had to refer to a clinical diagnosis of MDD that was compatible with *Diagnostic and Statistical Manual of Mental Disorders* (DSM) V or International Classification of Diseases (ICD) diagnostic criteria. We included studies with a formerly depressed patient sample if the primary outcome was depression relapse or recurrence. Studies in patients with diagnoses of dysthymia, bipolar disorder, depressive disorder due to another medical condition, or schizophrenia, alone or in combination with depression, were excluded in accordance with DSM V criteria.
- *Interventions*: Studies that administered thin or fine solid needles into known acupuncture points, either as an adjunctive therapy or monotherapy, were included. Studies involving full-body acupuncture, auricular acupuncture, or other specific body sites, with or without electrostimulation, were included. Studies involving acupuncture via laser, heat, or light were excluded, unless needles were also used. Studies involving dry needling, trigger point, acupressure, or acupoint stimulation were excluded, as were studies not referring to traditional acupuncture, unless needles were also used. Throughout the remainder of the

report, we use *acupuncture* to refer to traditional acupuncture without electrostimulation, unless otherwise specified.

- *Comparators*: Studies that included sham acupuncture (i.e., nonpenetrating needles or acupuncture at nonacupoints), nonspecific acupuncture at acupoints expected to affect depression, treatment as usual or standard care, waitlist control, no treatment, or other active treatments were included.
- *Outcomes*: Studies that reported one or more of the following outcomes were included: MDD symptoms, depression relapse, health-related quality of life.
- *Timing*: Studies could involve any treatment duration and follow-up period.
- *Setting*: Studies were not limited by setting.
- *Study design*: Included studies were limited to parallel group, individually randomized or cluster-randomized controlled trials only.

## Inclusion Screening

Two independent reviewers screened titles and abstracts of retrieved citations following a pilot exercise to ensure similar interpretation of the inclusion and exclusion criteria. Citations judged as potentially eligible by at least one reviewer were obtained for independent, full-text screening. The full-text publications were screened by two independent reviewers using the specified inclusion criteria. Any disagreements between the reviewers were resolved through discussion within the review team. Publications reporting results that derived from the same sample of participants were counted as a single study. An electronic database was used to track and document the flow of citations throughout this process, including the reasons for exclusion of full-text publications.

## Data Extraction

Information from each of the included studies was abstracted by two independent reviewers using electronic data collection forms designed by the project lead, with input from the project team. Reviewers pilot-tested the data collection forms on a few well-reported studies, modified the forms, and performed a final pilot of the forms on a random selection of included studies to ensure agreement of interpretation. All discrepancies were resolved by PhD-level staff with input from both reviewers in a group setting.

Study-level data were abstracted for the following information:

- *Participants*: gender, age, baseline depression scores
- *Interventions*: type of needle acupuncture (whole body, microsystem acupuncture, acupoints used in intervention), dosage (intensity, frequency, duration), and co-intervention(s)
- *Comparators*: type of comparator

- *Outcomes*—depressive symptoms, response to treatment (at least 50-percent reduction in depressive symptoms), remission (Hamilton Rating Scale for Depression [HRSD] <8; Patient Health Questionnaire-9 <5; Beck Depression Inventory [BDI]<1),<sup>3</sup> relapse, health-related quality of life, adverse events—for each follow-up point of measurement: domain, method of measurement, metric of data expression (e.g., means, proportions)
- *Timing*: time-points of outcome assessment
- *Setting*: geographic region, type of health care setting
- *Study design*: purpose, inclusion and exclusion criteria characteristics, starting and ending sample size, items relevant to risk of bias and quality ratings.

When multiple publications existed for a single study sample, descriptions of participants were compared to ensure that data from the same study sample were included in the review only once.

## Risk of Bias

Project leaders assessed the risk of bias of included RCTs using the Cochrane Risk of Bias tool (Higgins et al., 2011). Specifically, the reviewers assessed risk of bias related to the following: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants (performance bias), blinding of outcome assessors (detection bias), completeness of reporting outcome data (attrition bias), and selective outcome reporting (reporting bias). Other biases related to the U.S. Preventive Services Task Force’s criteria for internal validity of included studies also were assessed, namely those related to: equal distribution amongst groups of potential confounders at baseline; crossovers or contamination between groups; equal, reliable, and valid outcome measurement; clear definitions of interventions; and intention-to-treat (ITT) analysis (U.S. Preventive Services Task Force, 2008). These criteria were used to rate the quality of evidence of individual included studies using the following guidelines (see Table 3.1) (Lewin Group and ECRI Institute, 2014; U.S. Preventive Services Task Force, 2008):

- *Good*: Comparable groups are initially assembled and maintained throughout the study with at least 80-percent follow-up; reliable, valid measurement is used and applied equally to all groups; interventions are clearly described; all important outcomes are considered; appropriate attention is given to confounders in analysis; ITT analysis is used.
- *Fair*: One or more of the following issues is found in the study: some, though not major, differences between groups exist at follow-up; measurement instruments are acceptable but not ideal, though are generally applied equally; some but not all important outcomes

---

<sup>3</sup> The formal definition of *remission* used by the *VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder* (Management of Major Depressive Disorder Working Group, 2009) includes the requirement that the depressive symptom scores be maintained for at least one month. Studies did not necessary include that in their assessment of remission.

are considered; some but not all potential confounders are accounted for in analyses. ITT analysis is used.

- *Poor*: One or more of the following “fatal flaws” is found in the study: initially assembled groups are not comparable or maintained throughout the study; unreliable or invalid measurements are used or applied unequally across groups; key confounders are given little to no attention in analyses; ITT analysis is not used.

## Data Synthesis

The primary aim of this systematic review is to provide a comprehensive overview of studies (RCTs) with a high level of evidence that specifically target acupuncture treatment in patients with MDD. For each of the key questions and subquestions, we summarized findings in a narrative synthesis. Improvement in depression symptoms was assessed as depression scale score differences between intervention and control groups, the number of participants showing a response to treatment (as defined by the authors), and the number of patients in remission. In our narrative description of the studies, we present either mean changes in depression scale score or the actual score at the end of the intervention, depending on what was available for the study; standard errors are presented in parentheses (or brackets within parentheses). The effectiveness and comparative effectiveness was summarized by comparator given the variety of control and active interventions to which acupuncture was compared. We differentiated by depression severity where possible.

## Quality of Evidence

The quality of evidence was assessed for major outcomes using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach, in which the body of evidence is assessed based on the following dimensions: study limitations (low, medium, or high), directness (direct or indirect), consistency (consistent, inconsistent, or unknown), precision (precise or imprecise), and reporting bias (Egger et al., 1997) (suspected or undetected) (Brozek et al., 2009; Canfield and Dahm, 2011; Guyatt et al., 2008). We downgraded our rating of the quality of evidence when results were based on studies with substantial limitations, were inconsistent across individual studies, were based on a single study, or had conclusions that were based on indirect evidence.

The strength of evidence was graded on a four-item scale:

- *High* indicates that the review authors are very confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has few or no deficiencies. As such, the reviewers believe the findings are stable: that is, further research is very unlikely to change confidence in the effect estimate.
- *Moderate* indicates that the review authors are moderately confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has some deficiencies. As such, the reviewers believe that the findings are likely to be stable,



but further research may change confidence in the effect estimate and may even change the estimate.

- *Low* indicates that the review authors have limited confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has major or numerous (or both) deficiencies. As such, the reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the effect estimate lies close to the true effect.
- *Very low* indicates that the review authors have very little confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has very major deficiencies. As such, the true effect is likely to be substantially different from the estimated effect; thus, any estimate of effect is very uncertain.

The data sources, basic study characteristics, and each strength-of-evidence dimensional rating are summarized in Table 4.1, which details our reasoning for arriving at the overall strength of evidence rating.

## Protocol Deviations

The study selection criteria described in the protocol for this systematic review included the use of validated depression scales with a cut-off indicative of at least mild depression to identify the study sample. An initial screen of the identified literature indicated substantial clinical diversity among studies that used a depression scale. Depression is a symptom relevant to a number of mental disorders, patient characteristics vary, and it is unclear whether and how treatment effects would translate to patients with MDD. Therefore, in order to provide more-targeted information to answer the review questions, we limited included studies to those that required a clinical diagnosis of MDD as an eligibility criteria rather than applying the depression scale cut-offs as described in the systematic review protocol.



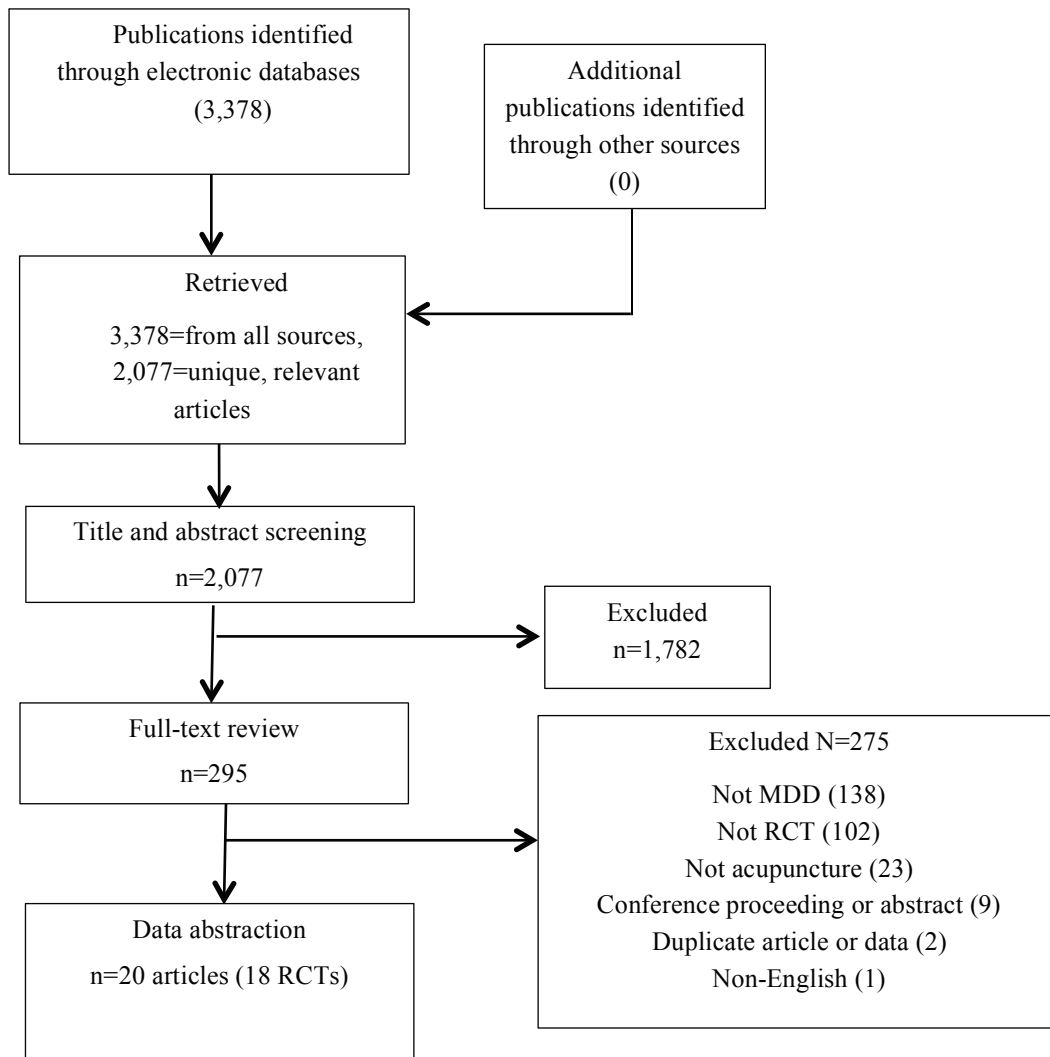
# Chapter Three: Results

---

## Results of Literature Searches

Our search of the electronic databases identified 3,378 publications (see Figure 3.1).

**Figure 3.1. Publication Review and Inclusion**



After duplicates across sources were removed, 2,077 publications were included for title and abstract screening, of which 1,782 were excluded for meeting one or more of the exclusion criteria. An additional 272 publications were excluded during full-text review (listed in Appendix B). A total of 18 studies met the inclusion criteria for our review.

## Description of Included Studies

Table 3.1 shows the number of studies contributing to answering each review question.

**Table 3.1. Evidence Base for Key Questions**

Key Question	Number of RCTs
1 Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in reducing depressive symptoms in adults with MDD?	11 RCTs
1a Among publications that address monotherapy acupuncture as a treatment for adults with MDD, how common and severe are adverse events?	6 RCTs
2 Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in reducing depressive symptoms in adults with MDD?	7 RCTs
2a Among publications that address adjunctive acupuncture for adults with MDD, how common and severe are adverse events?	5 RCTs
3 Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in decreasing relapse rates in adults with MDD?	0 RCTs
4 Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in decreasing relapse rates in adults with MDD?	0 RCTs
5 Is needle acupuncture, as a monotherapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in improving health-related quality of life in adults with MDD?	1 RCTs
6 Is needle acupuncture, as an adjunctive therapy, more effective than sham acupuncture, treatment as usual, waitlists, no treatment, or other active treatments in improving health-related quality of life in adults with MDD?	0 RCTs

### Key Question

For KQ 1, which examined the effect of needle acupuncture as monotherapy for depressive symptoms, we identified 11 RCTs that contributed information (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Chung et al., 2012; Huang et al., 2005; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Vazquez et al., 2011; Wang, Lu, et al., 2013). All 11 RCTs reported depressive symptoms using standardized scales as an outcome. Seven RCTs provided information on the response rate (number of patients with a 50-percent reduction in the depressive symptom score) to the intervention (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Huang et al., 2005; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010; Song and Liang, 2003). Five of the 11 identified studies provided

information on remission (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Chung et al., 2012; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010).

For KQ 1a, six studies provided information on the frequency and severity of adverse events that occurred with monotherapy acupuncture (Allen et al., 2006; Andreescu et al., 2011; Chung et al., 2012; Huang et al., 2005; Manber, Schnyer, Lyell, et al., 2010; Wang, Lee, et al., 2014).

For KQ 2 on the effect of needle acupuncture as adjunctive therapy for depressive symptoms, we identified seven RCTs, reported in nine publications, that included depressive symptoms using standardized scales as an outcome (Chen et al., 2014; Duan, Tu, Chen, et al., 2009; Duan, Tu, Jiao, and Qin, 2011; Qu et al., 2013; Roschke et al., 2000; Wang, Lu, et al., 2013; Yeung et al., 2011; Zhang, Ng, et al., 2012; Zhang, Ng, et al., 2013). Four studies provided information on clinical response (Duan, Tu, Chen, et al., 2009; Duan, Tu, Jiao, and Qin, 2011; Qu et al., 2013; Roschke et al., 2000; Zhang, Ng, et al., 2013), and two provided information on remission (Qu et al., 2013; Zhang, Ng, et al., 2013).

For KQ 2a, we found five studies that provided information on the frequency and severity of adverse events with adjunctive needle acupuncture used to treat MDD (Chen et al., 2014; Duan, Tu, Jiao, and Qin, 2011; Qu et al., 2013; Yeung et al., 2011; Zhang, Ng, et al., 2013).

We identified no studies that examined relapse after monotherapy needle acupuncture (KQ 3) or adjunctive needle acupuncture (KQ 4) for MDD.

We found two monotherapy acupuncture studies that provided information on health-related quality of life for MDD (KQ 5) (Andreescu et al., 2011; Chung et al., 2012).

For KQ 6, we found one adjunctive acupuncture study that provided information on health-related quality of life (Yeung et al., 2011).

## *Design*

All RCTs randomized individual participants rather than clusters of participants. The studies included in this review varied in size, ranging from 20 to 160 enrolled participants. Three studies included fewer than 50 participants; the majority (n=12) enrolled between 50 and 100 participants, and three included more than 100 participants. Six reported an *a priori* power calculation with a target sample size, two studies reported insufficient power for post-hoc analyses, and ten studies did not report information about power. Eight studies were two-arm RCTs, while ten were three-arm RCTs.

## *Setting*

The studies were performed predominately in China (n=11), with the rest conducted in the United States (n=5), Germany (n=1), and Mexico (n=1). Most of the studies took place at a single site (n=14); the number of sites ranged from one to four. Most of the studies took place in outpatient settings, including mental health clinics (n=15); other settings included inpatient settings, acupuncture clinics, and obstetric clinics.

## *Participants*

The average age of participants ranged from 30.5 to 49.1 years in the studies that reported patient characteristics. Four RCTs included only women. Of the remaining studies that included both men and women, the proportion of men in a study arm ranged from 5.3 to 42.9 percent.

## *Interventions and Providers*

Of the studies included in the review, six examined conventional acupuncture, 10 examined electroacupuncture, and two examined both. Studies were categorized as electroacupuncture if electrical stimulation was applied to any acupoints. Electroacupuncture was most often, but not exclusively, applied to the acupoints *Baihui* and *Yintang*. The frequency of acupuncture administration ranged from one to six times weekly. The duration of treatment ranged from three to 24 weeks.

The level of training and experience of the acupuncture providers varied. Three studies specified that the acupuncturists had a five-year undergraduate degree in Traditional Chinese Medicine (TCM), and one study specified that its only acupuncturist had a master's degree. Five studies stated that acupuncturists were certified and/or licensed; three studies specified certification was by the National Certification Commission for Acupuncture and Oriental Medicine (NCCAOM), and one study specified certification by the China Association of Acupuncture and Moxibustion. Two studies stated that acupuncture was provided by medical providers. Three studies specified that acupuncture was performed by experienced providers, but did not specify their training. When specified, the years of experience of the acupuncture providers ranged from less than two years to 15 years. Six studies did not report information on the training or experience of the acupuncture providers.

## *Comparators*

The included studies reported on a variety of comparators; eight studies each included two comparators. The most common comparator was antidepressants, reported in seven studies. Antidepressants combined with sham acupuncture were used as a comparator in four studies. Sham or nonspecific acupuncture alone was used as a comparator in 10 studies, while one study combined sham acupuncture with usual care. Less common comparators included massage (n=2) and waitlist (n=2).

## *Outcome Measures*

The length of follow-up ranged from immediately post-intervention to 10 weeks after treatment was completed. All studies reported depressive symptoms as an outcome. Eleven studies reported on clinical effectiveness or response, while six studies reported on remission. None of the studies assessed relapse. Three studies reported measures of health-related quality of life. Eleven studies reported adverse events or side effects.

## *Risk of Bias*

Tables 3.2 (monotherapy acupuncture) and 3.3 (adjunctive acupuncture) summarize the assessment of the risk of bias for the included publications using the Cochrane Risk of Bias tool for RCTs. One study obtained a “good” quality rating (Yeung et al., 2011); five studies were assigned a “fair” quality rating (Allen, Schnyer, and Hitt, 1998; Huang et al., 2005; Manber, Schnyer, Lyell, et al., 2010; Song, Halbreich, et al., 2009; Vazquez et al., 2011), and 12 studies were rated “poor” quality (Allen et al., 2006; Andreescu et al., 2011; Chen et al., 2014; Chung et al., 2012; Duan, Tu, Jiao, and Qin, 2011; Manber, Schnyer, Allen, et al., 2004; Qu et al., 2013; Roschke et al., 2000; Song, Zhou, et al., 2007; Wang, Lee, et al., 2014; Wang, Lu, et al., 2013; Zhang, Ng, et al., 2013). A common problem for these studies was a lack of ITT analysis and/or limited follow-up data (less than 80 percent of participants retained).

*Random sequence generation.* Nine studies had unclear selection bias because they did not report their method for randomizing study participants (Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Chen et al., 2014; Huang et al., 2005; Manber, Schnyer, Allen, et al., 2004; Roschke et al., 2000; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Wang, Lu, et al., 2013). The other studies reported adequate random sequence generation methods and were rated as low risk (Allen et al., 2006; Chung et al., 2012; Duan, Tu, Jiao, and Qin, 2011; Manber, Schnyer, Lyell, et al., 2010; Qu et al., 2013; Wang, Lee, et al., 2014; Wang, Lu, et al., 2013; Yeung et al., 2011; Zhang, Ng, et al., 2013).

*Allocation concealment.* Ten studies had unclear selection bias because they did not report their allocation concealment method (Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Chen et al., 2014; Huang et al., 2005; Manber, Schnyer, Allen, et al., 2004; Roschke et al., 2000; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Vazquez et al., 2011; Wang, Lu, et al., 2013). One study did not conceal allocation and was rated as high risk (Duan, Tu, Jiao, and Qin, 2011). The remaining studies did describe their method of allocation concealment and were rated as low risk (Allen et al., 2006; Chung et al., 2012; Manber, Schnyer, Lyell, et al., 2010; Qu et al., 2013; Sun et al., 2013; Wang, Lee, et al., 2014; Yeung et al., 2011; Zhang, Ng, et al., 2013).

*Blinding of participants and providers.* One study had unclear selection bias, because it did not report the approach for ensuring blinding of participants (Chung et al., 2012). Nine studies reported adequate blinding methods and were rated as low risk (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Roschke et al., 2000; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Vazquez et al., 2011; Yeung et al., 2011; Zhang, Ng, et al., 2013). Five studies did not report adequate blinding approaches and were rated as high risk (Duan, Tu, Jiao, and Qin, 2011; Huang et al., 2005; Qu et al., 2013; Wang, Lee, et al., 2014; Wang, Lu, et al., 2013). Three studies had adequate blinding for some study arms, but not others, and were rated as a mix of high risk/low risk or high risk/unclear (Chen et al., 2014; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010). While acupuncturists may

have been blinded to the study hypotheses, they were not blinded to the treatment being provided.

*Blinding of outcome assessors.* Two studies had unclear risk of detection bias because they did not report whether outcome assessors were blind to participation allocation to study arms (Chen et al., 2014; Huang et al., 2005;). Fifteen studies reported that the outcome assessors were blinded to intervention assignment or the study outcomes were self-reported instruments (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Chung et al., 2012; Duan, Tu, Jiao, and Chen, 2010; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010; Qu et al., 2013; Roschke et al., 2000; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Vazquez et al., 2011; Wang, Lee, et al., 2014; Yeung et al., 2011; Zhang, Ng, et al., 2012). One study was high risk because the outcome assessors were aware of study assignment (Wang, Lu, et al., 2013).

*Outcome data.* Six studies had low risk of attrition bias (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Huang et al., 2005; Manber, Schnyer, Lyell, et al., 2010; Wang, Lee, et al., 2014). Nine studies were at high risk for attrition bias (Chen et al., 2014; Chung et al., 2012; Duan, Tu, Jiao, and Chen, 2010; Manber, Schnyer, Allen, et al., 2004; Qu et al., 2013; Roschke et al., 2000; Song, Zhou, et al., 2007; Wang, Lu, et al., 2013; Zhang, Ng, et al., 2012). Three studies were unclear (Song, Halbreich, et al., 2009; Vazquez et al., 2011; Yeung et al., 2011).

*Selective outcome reporting.* Three studies had low risk of reporting bias because we were able to identify an *a priori* trial registration entry to verify the outcome measures employed in the study (Chung et al., 2012; Wang, Lee, et al., 2014; Zhang, Ng, et al., 2012). Thirteen studies had unclear risk of reporting bias because we were unable to identify such an entry (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Chen et al., 2014; Duan, Tu, Jiao, and Chen, 2010; Huang et al., 2005; Manber, Schnyer, Lyell, et al., 2010; Qu et al., 2013; Roschke et al., 2000; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Vazquez et al., 2011; Wang, Lu, et al., 2013; Yeung et al., 2011). Two studies were high risk because we identified a trial registration entry and the studies did not report on all identified outcomes (Andreescu et al., 2011; Manber, Schnyer, Allen, et al., 2004).

*Other.* Two studies did not provide an adequate description of the study to be able to determine whether other risks of biases existed (Chung et al., 2012; Roschke et al., 2000). Five studies were low risk for other biases because no other issues were identified (Huang et al., 2005; Song, Zhou, et al., 2007; Vazquez et al., 2011; Wang, Lu, et al., 2013; Yeung et al., 2011). The remainder of the studies suffered from one or more potential biases, which are detailed in Tables 3.2 and 3.3 (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Chen et al., 2014; Duan, Tu, Jiao, and Chen, 2010; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010; Qu et al., 2013; Song, Halbreich, et al., 2009; Wang, Lee, et al., 2014; Zhang, Ng, et al., 2012).



**Table 3.2. Study Quality/Risk of Bias for Each Monotherapy Acupuncture Randomized Controlled Trial**

<b>Study</b>	<b>Random Sequence Generation (selection bias)</b>	<b>Allocation Concealment (selection bias)</b>	<b>Blinding of Participants (performance bias)</b>	<b>Blinding of Outcome Assessors (detection bias)</b>	<b>Completeness of Reporting Outcome Data (attrition bias)</b>	<b>Selective Outcome Reporting (reporting bias)</b>	<b>Other Biases<sup>a</sup></b>	<b>USPSTF Quality Rating<sup>b</sup></b>
Allen, Schnyer, and Hitt, 1998	Unclear	Unclear	Low risk	Low risk	Low risk	Unclear	Difference between arms in baseline depression score	Fair
Allen et al., 2006	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	No ITT analysis	Poor
Andreescu et al., 2011	Unclear	Unclear	Low risk	Low risk	Low risk	High risk	No ITT analysis, patient cross-over	Poor
Chung et al., 2012	Low risk	Low risk	Unclear	Low risk	High risk	Low risk	Unclear	Poor
Huang et al., 2005	Unclear	Unclear	High risk	Unclear	Low risk	Unclear	None	Fair
Manber, Schnyer, Allen, et al., 2004	Unclear	Unclear	Low risk/high risk	Low risk	High risk	High risk	Modified ITT analysis required at least 1 post-randomization to be included	Poor
Manber, Schnyer, Lyell, et al., 2010	Low risk	Low risk	Low risk/high risk	Low risk	Low risk	Unclear	Baseline confounding	Fair
Song, Zhou, et al., 2007	Unclear	Unclear	Low risk	Low risk	High risk	Unclear	None	Poor
Song, Halbreich, et al., 2009	Unclear	Unclear	Low risk	Low risk	Unclear	Unclear	Funded by industry	Fair
Vazquez et al., 2011	Unclear	Unclear	Low risk	Low risk	Unclear	Unclear	None	Fair
Wang, Lu, et al., 2013	Low risk	Unclear	High risk	High risk	High risk	Unclear	None	Poor

<sup>a</sup> Other biases include balance of confounders, cross-overs/contamination, measurement, intervention definition, and ITT analysis.

<sup>b</sup> The USPSTF criteria (U.S. Preventive Services Task Force, 2008) for study quality involve assessment of various factors related to the internal validity of the study. "Good" is the highest ranking, which involves comparable groups with low attrition, with outcomes being reliably and validly measured and analyzed. "Fair" is the next highest rating and involves studies with one or a few potential concerns (e.g., some though not major differences between groups exist at follow-up), though intention-to-treat analysis was performed. "Poor" is the lowest ranking and involves studies with one or more "fatal flaws" (e.g., no intention-to-treat analysis).

**Table 3.3. Study Quality/Risk of Bias for Each Adjunctive Acupuncture Randomized Controlled Trial**

<b>Study</b>	<b>Random Sequence Generation (selection bias)</b>	<b>Allocation Concealment (selection bias)</b>	<b>Blinding of Participants (performance bias)</b>	<b>Blinding of Outcome Assessors (detection bias)</b>	<b>Completeness of Reporting Outcome Data (attrition bias)</b>	<b>Selective Outcome Reporting (reporting bias)</b>	<b>Other Biases<sup>a</sup></b>	<b>USPSTF Quality Rating<sup>b</sup></b>
Chen et al., 2014	Unclear	Unclear	High risk /Unclear	Unclear	High risk	Unclear	Modified ITT analysis	Poor
Duan, Tu, Jiao, and Qin, 2011; Duan, Tu, Jiao, and Chen, 2010	Low risk	High risk	High risk	Low risk	High risk	Unclear	No ITT analysis	Poor
Qu et al., 2013	Low risk	Low risk	High risk	Low risk	High risk	Unclear	No ITT analysis	Poor
Roschke et al., 2000	Unclear	Unclear	Low risk	Low risk	High risk	Unclear	Unclear	Poor
Wang, Lee, et al., 2014	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	No ITT analysis	Poor
Yeung et al., 2011	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	None	Good
Zhang, Ng, et al., 2012; Zhang, Ng, et al., 2013	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Those not compliant with fluoxetine had to withdraw from study	Poor

<sup>a</sup> Other biases include balance of confounders, cross-overs/contamination, measurement, intervention definition, and ITT analysis.

<sup>b</sup> The USPSTF criteria (U.S. Preventive Services Task Force, 2008) for study quality involve assessment of various factors related to the internal validity of the study. “Good” is the highest ranking, which involves comparable groups with low attrition, with outcomes being reliably and validly measured and analyzed. “Fair” is the next highest rating and involves studies with one or a few potential concerns (e.g., some though not major differences between groups exist at follow-up), though intention-to-treat analysis was performed. “Poor” is the lowest ranking and involves studies with one or more “fatal flaws” (e.g., no intention-to-treat analysis).

## KQ 1: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD?

We identified 11 studies on monotherapy acupuncture that included an assessment of depressive symptoms. Details of these studies are documented in the evidence table in Appendix C. Six RCTs were three-arm trials, and thus the same study will appear in multiple sections of this narrative synthesis.

### *Acupuncture Versus Waitlist Control*

Two studies compared acupuncture at acupoints thought to be associated with depressive symptoms to a waitlist control group (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998). Participants in both studies had mild to moderate depression, and in both studies, the intervention group received 12 acupuncture sessions over eight weeks, utilizing TCM-style acupuncture tailored to treat each patient's specific symptoms of depression.

The first study included 23 participants with MDD in the analytic sample of the acupuncture and waitlist arms (baseline modified HRSD score was 27.7 [standard error 6.8] and 26.9 [6.7] in the acupuncture and waitlist arms, respectively). Acupuncture was provided by trained and board-certified acupuncturists. The study found no significant differences in depressive symptom improvement between the acupuncture and waitlist control group among completers as measured by a modified version of the HRSD (-11.7 [7.3] and -6.1 [10.9] in the acupuncture and waitlist groups, respectively) (Allen, Schnyer, and Hitt, 1998), which was confirmed in an ITT analysis ( $p < 0.12$ ). At the end of the intervention, 50 percent of the acupuncture group and 27 percent of the waitlist group showed a clinical response (at least a 50-percent reduction on HRSD score; no statistical tests reported). By DSM-IV criteria (absence of both core symptoms of depression), 42 percent in the acupuncture group and 20 percent in the waitlist group were in remission at the end of the intervention.

In the second study, conducted by the same research group, a similar design was implemented but with a larger sample size ( $n=101$  in the acupuncture and waitlist groups; Allen et al., 2006). Acupuncture was provided by trained acupuncturists who were board certified by NCCAOM. In this sample of patients with mild to moderate MDD, baseline HRSD<sub>17</sub> score was 22.1 (4.8) and 22.8 (4.2) in the acupuncture and waitlist groups, respectively. There was statistically significantly greater improvement in depressive symptoms among patients who received acupuncture than among those on the waitlist control as measured by the BDI and HRSD<sub>17</sub> (change scores not reported,  $p < .001$ ) (Allen et al., 2006). However, there was no significant difference in the rate of response to treatment (22 percent versus 17 percent in the acupuncture and waitlist groups, respectively). There also was no significant difference in the

remission rate between groups as measured by a response plus HRSD<7 (16 percent versus 8 percent, respectively; p-value not reported) (Allen et al., 2006).

### *Acupuncture Versus Sham Acupuncture Using Nonpenetrating Needles*

One study compared cranial/body electroacupuncture, with points selected according to TCM principles, with a sham acupuncture treatment in which nonpenetrating needles were placed at the same acupoints used in the intervention group; acupuncture and sham acupuncture were performed by acupuncturists with three years of experience (Chung et al., 2012). The needles in both groups were electric-stimulated using the same modalities, and both groups were offered sessions twice weekly for four weeks. Thus, the sham acupuncture may not have been completely inert. Twenty pregnant women with mild MDD participated (baseline HRSD score was 14.4 [2.4] and 14.6 [2.3] in the electroacupuncture and sham acupuncture groups, respectively). The study authors reported no significant difference in reported depressive symptoms between treatment and sham acupuncture participants as measured by the BDI, the HRSD<sub>17</sub>, and the Edinburgh Postnatal Depression Scale (EPDS). Differences in results were nonsignificant post-treatment (HRSD 11.3 [4.8] versus 9.6 [3.4] in the electroacupuncture and sham acupuncture groups, respectively), as well as at a four-week follow-up (9.3 [4.7] and 8.6 [4.1] in the electroacupuncture and sham acupuncture groups, respectively). Treatment group was not statistically significantly associated with response rate at the end of treatment (12.5 percent versus 30.0 percent, p=0.5) or at follow-up (33.3 percent versus 60.0 percent, p=0.37). Treatment group was also not significantly associated with remission at the end of treatment (12.5 percent versus 16.7 percent, p=1.0) or at four-week follow-up (44.4 percent versus 47.4 percent, p=1.0) (Chung et al., 2012).

### *Depression-Specific Acupuncture Versus Acupuncture Targeting Acupoints Not Specific to Depression*

Eight studies compared acupuncture designed to reduce depression with placebo-like acupuncture targeting acupoints for symptoms not associated with depression (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998; Andreescu et al., 2011; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Vazquez et al., 2011). Four of the eight studies of individuals with MDD showed statistically significantly greater improvement in depressive symptoms in the depression-specific acupuncture group compared with the nonspecific acupuncture group (Allen, Schnyer, and Hitt, 1998; Manber, Schnyer, Lyell, et al., 2010; Song, Halbreich, et al., 2009; Vazquez et al., 2011), while the other four studies did not find a statistically significant effect (Allen et al., 2006; Andreescu et al., 2011; Manber, Schnyer, Allen, et al., 2004; Song, Zhou, et al., 2007).

Only one of the five studies that measured response rate reported a significantly higher response rate in the depression-specific acupuncture group than in the nonspecific acupuncture group (Manber, Schnyer, Lyell, et al., 2010). None of the four studies that measured remission

rate reported significantly higher response or remission rates in the depression-specific acupuncture group.

Two studies by Allen and colleagues assessed the efficacy of TCM acupuncture at acupoints associated with depressive symptoms relative to a control group that received acupuncture at acupoints not associated with treatment for depression (Allen et al., 2006; Allen, Schnyer, and Hitt, 1998). Patients in both acupuncture groups received 12 treatments over eight weeks. The first study included 23 women diagnosed with MDD in the mild to moderate range in the depression-specific acupuncture and nonspecific acupuncture groups (baseline HRSD scores 26.9 [6.7] versus 20.5 [4.5] in depression-specific acupuncture and nonspecific acupuncture groups, respectively,  $p < 0.05$ ). At the end of the intervention, women who received acupuncture specific to depression had a significantly greater reduction in depressive symptoms as measured by the HRSD (mean change =  $-11.7$ ) relative to women who received nonspecific acupuncture (mean change =  $-2.9$ ;  $p < 0.05$ ) (Allen, Schnyer, and Hitt, 1998). A similar trend was revealed when the BDI was used to assess depression symptoms; women who received depression-specific acupuncture had a greater reduction in BDI scores at the end of the intervention (mean change =  $-10.7$ ) relative to women who received nonspecific acupuncture (mean change =  $-3.4$ ;  $p < 0.05$ ) (Allen, Schnyer, and Hitt, 1998). The response rate in the two arms was 50 percent in the depression-specific acupuncture group and 27 percent in the nonspecific acupuncture group; statistical testing was not reported. By DSM-IV criteria (i.e., absence of both core symptoms of depression), 42 percent in the depression-specific acupuncture group and 9 percent in the nonspecific group were in remission at the end of the intervention; no statistical testing reported. In the second study, which employed a substantially larger sample size of 99 men and women with MDD in the depression-specific and nonspecific groups combined, a regression analysis revealed no significant difference in symptom improvement between the two acupuncture groups (as measured by the BDI and HRSD; change scores not reported) (Allen et al., 2006). Response rates were also not statistically different from one another in the group that received acupuncture targeted to depression symptoms (22 percent) relative to the control group that received acupuncture nonspecific to depression (39 percent) (Allen et al., 2006). There also was no significant difference in the remission rate between groups as measured by a response plus  $HRSD < 7$  (16 percent versus 33 percent, respectively; statistical test not reported) (Allen et al., 2006).

Like the Allen studies, Manber and colleagues also completed two studies on individually tailored acupuncture designed to treat depression according to the principles of TCM (Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010). Participants were pregnant women diagnosed with MDD who received 12 sessions of acupuncture over eight weeks. Symptom improvement in the depression-specific acupuncture group was compared with changes in an attention control group (reviewed in a section that follows), and also to a control group that received standardized acupuncture at points not associated with depression; sessions were the same duration and frequency as the depression-specific group. In the first study of 61

pregnant women with MDD, the training and experience of the providers were not described. Women who received depression-specific acupuncture had average symptom scores at the end of treatment that were not significantly different from women who received nonspecific acupuncture (9.6 [7.8] versus 12.6 [7.5], respectively (Manber, Schnyer, Allen, et al., 2004). Response rates (at least 50 percent reduction in HRSD and HRSD<14) were also not statistically different (68.8 percent versus 47.4 percent, respectively). Women who responded during the initial phase of the study continued with treatment until 10 weeks postpartum. Among the responders, there was not a significant difference in HRSD at 10 weeks postpartum (8.6 [6.5] versus 9.5 [7.4] in the specific and nonspecific acupuncture groups, respectively) or the BDI (6.9 [7.7] versus 10.8 [9.8], respectively). Among responders, a greater portion in the specific acupuncture group than the nonspecific acupuncture group was in remission (HRSD≤8) 10 weeks postpartum (85.7 versus 50.0, p=0.039). In the second study of 150 pregnant women with MDD, the intervention and comparator were provided by licensed acupuncturists who were board certified by NCCAOM. Depression symptom scores (as measured by the HRSD<sub>17</sub>) were significantly lower in the depression-specific acupuncture group than the nonspecific group (Cohen's d=0.39; 95% confidence interval [CI] 0.01, 0.77) (Manber, Schnyer, Lyell, et al., 2010). The study authors defined response as a 50-percent reduction in the HRSD<sub>17</sub>, a HRSD<sub>17</sub> score between 7 and 14, and failure to meet DSM-IV criteria for MDD. The response rate was significantly higher for the group receiving acupuncture specific to depression relative to the nonspecific group (number needed to treat [NNT] effect size=5.3; 95% CI, 2.8, 75.0). However, remission (defined as the absence of the core symptoms of MDD and HRSD<sub>17</sub>≤7) did not differ significantly between the two groups (34.8 percent and 27.5 percent for depression-specific and nonspecific acupuncture, respectively).

A study of 42 patients with MDD also used twelve 30-minute sessions of acupuncture based on TCM, but the treatment was standardized across patients and acupuncture points were stimulated at frequency 4 hertz (Hz) that was provided by a medical doctor who was an acupuncture specialist (Vazquez et al., 2011). Treatment-related changes in depressive symptoms were compared with a control group that received acupuncture at two points not associated with the treatment of depression. ITT analysis showed that patients who received standardized TCM electroacupuncture for depression had significantly greater reduction on the Carrol Rating Scale for Depression than patients who received nonspecific acupuncture (-10.4 versus -3.0, p=0.03). The study did not assess response or remission.

We identified three studies that compared cranial electroacupuncture *Yintang* and *Baihui* with acupuncture at points not on meridians or channels (Andreescu et al., 2011; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007). In a study of 57 participants with mild to moderate MDD, the active treatment was cranial electroacupuncture at *Baihui* and *Yintang*, which was compared with needling at nonchannel scalp points with sham electrostimulation. Both groups received treatments twice a week for six weeks from an acupuncturist with a master's degree in acupuncture and Chinese medicine and certified by NCCAOM who had been

practicing for five years. Baseline depression scores on the HRSD were 17.7 (3.9) in the active cranial electroacupuncture and 18.6 (2.9) in the control acupuncture group. The improvement in depression scores on the HRSD over the course of the intervention did not differ significantly between the two groups (−7.4 [6.2] and −7.9 [7.4] in the active electroacupuncture and control acupuncture groups, respectively). The response rate (≥50 percent reduction in HRSD score) also did not differ significantly between the two groups (40.0 percent and 44.4 percent in the active electroacupuncture and control acupuncture groups, respectively). The study did not assess remission.

Two additional studies, by a single research group, compared cranial electroacupuncture at *Yintang* and *Baihui* points with fluoxetine (described below in the section on medication controls) and with a group that received a combination of cranial acupuncture at points 1 cm from *Yintang* and *Baihui* points without electrical stimulation and a placebo drug (Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007). The training and experience of the providers were not described. In the first study, 90 patients with MDD received 45-minute treatments, five times per week for six weeks (Song, Zhou, et al., 2007). The baseline HRSD scores were 25.2 (3.5) in the electroacupuncture group and 25.4 (4.2) in the control acupuncture group. At the end of the intervention, there were no significant differences between the groups in depressive symptoms (12.0 [6.7] versus 12.9 [7.9] for electroacupuncture group and control acupuncture, respectively). The second study was very similar, but it included 95 patients with MDD (baseline HRSD score of 22.4 [2.9] and 22.8 [3.5] in the electroacupuncture and control acupuncture groups, respectively) and reduced the frequency of the treatments to three times a week for six weeks. In this study, the active cranial electroacupuncture group had significantly lower HRSD<sub>21</sub> scores on average (10.2) than the sham cranial acupuncture group (13.9;  $p < 0.05$ ) at the end of the intervention. The study did not assess response or remission.

### *Acupuncture Versus Attention Control*

In two studies, Manber and colleagues assessed the effect of acupuncture for depression among pregnant women diagnosed with MDD (Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010) as described above. Both study samples had an average HRSD baseline score indicating moderate depression. In both studies, the treatment group received 12 sessions of acupuncture tailored to the individual patient by an acupuncturist following the principles of TCM. The efficacy of acupuncture for depression was compared with acupuncture at points nonspecific to depression (reviewed above) and also to an attention control, reviewed here. The attention control group received a standardized Swedish massage of the same duration and frequency as the treatment group.

For the pilot study, the authors recruited 61 pregnant women with MDD (Manber, Schnyer, Allen, et al., 2004). Treatment response was defined as failure to meet full DSM-IV criteria for MDD, at least a 50-percent reduction in the patient's HRSD score, and an HRSD score no greater than 14. Although the acupuncture group (68.8 percent) had a better response rate to

treatment than the massage group (31.6 percent;  $p=0.03$ ), there was no significant difference between acupuncture and massage on the HRSD (10.3 [5.6] in massage group versus 9.2 [6.1] in acupuncture group) or BDI (10.0 [4.0] in massage group versus 9.2 [6.1] in acupuncture group) when scored continuously. Among those who responded to treatment initially, the remission rate ( $\text{HSRD} \leq 8$ ) 10 weeks postpartum was not significantly different in the acupuncture and massage groups (85.7 percent and 66.7 percent, respectively).

In the second larger trial, which included 150 pregnant women with MDD, there was no significant difference in HRSD scores from mixed-model analyses (Cohen's  $d=0.33$ ; 95% CI  $-0.10, 0.76$ ), response rate (34.8 percent versus 27.5 percent in electroacupuncture and control acupuncture groups, respectively), or remission rate (defined as the absence of core depressive symptoms and an HRSD score of 7 or less; 63 percent versus 50 percent) between the acupuncture and massage groups (Manber, Schnyer, Lyell, et al., 2010). The study authors reported a statistical power analysis indicating that the study was powered to detect a moderate effect size.

### *Acupuncture Versus Antidepressants*

Four studies compared electroacupuncture as monotherapy with antidepressant medications in adults with MDD (Huang et al., 2005; Luo, Jia and Li, 1985; Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007; Sun et al., 2013; Wang, Lu, et al., 2013). One study of 98 individuals with MDD compared six weeks of cranial electroacupuncture (six days per week) with six weeks of daily fluoxetine (20–40 mg) (Huang et al., 2005). The training and experience of the providers were not described. The baseline depression score was 23.5 (4.5) in the electroacupuncture group and 24.5 (5.2) in the antidepressant group. The two groups did not differ significantly postintervention on depressive symptoms as measured by the HRSD (9.7 [5.3] and 9.3 (2.9) in the electroacupuncture and antidepressant groups, respectively), BDI, Symptom Checklist (SCL)-90 depression subscale (1.5 [0.3] versus 1.5 [0.4]) or response rate (56 percent versus 64.6 percent in the acupuncture and antidepressant groups, respectively). The study did not assess remission.

In a series of two studies, Song and colleagues compared cranial electroacupuncture for depression with both control acupuncture plus placebo (reviewed earlier) and control acupuncture plus fluoxetine (Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007). The baseline HRSD in study one was 25.3 (3.5) and 25.1 (3.1) in electroacupuncture and control acupuncture groups, respectively; baseline HRSD scores in study two were 22.4 (2.9) and 22.2 (2.2) in the electroacupuncture and fluoxetine groups, respectively. After the six-week intervention, both studies reported that there were no significant differences between depressive symptoms in the cranial electroacupuncture group compared with the group that received fluoxetine (as measured by the HRSD) (Song, Halbreich, et al., 2009; Song, Zhou, et al., 2007). The postintervention depression score was 12.0 (6.7) and 12.4 (7.2) in the electroacupuncture



group and fluoxetine group in study one, and 10.2 (5.9) in the electroacupuncture group and 11.3 (6.6) in the fluoxetine group in study two. The studies did not assess response or remission.

Finally, in a sample of 60 patients with MDD, 24 weeks of cranial electroacupuncture (20 minutes, three times per week) provided by doctors with more than five years of acupuncture experience was compared with 24 weeks of paroxetine (20–60 mg/day) (Wang, Lu, et al., 2013). The baseline score on the Minnesota Multiphasic Personality Inventory (MMPI) depression subscale was 68.8 (8.2) in the acupuncture group and 66.4 (11.7) in the control group. At the end of the intervention, there was no statistically significant difference in depressive symptoms in the two groups (60.3 [11.2] and 54.8 [11.8] in the electroacupuncture and paroxetine groups, respectively). The authors also reported group means on the Self-Rating Depression Scale (SDS) but did not include a statistical test of the group differences. The study did not assess response or remission.

### **KQ 1a: Among Publications That Address Monotherapy Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events?**

Six of 11 RCTs assessing monotherapy acupuncture reported the occurrence of adverse events (Allen et al., 2006; Andreescu et al., 2011; Chung et al., 2012; Huang et al., 2005; Manber, Schnyer, Lyell, et al., 2010; Wang, Lu, et al., 2013). Five of these studies systematically assessed adverse events by using a structured instrument or by systematically asking participants about side effects (Allen et al., 2006; Andreescu et al., 2011; Chung et al., 2012; Huang et al., 2005; Manber et al., 2010).

Three studies formally compared adverse events between acupuncture and control groups: one study compared individually tailored acupuncture for depressive symptoms with two groups, (1) acupuncture at points nonspecific to depression and (2) massage (Manber, Schnyer, Lyell, et al., 2010); one study compared individually tailored acupuncture for depressive symptoms with acupuncture at acupoints not specific to depression (Allen et al., 2006); one study compared cranial electroacupuncture with sham electroacupuncture at nonacupoints on the scalp (Andreescu et al., 2011). Two studies found no significant differences in the occurrence of adverse events (Allen et al., 2006; Andreescu et al., 2011). The other study reported no differences in serious adverse events between its three arms (individually tailored acupuncture specific to depression, acupuncture at points nonspecific for depression, and prenatal massage); however, there were significantly more side effects in both the specific and nonspecific acupuncture groups than in the massage control group ( $p < 0.01$ ) (Manber, Schnyer, Lyell, et al., 2010).

Among the monotherapy studies that reported adverse events, there were few events and most were mild. Adverse events around the needling site included pain, bruises, and discomfort (Chung et al., 2012), as well as distending pain during needle stimulation (Huang et al., 2005).

One study that focused on pregnant women reported a small number of severe adverse events that were deemed unrelated to treatment, including premature delivery, neonatal demise, and pregnancy loss (Manber, Schnyer, Lyell, et al., 2010). One study reported two suicides, but those occurred in the nonspecific acupuncture control group (Allen et al., 2006).

## KQ 2: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD?

Seven studies examined acupuncture as an adjunctive treatment. Note that some studies had more than two study arms and appear in multiple categories below.

### *Acupuncture Plus Antidepressant Versus Antidepressants Alone*

Five studies compared acupuncture plus antidepressants with antidepressants alone. Four studies contained an arm that provided acupuncture using manual stimulation (Chen et al., 2014; Qu et al., 2013; Roschke et al., 2000; Wang, Lee, et al., 2014). Three studies contained an arm that used electroacupuncture (Chen et al., 2014; Duan, Tu, Jiao, and Qin, 2011; Duan, Tu, Jiao, and Chen, 2010; Qu et al., 2013); all three electrically stimulated *Baihui* and *Yintang*, and one study also stimulated *Fengchi* (Qu et al., 2013). The selection of body acupoints was typically based on TCM. Three studies compared response rates. Two studies compared remission rates.

The first study included 95 participants randomized to receive (1) acupuncture with only manual stimulation, plus antidepressant; (2) electroacupuncture plus antidepressant; or (3) antidepressant alone (Chen et al., 2014). Both acupuncture groups received acupuncture three times a week for six weeks, with the acupoints selected in accordance with the World Federation of Acupuncture-Moxibustion Societies; the training and experience of the acupuncture providers were not described. Both of the acupuncture arms and the antidepressant arm received 10 mg of Seroxat per day on days one and two and then 20 mg per day during the six-week intervention and during the four-week follow-up period. Baseline depression scores, measured by the depression dimension of the SCL-90, were significantly lower in the antidepressant group than the two acupuncture groups (Seroxat: 2.5 [0.7]; acupuncture: 3.5 [0.6]; electroacupuncture: 3.1 [0.6],  $p < 0.05$ ). Among those with at least one postintervention evaluation, there was significantly greater improvement over the course of the intervention in both acupuncture groups than the antidepressant alone group (SCL-90 at end of treatment; Seroxat: 2.2 [0.5]; acupuncture: 1.9 [0.7]; electroacupuncture: 2.1 [0.6],  $p < 0.05$ ). A month after the end of the intervention, there were no significant differences between the three groups. The study did not assess response or remission.

A second study randomized 160 participants to receive paroxetine along with (1) acupuncture with manual manipulation to achieve *di qi*, a sensation of numbness or tingling, using 10

acupoints commonly used in the treatment of depression; (2) cranial electroacupuncture; or (3) no acupuncture (Qu et al., 2013). Participants in the two acupuncture arms were treated three times a week for six weeks by acupuncturists with five years of undergraduate training in Chinese medicine and in practice for more than three years. All study participants received 20 to 40 mg of paroxetine per day. The baseline depression scores on the HRSD were 25.0 (5.2) for the electroacupuncture group, 25.1 (5.6) for the acupuncture group, and 23.3 (4.6) for the paroxetine group. Among those that completed at least one evaluation after treatment, the acupuncture groups had significantly greater improvement in depressive symptoms than the medication-only group at the end of treatment (electroacupuncture:  $-15.7$  [5.1], acupuncture group:  $-14.1$  [6.8], medication-only group:  $11.3$  [4.6]) and one month post-treatment. Qu et al. (2013) reported that more participants in the acupuncture arms had a therapeutic response (at least 50-percent reduction in HRSD) than those in the antidepressant alone group (69.6 percent, 69.8 percent, and 41.7 percent in the electroacupuncture, acupuncture with manual stimulation, and paroxetine groups, respectively,  $p=0.004$ ). The study also reported that the remission rate (HRSD score  $<8$  after treatment) was not significantly different between the three arms (28.6 percent, 22.6 percent, and 22.9 percent in the electroacupuncture, conventional acupuncture, and paroxetine groups, respectively) (Qu et al., 2013).

Forty-six participants in a third study were treated either with (1) four weeks of whole body acupuncture (three times a week in addition to 90–120 mg/day of mianserin) administered using a standard protocol by two clinicians who were experienced in traditional Chinese acupuncture or (2) mianserin alone (Roschke et al., 2000). There were not significant differences in improvement in depressive symptoms in the acupuncture plus mianserin group compared with the mianserin alone group on the Global Assessment Scale (GAS) or Bech-Rafaelsen Melancholia Scale (BRMS), although the comparison of scores on the GAS approached significance ( $p=0.052$ ). Actual changes in symptom scores were not reported. The authors defined response as at least a 25-point improvement in score on the GAS. Based on this definition, there was not a significant difference in response between the groups (18-percent response for acupuncture versus 4-percent response for mianserin). No study participants experienced a full remission.

A fourth study (Wang, Lee, et al., 2014) included 76 participants who received either (1) acupuncture five days a week for six weeks at a standardized set of points, with additional points selected based on TCM principles, plus selective serotonin reuptake inhibitors (SSRIs) or (2) SSRIs alone. Acupuncture was provided by an acupuncturist with 15 years of experience and certified by the China Association of Acupuncture and Moxibustion. Participants appeared moderately depressed on their average baseline HRSD score (acupuncture: 22.0 [0.6]; SSRI: 22.7 [0.3]). At the end of the six-week intervention, there was greater improvement in HRSD score in the acupuncture group (6.3 points [4.9]) than the SSRI only group (8.2 [0.4]). The average difference in improvement was  $-1.83$  (CI  $-2.07, -1.58$ ;  $p<0.05$ ) among those who completed the study. Response rates and remission rates were not reported.

A fifth study randomized 75 participants with mild to moderate depression to receive electroacupuncture plus antidepressants or antidepressants alone (Duan, Tu, Jiao, and Qin, 2011; Duan, Tu, Jiao, and Chen, 2010). The electroacupuncture group was treated five days per week for six weeks; *Baihui* and *Yintang* were electrically stimulated and conventional acupoints selected based on TCM principles. The training and experience of the providers were not described. All participants received 20 mg/day of fluoxetine for six weeks. Among those who completed the study, the electroacupuncture group showed greater improvement on depressive symptoms measured by the HRSD<sub>17</sub> than the antidepressant only control group (HRSD score decreased from 23.8 [4.0] to 10.1 [5.1] in the electroacupuncture group and from 25.1 [3.7] to 12.7 [5.5] in the fluoxetine only group,  $p < 0.05$ ). There was not, however, a significant difference between the groups in the percentage that experienced at least a 50-percent reduction in HRSD score (47.1 percent and 61.1 percent for fluoxetine and electroacupuncture groups, respectively). The study did not report remission rates.

#### ***Acupuncture Plus Usual Care Versus Sham Acupuncture Plus Usual Care***

One study ( $n=47$ ) compared the receipt of cranial electroacupuncture (points *Yintang*, *Baihui*, bilateral *Shenmen*, *Sishencong*, and *Anmian*) in addition to usual care (which included, but was not limited to, antidepressants for almost all participants and other medications for approximately half of the participants) with two sham acupuncture conditions: (1) sham acupuncture with nonpenetrating placebo needles at 1 inch away from the same cranial points plus usual care, and (2) minimal pricking at nonacupuncture points plus usual care (Yeung et al., 2011). Participants received electroacupuncture or one of the sham acuapunctures three times per week for three weeks. There were no significant differences in an ITT analysis between the groups in depressive symptoms as measured by the HRSD<sub>17</sub> at one week or four weeks after the intervention (HRSD at baseline, one-week post-treatment, and four weeks post-treatment for electroacupuncture (10.4 [3.9], 9.9 [4.5], 9.6 [5.1], minimal pricking (11.2 [3.9], 9.7 [2.6], 9.0 [3.8], and placebo needles (11.8 [3.9], 11.9 [5.3], 11.1 [5.3]). Response rates and remission rates were not reported.

#### ***Acupuncture Plus Antidepressants Versus Sham Acupuncture Using Nonpenetrating Needles Plus Antidepressants***

One study with 73 participants compared electroacupuncture plus fluoxetine with sham acupuncture using electrostimulation plus fluoxetine (Man et al., 2014; Zhang, Ng, et al., 2013). The study treated the intervention arm with cranial acupuncture at *Baihui* and *Yintang*, left *Sishencong* and *Toulinqi*, right *Sishencong* and *Toulinqi*, bilateral *Shuaigu*, bilateral *Taiyang*, and bilateral *Touwei* three times per week for three weeks, while the control group had nonpenetrating needles applied to the same acupoints (Zhang, Ng, et al., 2013). The providers were registered acupuncturists with five years of undergraduate training in Chinese health and more than three years of experience. Both arms received 10 to 40 mg/day of fluoxetine. Baseline

scores on the HRSD<sub>17</sub> were 23.9 (3.8) and 23.1 (3.6) in the electroacupuncture and sham acupuncture groups, respectively. The electroacupuncture group showed significantly greater improvement on the HRSD (−8.7, 95% CI −9.4, −7.9 for electroacupuncture; −6.3, 95% CI −6.9, −5.6 for sham acupuncture,  $p < 0.001$ ) and the SDS (−13.1, 95% CI −15.3, −10.8 for electroacupuncture; −8.4, 95% CI −10.4, −6.3 for sham acupuncture,  $p = 0.004$ ). There was not a significant difference in the proportion of participants between groups who experienced a response (19.4 percent for electroacupuncture versus 8.8 percent for sham acupuncture) or remission (HRSD < 8; 2.7 percent for electroacupuncture versus 2.9 percent for sham acupuncture).

### *Acupuncture Plus Antidepressants Versus Sham Acupuncture at Nonspecific Points Plus Antidepressants*

A second comparator arm in the Roschke et al. (2000) study, described above, compared antidepressants plus acupuncture with antidepressants plus sham acupuncture, which consisted of minimal pricking at nonspecific locations in the vicinity of the acupoints used in the intervention group three times a week for four weeks ( $n = 46$ ). Both groups also received 90–120 mg/day of mianserin (Roschke et al., 2000). The baseline HRSD score was comparable in the two groups (28 [5] versus 29 [5] in the acupuncture and sham acupuncture groups, respectively). This study found no significant difference between the two groups on two measures of depressive symptoms included in the study (GAS and BRMS). Actual changes, statistical tests, or  $p$ -values were not reported for depressive symptom scores (Roschke et al., 2000). The authors defined response as at least a 25-point improvement in score on the GAS. Based on this definition, there was not a significant difference in response between the groups (18-percent response for acupuncture versus 33-percent response for mianserin). No study participants experienced a full remission.

## **KQ 2a: Among Publications That Address Adjunctive Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events?**

Of the seven studies that examined adjunctive acupuncture, five reported the occurrence of adverse events during the course of the study (Chen et al., 2014; Duan, Tu, Jiao, and Chen, 2010; Duan, Tu, Jiao, and Qin, 2011; Qu et al., 2013, Roschke et al., 2000, Wang, Lee, et al., 2014; Yeung et al., 2011; Zhang, Ng, et al., 2012; Zhang, Ng, et al., 2013).

Two of the studies systematically assessed adverse events for adjunctive acupuncture with a structured instrument measuring side effects and compared the frequency of events between groups. One used treatment-emergent signs and symptoms (TESS) (Zhang, Ng, et al., 2013) and one used Åsberg's Side Effects Rating Scale (SERS) (Qu et al., 2013). Both studies compared cranial electroacupuncture plus antidepressants with antidepressants alone; one also compared

manual acupuncture plus antidepressants with antidepressants alone. Statistical comparisons detected no significant differences between any of the groups in adverse events (Qu et al., 2013; Zhang, Ng, et al., 2013).

For participants who received acupuncture, most of the recorded adverse events were mild in nature, such as discomfort or mild bleeding or bruising at the needling site (Yeung et al., 2011; Zhang, Ng, et al., 2012). Other commonly reported adverse side effects in acupuncture groups were headaches, dizziness, and nausea (Duan, Tu, Chen, et al., 2009; Qu et al., 2013; Yeung et al., 2011; Zhang, Ng, et al., 2012). Four studies mentioned sleep disturbances (Chen et al., 2014; Qu et al., 2013; Yeung et al., 2011; Zhang, Ng, et al., 2012), and two mentioned palpitations (Qu et al., 2013; Yeung et al., 2011). Two studies indicated that acupuncture participants withdrew because of treatment-related adverse events, including fainting due to needling (Qu et al., 2013; Zhang, Ng, et al., 2012). Among participants in both acupuncture and sham acupuncture interventions, more-severe adverse events were occasionally reported, such as heart attack (cranial electroacupuncture plus body acupuncture plus fluoxetine group; Duan, Tu, Jiao, and Chen, 2010; Duan, Tu, Jiao, and Qin, 2011) and hematoma (cranial electroacupuncture plus treatment as usual; Yeung et al., 2011). Studies were too small to adequately assess rare adverse events.

### **KQ 3: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD?**

We identified no studies that examined monotherapy acupuncture for MDD that reported on depression relapse. Of note, most studies followed patients only during the intervention period, which usually lasted just four to eight weeks.

### **KQ 4: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD?**

We identified no studies that examined acupuncture as an adjunctive therapy for MDD that included an assessment of relapse.

### **KQ 5: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD?**

One study (n=57) compared receiving cranial electroacupuncture twice a week for six weeks with receiving sham electroacupuncture (needling with sham electric current) at nonacupoints on the scalp. The results showed no significant differences in changes in quality of life between the cranial electroacupuncture and sham acupuncture groups, as measured by the SF-36 physical, mental, and pain components, as well as the Global Assessment of Functioning (Andreescu et al., 2011).

Of note, one study showed no differences between groups in improvement on the work, family, or social subscales of the Sheehan Disability Scale, which assesses quality of life impairments in a variety of domains (Chung et al., 2012). Participants received electroacupuncture at cranial and body acupoints twice per week for four weeks. This group was compared with a group that received sham acupuncture at the same points using nonpenetrating needles (n=20) (Chung et al., 2012).

### **KQ 6: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD?**

We did not identify any adjunctive studies reporting on quality of life; one study reported on disability. A study with 52 participants compared cranial electroacupuncture received three times per week for three weeks plus treatment as usual with sham acupuncture using placebo needles placed 1 inch from the acupoints plus treatment as usual (Yeung et al., 2011). This study found no significant differences between groups on the Sheehan Disability Scale for any of three domains (work, social, family) at the end of the intervention. The Yeung et al. (2011) study also compared cranial electroacupuncture plus treatment as usual with minimal acupuncture using superficial needling at nonacupuncture points. No significant differences were observed between groups on any of three domains of the Sheehan Disability Scale at the end of the intervention.





## Chapter Four: Discussion

---

### Summary of Findings

We identified 18 studies that examined the use of acupuncture in treating MDD. Eleven of these studies focused on acupuncture as a monotherapy, and seven examined its use as an adjunctive therapy to antidepressants or treatment as usual. The majority of studies focused on patients with mild to moderate depression. Assessment of the literature is complicated by a variety of factors, including variation in comparators used by studies. This variation produces a very small number of studies for each combination of a specific form of acupuncture (i.e., monotherapy, adjunctive) compared with a specific type of comparator (e.g., sham acupuncture using nonpenetrating needles, acupuncture at nonacupoints, waitlist). We found that the methodological quality of the studies was generally poor, with small sample size, limited blinding, high attrition, and limited use of ITT analysis. The presented information is based on a qualitative assessment of the literature. See Table 4.1 for a summary of the evidence.

#### *KQ 1: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD?*

We identified 11 RCTs assessing treatment effects of acupuncture as monotherapy on depressive symptoms in patients diagnosed with MDD. Studies used a variety of acupuncture schedules.

There was low quality of evidence that acupuncture is superior to waitlist in reducing depression scale scores, but the size of the treatment effect could not be determined and only two RCTs contributed to the finding.

There is very low quality of evidence that acupuncture is not statistically significantly different from sham acupuncture using nonpenetrating needles in reducing depression scale scores, but this result is based on one small RCT only and the true effect may be substantially different.

Eight RCTs compared the effect of acupuncture at acupoints specifically targeting depression on depression scale scores with acupuncture targeting acupoints not specific to depression. The direction of effects varied, sometimes favoring depression-specific acupuncture, sometimes the nonspecific acupuncture, and some studies showed no statistically significant difference between study arms. The quality of the evidence is very low, and it is not possible to determine with confidence whether depression-specific acupuncture is superior to control acupuncture targeting nonspecific points.

There was low quality of evidence that acupuncture is not statistically significantly different from massage in reducing depression scale score, but the statistical power to detect differences between study arms was unclear and the result is based on one fair and one poor quality RCT.

Four fair and poor quality RCTs compared acupuncture and antidepressants. Differences in depression scale scores varied somewhat across arms. Two studies reported no statistically significant differences between study arms, and two studies did not report statistical tests; however, none of the RCTs reported a statistical power calculation to determine whether the studies were sufficiently powered to detect differences. Hence, it is difficult to draw conclusions from the very low quality of evidence.

Results for an alternative measure of depression improvement, the number of patients showing a treatment response (usually defined as a 50-percent reduction in depression scale scores), showed inconclusive findings. Effect estimates for the rate of treatment responders comparing acupuncture with waitlist, sham acupuncture using nonpenetrating needles or using unspecific acupoints, massage, or antidepressants were hampered by inconsistent results across individual studies, or results were based on only one or two RCTs reporting on the outcome. Hence, all results were graded as very low quality evidence.

Four studies reported on the outcome remission. Acupuncture arms reported a higher remission rate than waitlist in two RCTs, but the one study testing the statistical significance of results did not find results different from chance. Acupuncture versus sham acupuncture using nonpenetrating needles reported a higher, but not statistically significantly different, rate in the sham acupuncture group, but the result is based on a single RCT. Remission rates varied comparing targeted acupuncture and acupuncture using nonspecific acupoints and sometimes favored the depression-specific acupuncture, sometimes the control arm across four RCTs. Two RCTs comparing acupuncture and massage showed inconsistent results. All evidence statements for the outcome remission were determined to be very low quality of evidence because of the methodological quality, inconsistency in or lack of replication, or the imprecision and lack of statistical power to detect a difference between alternative interventions.

***KQ 1a: Among Publications That Address Monotherapy Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events?***

Six RCTs of monotherapy acupuncture reported the occurrence of adverse events. Five of these studies systematically assessed adverse events by using a structured instrument or by systematically asking participants about side effects, but only three studies formally compared adverse events between acupuncture and control groups. Of the studies that conducted formal comparisons, two studies compared acupuncture tailored to treat depressive symptoms with acupuncture at points nonspecific to depression; one study compared acupuncture with massage. Both studies comparing depression-specific acupuncture with nonspecific acupuncture found no significant differences in the occurrence of adverse events. The study that compared depression-specific acupuncture with massage and reported significantly more side effects that did not result

in terminating treatment in the acupuncture group. Among the monotherapy studies that reported on adverse events, there were few events and most were mild, such as pain, bruises, or discomfort at acupuncture sites. Severe adverse events either occurred in the comparator group or were deemed not related to the acupuncture. However, studies were too small to detect rare adverse events. Overall, the evidence is low to very low.

*KQ 2: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Reducing Depressive Symptoms in Adults with MDD?*

Seven RCTs assessed acupuncture as an adjunctive therapy. Five studies compared acupuncture adjunctive to antidepressants with antidepressants alone. One study compared acupuncture plus usual care with sham acupuncture at nonacupoints plus usual care. Another study compared acupuncture plus usual care with sham acupuncture using nonpenetrating needles plus usual care.

The combination of acupuncture plus antidepressants tended to show lower depression scale scores or reported a greater reduction in scores than antidepressant arms alone, but the size of the effect varied and the difference was only statistically significantly different in three of five studies.

The RCT comparing acupuncture and minimal pricking at nonacupoints showed no difference between arms; both arms received treatment as usual. The RCT comparing acupuncture and sham acupuncture using nonpenetrating needles also showed no statistically significant differences; both arms received treatment as usual. One RCT reported a comparison with nonspecific acupoints and found no statistically significant differences. A comparison of acupuncture plus antidepressants with sham acupuncture using nonpenetrating needles plus antidepressants showed a statistically significant difference between arms in favor of true acupuncture, but the result is based on one, poor quality RCT and the quality of evidence is very low.

Three RCTs that compared acupuncture plus antidepressants with antidepressants alone reported the rate of treatment responders. All three favored the combination groups, but only one RCT reported a statistically significant difference. All three studies contributing to this result were of poor quality; hence, our confidence in the finding is limited. One RCT comparing acupuncture plus antidepressants with sham acupuncture using nonpenetrating needles plus antidepressants found a higher response rate in the true acupuncture group, but the difference was not statistically significant and the study was a poor quality RCT.

Effects on remission rates showed no differences between acupuncture plus antidepressants versus antidepressants alone, acupuncture plus treatment as usual versus sham acupuncture using nonpenetrating needles plus treatment as usual, or acupuncture plus antidepressants versus sham acupuncture using nonpenetrating needles plus antidepressants. The rate of patients achieving

remission was low, and the quality of the evidence was very low for all findings because of the methodological quality and the inconsistency in and imprecision of the effect estimates.

***KQ 2a: Among Publications That Address Adjunctive Acupuncture as a Treatment for Adults with MDD, How Common and Severe Are Adverse Events?***

Five studies reported on the occurrence of adverse events during the course of the study, but only two studies systematically assessed adverse events for adjunctive acupuncture with a structured instrument measuring side effects and compared the frequency of events between groups. Both studies compared acupuncture and antidepressants with antidepressants alone. Statistical comparisons detected no significant differences between any of the groups in adverse events. For participants who received acupuncture, most recorded adverse events were mild in nature, such as discomfort and mild bleeding or bruising at the needling site. Among participants in both acupuncture and sham acupuncture interventions, more-severe adverse events were occasionally reported, such as heart attack (cranial electroacupuncture plus body acupuncture plus fluoxetine group), but, in general, studies were too small to adequately assess rare adverse events. There is very low quality evidence on the frequency and severity of adverse events.

***KQ 3: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD?***

We identified no RCTs of acupuncture as monotherapy that examined depression relapse rates; the review is not able to answer this question.

***KQ 4: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Decreasing Relapse Rates in Adults with MDD?***

We identified no RCTs of acupuncture as adjunctive therapy that examined depression relapse rates; the review is not able to answer this question.

***KQ 5: Is Needle Acupuncture, as a Monotherapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD?***

There was only one, poor quality study that examined the effect of monotherapy acupuncture on health-related quality of life. The study did not find a statistically significant difference in quality of life between the electroacupuncture group and the control group that used nonspecific acupoints, but the finding is based on very low quality of evidence.

*KQ 6: Is Needle Acupuncture, as an Adjunctive Therapy, More Effective Than Sham Acupuncture, Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments in Improving Health-Related Quality of Life in Adults with MDD?*

We identified no RCTs of acupuncture as adjunctive therapy that examined health-related quality of life; the review is not able to answer this question.

**Table 4.1. Summary of Findings and Quality of Evidence**

Outcome, Intervention, Comparator	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
<b>KQ 1: Monotherapy acupuncture and depressive symptoms: Effect on depressive scale scores</b>							
Comparison: Acupuncture versus waitlist	2 RCTs (Allen, Schnyer, and Hitt, 1998; Allen et al., 2006); 143 enrolled, 119 completed	Acupuncture: -11.7 (7.3) Waitlist: -6.1 (10.9) (p<0.12)  Regression analysis showed greater improvement in acupuncture group (p<0.001)	1 fair and 1 poor quality RCT (-1)	Direction consistent	Direct	Imprecise (-1)	Low
Comparison: Acupuncture versus sham (nonpenetrating needles)	1 RCT (Chung et al., 2012); 20 enrolled, 14 completed	Electroacupuncture (EA): 11.3 (4.8) Sham: 9.6 (3.4) (p=0.21)	1 small poor quality RCT (-2)	No replication (-2)	Direct	Imprecise (-1)	Very low
Comparison: Depression-specific acupuncture versus nonspecific acupuncture (targeting acupoints not specific to depression)	8 RCTs (Allen, Schnyer, and Hitt, 1998; Allen et al., 2006; Andreescu et al., 2011; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010; Song, Zhou, et al., 2007; Song, Halbreich, et al., 2009; Vazquez et al., 2011); 704 enrolled, 604 completed	Acupuncture: -11.7 (7.3) Sham: -2.9 (7.9) (p<0.05)  No difference in improvement (p>0.2)  EA: -6.6 (5.9) Sham: -7.6 (6.6) (p=0.69)  Acupuncture: 9.6 (7.8) Sham: 12.6 (7.5) (n.s.)  Acupuncture showed more improvement than sham (Cohen's d 0.46, p<0.05)  EA: 12.0 (6.7) Sham EA: 12.9 (7.9)  EA: 10.2 (5.9) Sham: 13.9 (6.3)	Fair and poor quality RCTs (-1)	Very inconsistent (-2)	Direct	Varies (-1)	Very low

Outcome, Intervention, Comparator	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
		EA: 1.3 (0.8) Sham: 1.5 (0.8)					
Comparison: Depression-specific acupuncture versus massage	2 RCTs (Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010); 211 enrolled, 162 completed	Acupuncture: 9.6 (7.8) Massage: 10.3 (5.6) (n.s.)  Acupuncture not different from massage group (p=0.13)	1 fair and 1 poor quality RCT (-1)	Consistent	Direct	Imprecise, statistical power unclear (-1)	Low
Comparison: Acupuncture versus antidepressants	4 RCTs (Huang et al., 2005; Song, Zhou, et al., 2007; Song, Halbreich, et al., 2009; Wang, Lu, et al., 2013); 343 enrolled, 322 completed	EA: 9.7 (5.3) Fluoxetine: 9.3 (2.9)  EA + placebo: 25.3 (3.5) Fluoxetine + sham: 25.1 (3.1)  EA: 10.2 (5.9) Fluoxetine: 11.3 (6.6) (n.s.)  EA: 13.8 (6.2) Paroxetine: 11.4 (7.2) (n.s.)	2 fair, 2 poor quality RCTs (-1)	Inconsistent (-1)	Direct	Imprecise, none reported a power calculation (-2)	Very low
<b>KQ 1: Monotherapy acupuncture and depressive symptoms: Effect on response rate</b>							
Comparison: Acupuncture versus waitlist	2 RCTs (Allen, Schnyer, and Hitt, 1998; Allen et al., 2006); 143 enrolled, 119 completed	Acupuncture: 50% Waitlist: 27%  Acupuncture: 22% Waitlist: 17% (n.s.)	1 fair and 1 poor quality RCT (-1)	Direction consistent but not size of effect (-1)	Direct	Imprecise (-1)	Very low
Comparison: Acupuncture versus sham (nonpenetrating needles)	1 RCT (Chung et al., 2012); 20 enrolled, 14 completed	EA: 33% Sham: 60% (p=0.37)	1 small poor quality RCT (-2)	No replication (-2)	Direct	Imprecise (-1)	Very low

<b>Outcome, Intervention, Comparator</b>	<b>Study Design (number of RCTs and participants)</b>	<b>Findings (direction and magnitude of effect)</b>	<b>Study Limitations</b>	<b>Inconsistency</b>	<b>Indirectness</b>	<b>Imprecision</b>	<b>GRADE of Evidence for Outcome</b>
Comparison: Depression-specific acupuncture versus nonspecific acupuncture (targeting acupoints not specific to depression)	5 RCTs (Allen, Schnyer, and Hitt, 1998; Allen et al., 2006; Andreescu et al., 2011; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010); 457 enrolled, 376 completed	Acupuncture: 50% Sham: 27%  Acupuncture: 22% Sham: 39% (p<0.07)  EA: 40% Sham: 44% (p=0.77)  Acupuncture: 69% Sham: 47% (p<0.17)  Acupuncture: 63% Sham: 38% (p<0.05)	Fair and poor quality RCTs (-1)	Very inconsistent (-2)	Direct	Varied across studies	Very low
Comparison: Depression-specific acupuncture versus massage	2 RCTs (Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010); 211 enrolled, 162 completed	Acupuncture: 69% Massage: 32% (p=0.03)  Acupuncture: 63% Massage: 50% (p=0.20)	1 fair and 1 poor quality RCT (-1)	Inconsistent (-1)	Direct	Imprecise, statistical power unclear (-1)	Very low
Comparison: Acupuncture versus antidepressants	1 RCT (Huang et al., 2005); 98 participants	EA: 56% Fluoxetine: 65% (n.s.)	1 fair quality RCT (-1)	No replication (-2)	Direct	Imprecise (-1)	Very low
<b>KQ 1: Monotherapy acupuncture and depressive symptoms: Effect on remission rate</b>							
Comparison: Acupuncture versus waitlist	2 RCTs (Allen, Schnyer, and Hitt, 1998; Allen et al., 2006); 143 enrolled, 119 completed	Acupuncture: 42% Waitlist: 20%  Acupuncture: 16% Waitlist: 8% (n.s.)	1 fair and 1 poor quality RCT (-1)	Consistent	Direct	Imprecise, power unlikely (-1)	Very low
Comparison: Acupuncture versus sham (nonpenetrating needles)	1 RCT (Chung et al., 2012); 20 enrolled, 14 completed	EA: 44% Sham: 50% (p=1.00)	1 small poor quality RCT (-2)	No replication (-2)	Direct	Imprecise, power insufficient (-2)	Very low



<b>Outcome, Intervention, Comparator</b>	<b>Study Design (number of RCTs and participants)</b>	<b>Findings (direction and magnitude of effect)</b>	<b>Study Limitations</b>	<b>Inconsistency</b>	<b>Indirectness</b>	<b>Imprecision</b>	<b>GRADE of Evidence for Outcome</b>
Comparison: Depression-specific acupuncture versus nonspecific acupuncture (targeting acupoints not specific to depression)	4 RCTs (Allen, Schnyer, and Hitt, 1998; Allen et al., 2006; Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010); 400 enrolled, 326 completed	Acupuncture: 42% Sham: 9%  Acupuncture: 16% Sham: 33% (p<0.06)  Acupuncture: 86% Sham: 50%  Acupuncture: 35% Sham: 28% (p=0.47)	Fair and poor quality RCTs (-1)	Very inconsistent (-2)	Direct	Precision varied across RCTs, none reported power calculation for remission (-1)	Very low
Comparison: Acupuncture versus massage	2 RCTs (Manber, Schnyer, Allen, et al., 2004; Manber, Schnyer, Lyell, et al., 2010); 211 enrolled, 162 completed	Acupuncture: 86% Massage: 67%  Acupuncture: 35% massage: 31% (p=0.72)	1 fair and 1 poor quality RCT (-1)	Inconsistent (-1)	Direct	Imprecise, power unlikely (-2)	Very low
<b>KQ 1a: Monotherapy acupuncture adverse events: Serious adverse events</b>							
Comparison: Depression-specific acupuncture versus nonspecific acupuncture (targeting acupoints not specific to depression)	3 RCTs (Allen et al., 2006; Andreescu et al., 2011; Manber, Schnyer, Lyell, et al., 2010); 261 enrolled, 211 completed	1 RCT reported no serious adverse events. Study of pregnant women reported 10 adverse events that were deemed unrelated to treatment.  Depression-specific acupuncture: premature delivery of twins with one neonatal demise and the surviving twin receiving prolonged neonatal intensive care (n=1); congenital defects among neonate (n=1); preclampsia (n=2)  Nonspecific acupuncture: pregnancy loss (n=1); hospitalization with dehydration and low amniotic fluid (n=1);	1 fair, 2 poor quality RCTs (-1)	Reporting varied, consistency could not be assessed (-1)	Direct	Imprecise, not powered to detect rare events (-2)	Very low

Outcome, Intervention, Comparator	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
		<p>Massage: congenital defects among neonate (n=1); hospitalization for esophageal spasms (n=1); hospitalization for isolated atrial fibrillation (n=1); hospitalization for premature contractions (n=1)</p> <p>Third study reported that one person in nonspecific acupuncture arm committed suicide</p>					
Comparison: Acupuncture versus massage	1 RCT (Manber, Schnyer, Lyell, et al., 2010); 98 enrolled, 77 completed	<p>Premature delivery of twins with one neonatal demise and surviving twin receiving prolonged neonatal intensive care (n=1); congenital defects (n=1); preeclampsia (n=2) in acupuncture group (all events deemed unrelated to the intervention)</p> <p>Massage: congenital defects (n=1); hospitalization for esophageal spasms (n=1); hospitalization for atrial fibrillation (n=1); hospitalization for premature contractions (n=1)</p>	1 fair quality RCT (-1)	No replication (-2)	Direct	Imprecise, not powered to detect rare events (-2)	Very low
<b>KQ 1a: Monotherapy acupuncture: All adverse events</b>							
Comparison: Depression-specific acupuncture versus nonspecific acupuncture (targeting acupoints not specific to depression)	3 RCTs (Allen et al., 2006; Andreescu et al., 2011; Manber, Schnyer, Lyell, et al., 2010); 261 enrolled, 211 completed	<p>1 RCT reported no adverse events.</p> <p>1 RCT reported a comparable number of mostly mild adverse events in both arms (e.g., pain symptoms, somatic symptoms); more than 60% of participants experienced at least one adverse event. Five participants</p>	1 fair, 2 poor quality RCTs (-1)	Reporting varied, inconsistent (-2)	Direct	Imprecise (-1)	Very low

Outcome, Intervention, Comparator	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
		reported needle-related pain, with one person discontinuing treatment.  Third RCT reported mostly mild side effects, both related and unrelated to treatment. Treatment-related side effects included transient discomfort and bleeding at needling sites.					
Comparison: Acupuncture versus massage	1 RCT (Manber, Schnyer, Lyell, et al., 2010); 98 enrolled, 77 completed	Mostly mild side effects, both related and unrelated to treatment. Treatment-related side effects in acupuncture arm included transient discomfort and bleeding at needling sites. Treatment-related side effects in massage arm included temporary discomfort. Significantly fewer people in the massage arm experienced side effects than in the intervention arm.	1 fair quality RCT (-1)	No replication (-2)	Direct	Imprecise (-1)	Very low
<b>KQ 2: Adjunctive therapy acupuncture and depressive symptoms: Effect on depression scale scores</b>							
Comparison: Acupuncture plus antidepressants versus antidepressants alone	5 RCTs (Chen et al., 2014; Duan, Tu, Jiao, and Qin, 2011; Qu et al., 2013; Roschke et al., 2000; Wang, Lee, et al., 2014); 476 enrolled, 448 completed	Acupuncture + seroxat: 1.9 (0.6) EA + seroxat: 2.1 (0.6) Seroxat alone: 2.1 (0.5) (p>0.05)  EA + fluoxetine: 10.1 (5.1) Fluoxetine alone: 12.7 (5.5) (p<0.01)  Acupuncture + paroxetine: -14.8 (5.5) EA + paroxetine: -17.1 (6.1) Paroxetine alone: -13.1 (3.8) (p=0.013)  Acupuncture + mianserin versus	Poor quality RCTs (-2)	Inconsistent (-1)	Direct	Varied across RCTs	Very Low

<b>Outcome, Intervention, Comparator</b>	<b>Study Design (number of RCTs and participants)</b>	<b>Findings (direction and magnitude of effect)</b>	<b>Study Limitations</b>	<b>Inconsistency</b>	<b>Indirectness</b>	<b>Imprecision</b>	<b>GRADE of Evidence for Outcome</b>
		sham + mianserin versus mianserin alone (p=0.226)  Acupuncture: 6.3 (0.49) SSRI: 8.2 (0.4) (p<0.05)					
Comparison: Acupuncture plus TAU versus sham (minimal pricking at nonacupoints) plus TAU	1 RCT (Yeung et al., 2011); 52 enrolled, 47 completed	EA: 9.6 (5.1) Sham: 9.0 (3.8) (n.s.)	1 good quality RCT	No replication (-2)	Direct	Imprecise (-1)	Very low
Comparison: Acupuncture plus TAU versus sham (nonpenetrating needles at acupoints) plus TAU	1 RCT (Yeung et al., 2011); 52 enrolled, 47 completed	EA + TAU: 9.6 (5.1) Sham + TAU: 11.1 (5.3) (n.s.)	1 good quality RCT	No replication (-2)	Direct	Imprecise (-1)	Very low
Comparison: Depression-specific acupuncture plus antidepressants versus nonspecific acupuncture (nonspecific points) plus antidepressants	1 RCT (Roschke et al., 2000); 46 enrolled, 46 completed	Acupuncture + mianserin versus sham + mianserin: n.s.	1 poor quality RCT (-2)	No replication (-2)	Direct	Imprecise (-1)	Very low
Comparison: Acupuncture plus antidepressants versus sham (nonpenetrating needles at same acupoints) plus antidepressants	1 RCT (Zhang, Ng, et al., 2013); 73 enrolled, 63 completed	Acupuncture + fluoxetine: -8.7 (95% CI -9.4, -7.9) Sham: + fluoxetine -6.3 (95% CI -6.9, -5.6) (p<0.001)	1 poor quality RCT (-1)	No replication (-2)	Direct	Imprecise (-1)	Very low

Outcome, Intervention, Comparator	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
<b>KQ 2: Adjunctive acupuncture and depressive symptoms: Effect on response rate</b>							
Comparison: Acupuncture plus antidepressants versus antidepressants alone	3 RCTs (Duan, Tu, Jiao, and Chen, 2010; Qu et al., 2013; Roschke et al., 2000); 476 enrolled, 448 completed	EA + fluoxetine: 83% Fluoxetine alone: 74% (p=0.17)  Acupuncture + paroxetine: 70% EA + paroxetine: 70% Paroxetine alone: 42% (p=0.004)  Acupuncture + mianserin: 18% Sham + mianserin: 33% Mianserin alone: 4% (p=0.025)	Poor quality RCTs (-2)	Direction consistent	Direct	Varies across RCTs	Low
Comparison: Acupuncture plus antidepressants versus antidepressants plus sham (nonpenetrating needles at same acupoints)	1 RCT (Zhang, Ng, et al., 2013); 73 enrolled, 63 completed	EA + fluoxetine: 19% Sham + fluoxetine: 9% (n.s.)	1 poor quality RCT (-2)	No replication (-2)	Direct	Imprecise (-1)	Very low
<b>KQ 2: Adjunctive acupuncture and depressive symptoms: Effect on remission rate</b>							
Comparison: Acupuncture plus antidepressants versus antidepressants alone	2 RCTs (Qu, et al., 2013; Roschke et al., 2000); 206 enrolled, 189 completed	Acupuncture + paroxetine: 23% EA + paroxetine: 29% Paroxetine alone: 23% (p=0.723)  Acupuncture + mianserin: 0% Mianserin alone: 0%	Poor quality RCTs (-2)	Inconsistent (-1)	Direct	Imprecise, not powered for remission (-1)	Very low
Comparison: Acupuncture plus TAU versus sham (nonpenetrating needles) plus TAU	1 RCT (Zhang, Ng, et al., 2013); 73 enrolled, 63 completed	EA + TAU: 3% Sham + TAU: 3% (p=0.998)	1 good quality RCT	No replication (-2)	Direct	Imprecise, not powered for remission (-1)	Very low
Comparison: Acupuncture plus anti-depressants versus sham (nonpenetrating needles at same acupoints) plus antidepressants	1 RCT (Roschke et al., 2000); 52 enrolled, 47 completed	Acupuncture + mianserin: 0% Sham + mianserin: 0%	1 poor quality RCT (-2)	No replication (-2)	Direct	Precise	Very low

Outcome, Intervention, Comparator	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
<b>KQ 2a: Adjunctive acupuncture adverse events: All adverse events/side effects</b>							
Comparison: Acupuncture plus antidepressants versus antidepressants	2 RCT (Zhang, Ng, et al., 2013; Qu et al., 2013); 54 enrolled, 51 completed,	At least 5% of participants in each arm experienced adverse events. Common adverse events included dizziness, tiredness, nausea, headache, and discomfort during needling sensation	2 poor quality RCTs (-2)	Reporting varies, consistency unclear (-1)	Direct	Imprecise (-1)	Very low
<b>KQ 3: Monotherapy acupuncture and depression relapse</b>							
	0 RCTs	N/A	N/A	N/A	N/A	N/A	No evidence
<b>KQ 4: Adjunctive acupuncture and depression relapse</b>							
	0 RCTs	N/A	N/A	N/A	N/A	N/A	No evidence
<b>KQ 5: Monotherapy acupuncture effect on quality of life</b>							
Comparison: Acupuncture versus sham (needling at nonacupuncture points)	1 RCT (Andreescu et al., 2011); 57 enrolled, 46 completed	Physical Component EA: 0.5 (6.9) Sham: -1.7 (8.0) (p=0.32)  Mental Component EA: 6.2 (13.6) Sham: 14.1 (17.5) (p=0.09)  Bodily Pain Index EA: -1.0 (18.3) Sham: 6.8 (19.7) (p=0.17)	One poor quality RCT (-2)	No replication (-2)	Direct	Imprecise (-1)	Very low
<b>KQ 6: Adjunctive acupuncture effect on quality of life</b>							
	0 RCTs	N/A	N/A	N/A	N/A	N/A	No evidence
NOTE: n.s. = no significant effect; N/A = not applicable.							

## Other Reviews in This Area

The results of this review are comparable to the conclusions of most previous reviews on acupuncture for MDD. Other reviews have concluded that the evidence is generally weak, with a high risk of bias in many studies (Ernst, Lee, and Choi, 2011; Smith, Hay, and MacPherson, 2010). They have also found that there is little evidence of a consistent benefit from acupuncture compared with waitlist control or sham acupuncture (Ernst, Lee, and Choi, 2011; Leo and Ligot, 2007; Smith, Hay, and MacPherson, 2010; Zhang, Chen, et al., 2010). They also concluded that acupuncture may have a beneficial effect when combined with antidepressants (Chan et al., 2015; Smith, Hay, and MacPherson, 2010) and that most studies did not find a difference between acupuncture as monotherapy and antidepressants (Leo and Ligot, 2007; Smith, Hay, and MacPherson, 2010; Zhang, Chen, et al., 2010). Two other reviews were more favorable in their conclusions, stating that acupuncture could reduce the severity of depression (Wang, Qi, et al., 2008) and was effective for treating anxiety and depression in pregnant women (Sniezek and Siddiqui, 2013). The current review included a larger number of studies than the Wang, Qi, et al. (2008) review; we also did not include three of the studies from that review because the study was not focused on MDD (n=1), the report was not in English (n=1), or the intervention was not needle acupuncture (n=1). The review by Sniezek and Siddiqui (2013) focused on pregnant women and was not restricted to study samples with MDD.

## Strengths and Limitations

This study has a number of strengths, including a comprehensive search of electronic databases, the use of two independent reviewers to perform study selection and data abstraction, and the assessment of risk of bias and strength of evidence to develop the review's conclusions. Furthermore, we contacted investigators of recently completed registered trials to inquire about completed articles or reports that had not yet been published. In addition, this review systematically documents the available evidence on acupuncture for MDD, the condition that is the focus of the VA/DoD clinical guidelines (Management of Major Depressive Disorder Working Group, 2008), rather than depressive disorders more broadly, and this review assesses the quality of evidence by specific outcomes. However, there are also some limitations worth noting. We did not request study authors to provide data beyond what was contained in publications or in-press manuscripts. Most of the studies focused on a sample with a mix of mild to moderate depression; thus, the results of this review may not be generalizable to individuals with more-severe depression. Further, the study results were not stratified by severity of depression; thus, we were unable to ascertain whether the efficacy of acupuncture varied by depression severity. Many of the articles had fairly small samples and were of poor quality, largely due to lack of ITT analysis, poor follow-up, or baseline differences between study arms. Other studies provided so little detail on their design and implementation that it was impossible

to fully assess the potential risks of bias. Thus, poor quality of the underlying studies limits the ability to draw strong conclusions about the effect of acupuncture on depression. Furthermore, there was a great deal of heterogeneity across studies in the frequency and duration of the acupuncture interventions, as well the types of comparators used. Lastly, we did not perform meta-analyses, which would have provided more-precise estimates of effects for comparing acupuncture and antidepressants, both as monotherapy and adjunctive to antidepressants; instead, we relied on the results reported in the articles.

## Implications for Future Research and Practice

Our conclusions are mostly consistent with other reviews on the use of acupuncture to treat MDD. Acupuncture may be superior to waitlist. The limited evidence suggests a higher rate of responders with adjunctive acupuncture plus antidepressants than antidepressants alone, but the studies were of poor quality. Findings for effect estimates of acupuncture compared with other comparators are inconclusive. The effectiveness of acupuncture delivered as monotherapy was not significantly different from the effectiveness of antidepressants in the studies we reviewed. However, these studies were not adequately powered to demonstrate similarity across groups. There is also a lack of evidence that acupuncture at acupoints specific to the treatment of depression is more effective than nonspecific acupuncture or forms of sham acupuncture, including needling at nonacupuncture points or using nonpenetrating needles. Few studies reported on patients achieving remission. The effect of acupuncture on relapse rates could not be determined. Too few studies assessed quality of life to estimate treatment effects. Reported adverse events were typically mild in nature, but the assessment lacked rigor and studies were not designed to detect rare events. We conclude that the generally poor methodological quality of the body of evidence prevents any strong conclusions about needle acupuncture for MDD.

Future studies should improve on the weaknesses pervasive in the current body of work, including a lack of patient blinding to assigned conditions, suboptimal participant retention, and the lack of ITT analyses. Though patient blinding is critical because of the previously demonstrated impact of patient expectancies for acupuncture outcomes (Colagiuri and Smith, 2012), the use of sham acupuncture is a source of debate. Some have raised concerns that many forms of sham acupuncture may be active interventions (Lund and Lundeberg, 2006). Further research examining the effect of acupuncture on depression should include large samples that allow results to be stratified by disease severity, focus on better understanding whether there is a minimum frequency or duration of acupuncture for it to be effective, and include measures of health-related quality of life.



## Appendix A: PubMed Search Strategy

---

### **Search Term**

(depress\* OR depression[MeSH] OR “depressive disorder”[MeSH] OR “mood disorders”[MeSH] OR “mood disorder” OR “Mood disorders” OR “depressive disorder” OR “depressive disorders” OR (“mood” [Title/Abstract] AND “disturbance”[Title/Abstract]) OR “affective disorders” OR “affective disorder”)

AND

“Acupuncture” OR acupuncture therapy[MeSH] OR Acupuncture[MeSH] OR (needle[Title/Abstract] AND meridian[Title/Abstract]) OR “auricular acupuncture” OR “traditional Chinese Medicine” OR electroacupuncture OR electroacupuncture[MeSH] OR acupressure[MeSH] OR acupressure

**Limits: English; Not: Editorial or Comment; NOT other animals**

more “rat” and “rats” removed (and other animals)



## Appendix B: Excluded Full-Text Articles

---

### *Reason Excluded: Abstract Only*

Ma, X., Z. Guo, S. Wang, W. Zhangm, T. Guo, J. Chen, L. Sun, Y. Wang, X. Zhang, C. Zhang, and L. Sun, “Effects of Electroacupuncture (EA) Combined with Antidepressants on Depression: A Randomized Controlled Trial,” *Journal of Alternative & Complementary Medicine*, Vol. 20, No. 5, 2014, pp. A8–A8.

### *Reason Excluded: Does Not Report Depressive Symptom Data*

Wang, S., Y. Wang, L. Sun, Z. Guo, X. Yang, T. Ya, and C. Zhang, “The Study on Alleviating Side Effects of Medicine and Improving Quality of Life in Treatment of Mild or Moderate Depression by Combining Acupuncture and Paroxetine,” *Journal of Alternative Complementary Medicine*, Vol. 20, 2014, pp. A46–A47.

### *Reason Excluded: Duplicate Article*

Manber, R., R. Schnyer, A. Chambers, D. Lyell, A. Caughey, and E. Carlyle, “Acupuncture for Depression During Pregnancy,” *American Journal of Obstetrics and Gynecology*, Vol. 201, No. 6, Suppl. 1, 2009.

### *Reason Excluded: Letter*

Wiwantkit, V., “Filiform Needle Acupuncture for Poststroke Depression,” *Neural Regeneration Research*, Vol. 9, No. 12, 2014, p. 1248.

### *Reason Excluded: Not English Language*

Keding, A., “Acupuncture and Counseling for Depression: Demonstration of the Efficacy of Using SMS Text Messages on a Large Randomized Controlled Trial,” *Revista Internacional de Acupuntura*, Vol. 8, No. 151, 2014.

### *Reason Excluded: Secondary Analysis of Data Included in Review*

Hopton, A., H. MacPherson, A. Keding, and S. Morley, “Acupuncture, Counselling or Usual Care for Depression and Comorbid Pain: Secondary Analysis of a Randomised Controlled Trial,” *British Medical Journal Open*, Vol. 4, No. 5, 2014, p. e004964.

***Reason Excluded: Unable to Identify Effect of Acupuncture***

Fan, L., W. B. Fu, N. G. Xu, J. H. Liu, Z. P. Li, and A. H. Ou, "Impacts of Acupuncture and Moxibustion on Outcome Indices of Depression Patients' Subjective Reports," *World Journal of Acupuncture - Moxibustion*, Vol. 23, No. 2, 2013, pp. 22–28.

Zhang, W. J., X. B. Yang, and B. L. Zhong, "Combination of Acupuncture and Fluoxetine for Depression: A Randomized, Double-Blind, Sham-Controlled Trial," *Journal of Alternative and Complementary Medicine*, Vol. 15, No. 8, August 2009, pp. 837–844.

***Reason Excluded: Case Report***

Errington-Evans, N., "Acupuncture in Chronic Non-Responding Anxiety/Depression Patients: A Case Series," *Acupuncture in Medicine*, Vol. 27, No. 3, September 2009, pp. 133–134.

Grant, L., "Treating Young Adults with Acupuncture," *Journal of Chinese Medicine*, No. 73, 2003, pp. 5–8.

Hu, J., "Acupuncture Treatment of Melancholia," *Journal of Traditional Chinese Medicine*, Vol. 23, No. 1, March 2003, pp. 75–77.

Macpherson, H., L. Thorpe, K. Thomas, and D. Geddes, "Acupuncture for Depression: First Steps Toward a Clinical Evaluation," *Journal of Alternative and Complementary Medicine*, Vol. 10, No. 6, December 2004, pp. 1083–1091.

Tao, H., "Acupuncture Treatment of Depressive Syndrome," *Journal of Traditional Chinese Medicine*, Vol. 25, No. 2, June 2005, pp. 106–107.

Zhang, C., J. Li, and S. Wang, "Treatment of Melancholia in Germany by Acupuncture Method for Resuscitation," *Journal of Traditional Chinese Medicine*, Vol. 24, No. 1, March 2004, pp. 22–23.

***Reason Excluded: Background***

"Alternatives to Antidepressants During Pregnancy," *Harvard Mental Health Letter*, Vol. 27, No. 2, 2010, pp. 4–5.

Das, A., "Acupuncture Found of Major Importance in Depressive Syndromes," *American Journal of Acupuncture*, Vol. 8, No. 4, 1980, pp. 335–339.

Dhar, H. L., and T. Vasanti, "Endogenous Depression, Thyroid Function and Acupuncture," *Indian Journal of Physiology and Pharmacology*, Vol. 45, No. 1, January 2001, pp. 125–126.

Fialka-Moser, V., "Acupuncture Shown to Be Useful for Depression," *Focus on Alternative & Complementary Therapies*, Vol. 5, No. 4, 2000, pp. 262–263.

Halbreich, U. M., D. Zhou, C. Song, Y. Dwivedi, and G. Pandey, "Effects of Antidepressant Treatment with Electroacupuncture and Fluoxetine on Interleukins and Signal Transduction

Aspects,” *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, Vol. 29, Suppl. 1, 2004, S179–180.

Lewis, S., “Broken Heart Syndrome: Perspectives from East and West,” *Advances in Mind-Body Medicine*, Vol. 21, No. 2, 2005, pp. 3–5.

Reuben, C., “Amino Acids Enhance Acupuncture Results for Patients with Anxiety, Depression, and Insomnia,” *California Journal of Oriental Medicine (CJOM)*, Vol. 24, No. 1, 2013, pp. 14–20.

#### ***Reason Excluded: Not an RCT***

Blitzer, L. E., D. J. Atchison-Nevel, and M. C. Kenny, “Using Acupuncture to Treat Major Depressive Disorder: A Pilot Investigation,” *Clinical Acupuncture & Oriental Medicine*, Vol. 4, No. 4, 2003, pp. 144–147.

Gallagher, S. M., J. J. Allen, S. K. Hitt, R. N. Schnyer, and R. Manber, “Six-Month Depression Relapse Rates Among Women Treated with Acupuncture,” *Complementary Therapies in Medicine*, Vol. 9, No. 4, December 2001, pp. 216–218.

Hull, A., M. Reinhard, K. McCarron, N. Allen, M.C. Jecmen, J. Akhter, A. Duncan, and K. Soltes, “Acupuncture and Meditation for Military Veterans: First Steps of Quality Management and Future Program Development,” *Global Advances in Health and Medicine*, Vol. 3, No. 4, 2014, pp. 27–31.

Liu, Y. H., Z. G. Duan, S. Zeng, S. Wan, Y. Q. Cao, and T. Liu, “Impacts of Acupuncture on Brainstem Evoked Potentials in Patients with Primary Depression,” *World Journal of Acupuncture - Moxibustion*, Vol. 23, No. 3, 2013, pp. 39–45.

Mischoulon, D., C. D. Brill, V. E. Ameral, M. Fava, and A. S. Yeung, “A Pilot Study of Acupuncture Monotherapy in Patients with Major Depressive Disorder,” *Journal of Affective Disorders*, Vol. 141, No. 2–3, December 10, 2012, pp. 469–473.

Pohl, A., and C. Nordin, “Clinical and Biochemical Observations During Treatment of Depression with Electroacupuncture: A Pilot Study,” *Human Psychopharmacology*, Vol. 17, No. 7, October 2002, pp. 345–348.

Shi, X., G. Litscher, H. Wang, L. Wang, Z. Zhao, D. Litscher, J. Tao, I. Gaischek, and Z. Sheng, “Continuous Auricular Electroacupuncture Can Significantly Improve Heart Rate Variability and Clinical Scores in Patients with Depression: First Results from a Transcontinental Study,” *Evidence-Based Complementary and Alternative Medicine*, Vol. 2013, 2013, p. 894096.

- Tufan, Z. K., H. Arslan, F. Yildiz, C. Bulut, H. Irmak, S. Kinikli, and A. P. Demiroz, "Acupuncture for Depression and Myalgia in Patients with Hepatitis: An Observational Study," *Acupuncture in Medicine*, Vol. 28, No. 3, September 2010, pp. 136–139.
- Wang, H., "Acupuncture Treatment of Depressive Syndromes After Cerebral Vascular Accidents," *Journal of Traditional Chinese Medicine*, Vol. 22, No. 4, December 2002, pp. 274–275.
- Yeung, A. S., V. E. Ameral, S. E. Chuzi, M. Fava, and D. Mischoulon, "A Pilot Study of Acupuncture Augmentation Therapy in Antidepressant Partial and Non-Responders with Major Depressive Disorder," *Journal of Affective Disorders*, Vol. 130, No. 1–2, April 2011, pp. 285–289.
- Youn, J. I., K. K. Sung, B. K. Song, M. Kim, and S. Lee, "Effects of Electro-Acupuncture Therapy on Post-Stroke Depression in Patients with Different Degrees of Motor Function Impairments: A Pilot Study," *Journal of Physical Therapy Science*, Vol. 25, No. 6, June 2013, pp. 725–728.
- Reason Excluded: Conference Proceeding***
- "Major Depressive Disorder," *Acupuncture in Medicine*, Vol. 30, No. 2, 2012, pp. 145–146.
- "Research Reveals Depression Options," *Nursing Standard*, Vol. 28, No. 5, 2013, p. 10.
- Guo, T., Y. Wang, L. Sun, W. Zhang, and W. Ma, "Acupuncture Combined with an Antidepressant Has a Better Effect on Major Depression: A Multi-Center, Randomized, Controlled Clinical Trial [Abstract]," *BMC Complementary and Alternative Medicine [Abstracts of the International Research Congress on Integrative Medicine and Health; 2012 May 15–18; Portland, OR, United States]*, Vol. 12, 2012.
- Halbreich, U. "Systematic Reviews of Clinical Trials of Acupuncture as Treatment for Depression: How Systematic and Accurate Are They?" *CNS Spectrums*, Vol. 13, No. 4, 2008, 293–294, 299–300.
- Lee, H., and R. Manber, "Can Acupuncture Be a Treatment Option for Depression During Pregnancy?" *Focus on Alternative & Complementary Therapies*, Vol. 10, No. 3, 2005, pp. 210–211.
- Macpherson, H., K. Thomas, B. Armstrong, B. De Valois, C. Relton, B. Mullinger, A. White, A. Flower, and V. Scheid, "Developing Research Strategies in Complementary and Alternative Medicine," *Complementary Therapies in Medicine*, Vol. 16, No. 6, 2008, pp. 359–362.
- White, A., P. Bajaj, M. Meinen, and A. Sheikh, "Depression," *Acupuncture in Medicine*, Vol. 31, No. 3, 2013, pp. 338–339.

***Reason Excluded: Does Not Report Data for Acupuncture for MDD***

- “Applying the Evidence London 26 September 2000 NHS Alliance and Exeter University’s Department of Complementary Medicine,” *Complementary Therapies in Medicine*, Vol. 8, No. 4, 2000, pp. 286–287.
- Anju, S., and C. Collette Breuner, “Complementary, Holistic, and Integrative Medicine: Depression, Sleep Disorders, and Substance Abuse,” *Pediatrics*, Vol. 130, 2012, pp. 422–425.
- Carter, K. O., M. Olshan-Perlmutter, H. J. Norton, and M. O. Smith, “Nada Acupuncture Prospective Trial in Patients with Substance Use Disorders and Seven Common Health Symptoms,” *Medical Acupuncture*, Vol. 23, No. 3, 2011, pp. 131–135.
- Chen, J., J. Guo, J. Sun, W. Jiang, and B. Wu, “TCM Treatment of Parkinson’s Syndrome—A Report of 40 Cases,” *Journal of Traditional Chinese Medicine*, Vol. 23, No. 3, 2003, pp. 168–169.
- Clavey, S., “The Treatment of Postnatal Depression with Chinese Herbal Medicine and Acupuncture,” *Journal of Chinese Medicine*, No. 101, 2013, pp. 19–24.
- Davis, W. M., “New Directions in Treating Depression,” *Drug Topics*, Vol. 142, No. 22, 1998, pp. 85–94.
- Deng, G. E., S. M. Rausch, L. W. Jones, A. Gulati, N. B. Kumar, H. Greenlee, M. C. Pietanza, and B. R. Cassileth, “Complementary Therapies and Integrative Medicine in Lung Cancer: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines,” *Chest*, Vol. 143, No. 5, Suppl., May 2013, pp. e420S–436S.
- Deng, G., Y. Chan, D. Sjoberg, A. Vickers, K. S. Yeung, M. Kris, D. Straus, and B. Cassileth, “Acupuncture for the Treatment of Post-Chemotherapy Chronic Fatigue: A Randomized, Blinded, Sham-Controlled Trial,” *Support Care Cancer*, Vol. 21, No. 6, June 2013, pp. 1735–1741.
- Ernst, E., “Complementary Medicine: Does It Have a Role in the Medical Care of Elderly People?” *Reviews in Clinical Gerontology*, Vol. 7, No. 4, 1997, pp. 353–358.
- Field, T., “Pregnancy and Labor Alternative Therapy Research,” *Alternative Therapies in Health and Medicine*, Vol. 14, No. 5, September–October 2008, pp. 28–34.
- Frenkel, M., and V. Shah, “Complementary Medicine Can Benefit Palliative Care—Part 2,” *European Journal of Palliative Care*, Vol. 15, No. 6, 2008, pp. 288–293.
- Kou, M. J., and J. X. Chen, “Integrated Traditional and Western Medicine for Treatment of Depression Based on Syndrome Differentiation: A Meta-Analysis of Randomized Controlled

- Trials Based on the Hamilton Depression Scale,” *Journal of Traditional Chinese Medicine*, Vol. 32, No. 1, 2012, pp. 1–5.
- Kraft, K., “CAM for Depression, Anxiety, Grief, and Other Symptoms in Palliative Care,” *Progress in Palliative Care*, Vol. 20, No. 5, 2012, pp. 272–277.
- Linde, K., and S. N. Willich, “How Objective Are Systematic Reviews? Differences Between Reviews on Complementary Medicine,” *Journal of the Royal Society of Medicine*, Vol. 96, No. 1, 2003, pp. 17–22.
- Longacre, M., E. Silver-Highfield, P. Lama, and M. Grodin, “Complementary and Alternative Medicine in the Treatment of Refugees and Survivors of Torture: A Review and Proposal for Action,” *Torture*, Vol. 22, No. 1, 2012, pp. 38–57.
- Mamtani, R., and A. Cimino, “A Primer of Complementary and Alternative Medicine and Its Relevance in the Treatment of Mental Health Problems,” *Psychiatric Quarterly*, Vol. 73, No. 4, Winter 2002, pp. 367–381.
- Manheimer, E., and B. Berman, “Exploring, Evaluating, and Applying the Results of Systematic Reviews of CAM Therapies,” *Explore: The Journal of Science and Healing*, Vol. 1, No. 3, 2005, pp. 210–214.
- Swanson, B., J. K. Keithley, J. M. Zeller, and D. Cronin-Stubbs, “Complementary and Alternative Therapies to Manage HIV-Related Symptoms,” *JANAC: Journal of the Association of Nurses in AIDS Care*, Vol. 11, No. 5, 2000, pp. 40–60.
- Vickers, A., “Recent Advances: Complementary Medicine,” *BMJ: British Medical Journal*, Vol. 321, No. 7262, 2000, pp. 683–686.
- Volinn, E., B. Yang, J. He, X. Sheng, J. Ying, W. Volinn, J. Zhang, and Y. Zuo, “West China Hospital Set of Measures in Chinese to Evaluate Back Pain Treatment,” *Pain Medicine*, Vol. 11, No. 5, May 2010, pp. 637–647.
- Weidenhammer, W., K. Linde, A. Streng, A. Hoppe, and D. Melchart, “Acupuncture for Chronic Low Back Pain in Routine Care: A Multicenter Observational Study,” *Clinical Journal of Pain*, Vol. 23, No. 2, February 2007, pp. 128–135.
- Zhang, G., and J. Ruan, “Treatment of Mental Depression Due to Liver-Qi Stagnancy with Herbal Decoction and by Magnetic Therapy at the Acupoints—A Report of 45 Cases,” *Journal of Traditional Chinese Medicine*, Vol. 24, No. 1, 2004, pp. 20–21.
- Zoorob, R., S. Chakrabarty, H. O’Hara, and C. Kihlberg, “Which CAM Modalities Are Worth Considering?” *Journal of Family Practice*, Vol. 63, No. 10, 2014, pp. 585–590.



*Reason Excluded: Nonsystematic Review*

Bazzan, A. J., G. Zabrecky, D. A. Monti, and A. B. Newberg, "Current Evidence Regarding the Management of Mood and Anxiety Disorders Using Complementary and Alternative Medicine," *Expert Review of Neurotherapeutics*, Vol. 14, No. 4, 2014, pp. 411–423.

Born, L., D. Zinga, and S. D. Phillips, "Update on the Treatment of Depression During Pregnancy," *Therapy*, Vol. 3, No. 1, 2006, pp. 153–161.

Chen, J. P., H. Chen, and H. Chung, "Depressive Disorders in Asian American Adults," *Western Journal of Medicine*, Vol. 176, No. 4, 2002, pp. 239–244.

Cohen, A.J., A. Menter, and L. Hale, "Acupuncture: Role in Comprehensive Cancer Care—A Primer for the Oncologist and Review of the Literature," *Integrative Cancer Therapies*, Vol. 4, No. 2, 2005, pp. 131–143.

Deligiannidis, K. M., and M. P. Freeman, "Complementary and Alternative Medicine for the Treatment of Depressive Disorders in Women," *Psychiatric Clinics of North America*, Vol. 33, No. 2, June 2010, pp. 441–463.

———, "Complementary and Alternative Medicine Therapies for Perinatal Depression," *Best Practice & Research Clinical Obstetrics & Gynaecology*, August 26, 2013.

Dimidjian, S., and S. Goodman, "Nonpharmacologic Intervention and Prevention Strategies for Depression During Pregnancy and the Postpartum," *Clinical Obstetrics and Gynecology*, Vol. 52, No. 3, 2009, pp. 498–515.

Hagelskamp, C., A. Scammell, S. Au, and G. Leavey, "Acupuncture as Treatment for Depression in Primary Care: Current Position and Future Hopes," *Primary Care Mental Health*, Vol. 1, No. 2, 2003, pp. 75–79.

Horowitz, S., "Acupuncture for Treating Mental Health Disorders," *Alternative & Complementary Therapies*, Vol. 15, No. 3, 2009, pp. 135–141.

Johnston, M. F., C. Yang, K. K. Hui, B. Xiao, X. Li, and A. Rusiewicz, "Acupuncture for Chemotherapy-Associated Cognitive Dysfunction: A Hypothesis-Generating Literature Review to Inform Clinical Advice," *Integrative Cancer Therapies*, Vol. 6, No. 1, 2007, pp. 36–41.

Jonas, W. B., J. A. G. Walter, M. Fritts, and R. C. Niemtzow, "Acupuncture for the Trauma Spectrum Response: Scientific Foundations, Challenges to implementation," *Medical Acupuncture*, Vol. 23, No. 4, 2011, pp. 249–262.

Kim, Y. H. J., "The Effectiveness of Acupuncture for Treating Depression: A Review," *Alternative and Complementary Therapies*, Vol. 13, No. 3, 2007, pp. 129–131.

- Korngold, E., and H. Beinfield, "Chinese Medicine and the Mind," *Explore: The Journal of Science and Healing*, Vol. 2, No. 4, 2006, pp. 321–333.
- Larzelere, M. M., and P. Wiseman, "Anxiety, Depression, and Insomnia," *Primary Care*, Vol. 29, No. 2, June 2002, pp. 339–360, vii.
- Luo, H., Y. Jia, X. Feng, X. Zhao, and L. C. Tang, "Advances in Clinical Research on Common Mental Disorders with Computer Controlled Electro-Acupuncture Treatment," *Advances in Experimental Medicine and Biology*, Vol. 363, 1995, pp. 109–122.
- MacPherson, H., "Acupuncture for Depression: State of the Evidence," *Acupuncture in Medicine*, Vol. 32, No. 4, 2014, pp. 304–305.
- Manber, R., J. J. Allen, and M. E. Morris, "Alternative Treatments for Depression: Empirical Support and Relevance to Women," *Journal of Clinical Psychiatry*, Vol. 63, No. 7, July 2002, pp. 628–640.
- Maurer, D., and R. Colt, "An Evidence-Based Approach to the Management of Depression," *Primary Care—Clinics in Office Practice*, Vol. 33, No. 4, 2006, pp. 923–941.
- Meng, F.-Q., H.-C. Luo, and U. Halbreich, "Concepts, Techniques, and Clinical Applications of Acupuncture," *Psychiatric Annals*, Vol. 32, No. 1, 2002, pp. 45–49.
- O'Regan, D., and J. Filshie, "Acupuncture and Cancer," *Autonomic Neuroscience*, Vol. 157, No. 1–2, October 28, 2010, pp. 96–100.
- Pilkington, K., "Acupuncture Therapy for Psychiatric Illness," *International Review of Neurobiology*, Vol. 111, 2013, pp. 197–216.
- Reid, T., "Depression—A Multifaced Problem," *European Journal of Oriental Medicine*, Vol. 6, No. 5, 2010, pp. 32–47.
- Ross, S. M., "Mild to Moderate Depression: A Complementary and Integrative Therapies Approach," *Holistic Nursing Practice*, Vol. 24, No. 5, 2010, pp. 303–309.
- Samuels, N., C. Gropp, S. R. Singer, and M. Oberbaum, "Acupuncture for Psychiatric Illness: A Literature Review," *Behavioral Medicine*, Vol. 34, No. 2, Summer 2008, pp. 55–64.
- Schneider, C., and N. Korsen, "Complementary and Alternative Medical Approaches to Treating Depression in a Family Practice Setting," *Clinics in Family Practice*, Vol. 4, No. 4, 2002, pp. 873–893.
- Stania, D., D. Vanessa, G. Wanda, and C. Peter, "Identification and Treatment of Depression in Minority Populations," *International Journal of Psychiatry in Medicine*, Vol. 42, No. 1, 2011, pp. 69–83.
- Steeffel, L., "Treating Depression: Helping the Body Heal the Mind," *Alternative & Complementary Therapies*, Vol. 2, No. 1, January–February, 1996, pp. 1–4.

- Stevinson, C., “Evidence for the Efficacy of Complementary Therapies in Depression,” *Focus on Alternative & Complementary Therapies*, Vol. 4, No. 3, 1999, pp. 111–114.
- Ulett, G. A., S. P. Han, and J. S. Han, “Electroacupuncture: Mechanisms and Clinical Application,” *Biological Psychiatry*, Vol. 44, No. 2, July 1998, pp. 129–138.
- Van Der Watt, G., J. Laugharne, and A. Janca, “Complementary and Alternative Medicine in the Treatment of Anxiety and Depression,” *Current Opinion in Psychiatry*, Vol. 21, No. 1, January 2008, pp. 37–42.
- Weier, K. M., and M. W. Beal, “Complementary Therapies as Adjuncts in the Treatment of Postpartum Depression,” *Journal of Midwifery & Women’s Health*, Vol. 49, No. 2, March–April 2004, pp. 96–104.
- Wu, J., A. S. Yeung, R. Schnyer, Y. Wang, and D. Mischoulon, “Acupuncture for Depression: A Review of Clinical Applications,” *Canadian Journal of Psychiatry*, Vol. 57, No. 7, July 2012, pp. 397–405.
- Zhang, J., J. Chen, J. Chen, X. Li, X. Lai, Z. S., and S. Wang., “Early Filiform Needle Acupuncture for Poststroke Depression: A Meta-Analysis of 17 Randomized Controlled Clinical Trials,” *Neural Regeneration Research*, Vol. 9, No. 7, 2014, pp. 773–784.
- Zhang, Y., Wang, Z.Z., Sun, H.M., Li, P., Li, Y.F, Chen, “Systematic Review of Traditional Chinese Medicine for Depression in Parkinson’s Disease,” *American Journal of Chinese Medicine*, Vol. 42, No. 5, 2014, pp. 1035–1051.

#### ***Reason Excluded: Systematic Review***

- Cao, H., J. Liu, and G. T. Lewith, “Traditional Chinese Medicine for Treatment of Fibromyalgia: A Systematic Review of Randomized Controlled Trials,” *Journal of Alternative and Complementary Medicine*, Vol. 16, No. 4, April 2010, pp. 397–409.
- Cao, H., S. Bouchier, and J. Liu, “Does Syndrome Differentiation Matter? A Meta-Analysis of Randomized Controlled Trials in Cochrane Reviews of Acupuncture,” *Medical Acupuncture*, Vol. 24, No. 2, 2012, pp. 68–76.
- Chan, Y., W. Lo, S. Yang, Y. Chen, J. Lin, “The Benefit of Combined Acupuncture and Antidepressant Medication for Depression: A Systematic Review and Meta-Analysis,” *Journal of Affective Disorders*, Vol. 176c, 2015, pp. 106–117.
- Dennis, C. L., and K. Allen, “Interventions (Other Than Pharmacological, Psychosocial or Psychological) for Treating Antenatal Depression,” *Cochrane Database of Systematic Reviews*, No. 4, 2008, p. CD006795.

- Dennis, C. L., and T. Dowswell, "Interventions (Other Than Pharmacological, Psychosocial or Psychological) for Treating Antenatal Depression," *Cochrane Database of Systematic Reviews*, Vol. 7, 2013, p. CD006795.
- Dirmaier, J., M. Steinmann, T. Krattenmacher, B. Watzke, D. Barghaan, U. Koch, and H. Schulz, "Non-Pharmacological Treatment of Depressive Disorders: A Review of Evidence-Based Treatment Options," *Reviews on Recent Clinical Trials*, Vol. 7, No. 2, May 2012, pp. 141–149.
- Ernst, E., "Acupuncture: What Does the Most Reliable Evidence Tell Us?" *Journal of Pain and Symptom Management*, Vol. 37, No. 4, 2009, pp. 709–714.
- Ernst, E., J. I. Rand, and C. Stevinson, "Complementary Therapies for Depression: An Overview," *Archives of General Psychiatry*, Vol. 55, No. 11, November 1998, pp. 1026–1032.
- Ernst, E., M. S. Lee, and T. Y. Choi, "Acupuncture for Depression? A Systematic Review of Systematic Reviews," *Evaluation & the Health Professions*, Vol. 34, No. 4, December 2011, pp. 403–412.
- Freeman, M. P., C. Helgason, and R. A. Hill, "Selected Integrative Medicine Treatments for Depression: Considerations for Women," *Journal of the American Medical Women's Association (1972)*, Vol. 59, No. 3, Summer 2004, pp. 216–224.
- Freeman, M. P., M. Fava, J. Lake, M. H. Trivedi, K. L. Wisner, and D. Mischoulon, "Complementary and Alternative Medicine in Major Depressive Disorder: The American Psychiatric Association Task Force Report," *Journal of Clinical Psychiatry*, Vol. 71, No. 6, June 2010, pp. 669–681.
- Garcia, M. K., J. Mcquade, R. Haddad, S. Patel, R. Lee, P. Yang, J. L. Palmer, and L. Cohen, "Systematic Review of Acupuncture in Cancer Care: A Synthesis of the Evidence," *Journal of Clinical Oncology*, Vol. 31, No. 7, March 1, 2013, pp. 952–960.
- Jorm, A. F., H. Christensen, K. M. Griffiths, and B. Rodgers, "Effectiveness of Complementary and Self-Help Treatments for Depression," *Medical Journal of Australia*, Vol. 176, Suppl., May 20, 2002, pp. S84–S96.
- Kalavapalli, R., and R. Singareddy, "Role of Acupuncture in the Treatment of Insomnia: A Comprehensive Review," *Complementary Therapies in Clinical Practice*, Vol. 13, No. 3, August 2007, pp. 184–193.
- Lavretsky, H., "Complementary and Alternative Medicine Use for Treatment and Prevention of Late-Life Mood Disorders," *Clinical Geriatrics*, Vol. 18, No. 6, 2010, pp. 32–37.
- Lee, C., C. Crawford, D. Wallerstedt, A. York, A. Duncan, J. Smith, M. Sprengel, R. Welton, and W. Jonas, "The Effectiveness of Acupuncture Research Across Components of the

- Trauma Spectrum Response (TSR): A Systematic Review of Reviews,” *Systematic Reviews*, Vol. 1, 2012, p. 46.
- Leo, R. J., and J. S. Ligot, Jr., “A Systematic Review of Randomized Controlled Trials of Acupuncture in the Treatment of Depression,” *Journal of Affective Disorders*, Vol. 97, No. 1–3, January 2007, pp. 13–22.
- Lett, H. S., J. Davidson, and J. A. Blumenthal, “Nonpharmacologic Treatments for Depression in Patients with Coronary Heart Disease,” *Psychosomatic Medicine*, Vol. 67, Suppl. 1, May–June 2005, pp. S58–S62.
- Manheimer, E., S. Wieland, E. Kimbrough, K. Cheng, and B. M. Berman, “Evidence from the Cochrane Collaboration for Traditional Chinese Medicine Therapies,” *Journal of Alternative and Complementary Medicine*, Vol. 15, No. 9, 2009, pp. 1001–1014.
- Meeks, T. W., J. L. Wetherell, M. R. Irwin, L. S. Redwine, and D. V. Jeste, “Complementary and Alternative Treatments for Late-Life Depression, Anxiety, and Sleep Disturbance: A Review of Randomized Controlled Trials,” *Journal of Clinical Psychiatry*, Vol. 68, No. 10, October 2007, pp. 1461–1471.
- Mukaino, Y., J. Park, A. White, and E. Ernst, “The Effectiveness of Acupuncture for Depression—A Systematic Review of Randomised Controlled Trials,” *Acupuncture in Medicine*, Vol. 23, No. 2, June 2005, pp. 70–76.
- Nahas, R., and O. Sheikh, “Complementary and Alternative Medicine for the Treatment of Major Depressive Disorder,” *Canadian Family Physician*, Vol. 57, No. 6, June 2011, pp. 659–663.
- Pilkington, K., “Anxiety, Depression and Acupuncture: A Review of the Clinical Research,” *Autonomic Neuroscience*, Vol. 157, No. 1–2, October 28, 2010, pp. 91–95.
- Pilkington, K., H. Rampes, and J. Richardson, “Complementary Medicine for Depression,” *Expert Review of Neurotherapeutics*, Vol. 6, No. 11, November 2006, pp. 1741–1751.
- Qureshi, N. A., and A. M. Al-Bedah, “Mood Disorders and Complementary and Alternative Medicine: A Literature Review,” *Neuropsychiatric Disease and Treatment*, Vol. 9, 2013, pp. 639–658.
- Ravindran, A. V. and T. L. Da Silva, “Complementary and Alternative Therapies as Add-On to Pharmacotherapy for Mood and Anxiety Disorders: A Systematic Review,” *Journal of Affective Disorders*, Vol. 150, No. 3, 2013, pp. 707–719.
- Ravindran, A. V., R. W. Lam, M. J. Filteau, F. Lesperance, S. H. Kennedy, S. V. Parikh, and S. B. Patten, “Canadian Network for Mood and Anxiety Treatments (Canmat) Clinical Guidelines for the Management of Major Depressive Disorder in Adults. vs. Complementary and Alternative Medicine Treatments,” *Journal of Affective Disorders*, Vol. 117, Suppl. 1, October 2009, pp. S54–S64.

- Sartorius, N., T. C. Baghai, D. S. Baldwin, B. Barrett, U. Brand, W. Fleischhacker, G. Goodwin, H. Grunze, M. Knapp, B. E. Leonard, J. Lieberman, Y. Nakane, R. M. Pinder, A. F. Schatzberg, J. Svestka, P. Baumann, K. Ghalib, J. C. Markowitz, F. Padberg, M. Fink, T. Furukawa, K. N. Fountoulakis, P. Jensen, S. Kanba, and A. Riecher-Rossler, “Antidepressant Medications and Other Treatments of Depressive Disorders: A CINP Task Force Report Based on a Review of Evidence,” *International Journal of Neuropsychopharmacology*, Vol. 10, Suppl. 1, 2007, pp. S1–S207.
- Schroer, S., and J. Adamson, “Acupuncture for Depression: A Critique of the Evidence Base,” *Cns Neuroscience & Therapeutics*, Vol. 17, No. 5, 2011, pp. 398–410.
- Smith, C. A., P. P. Hay, and H. MacPherson, “Acupuncture for Depression,” *Cochrane Database of Systematic Reviews*, No. 1, 2010, pp. 1–3.
- Sniezek, D. P., and I. J. Siddiqui, “Acupuncture for Treating Anxiety and Depression in Women: A Clinical Systematic Review,” *Medical Acupuncture*, Vol. 25, No. 3, 2013, pp. 164–172.
- Stub, T., T. Alraek, and J. P. Liu, “Acupuncture Treatment for Depression—A Systematic Review and Meta-Analysis,” *European Journal of Integrative Medicine*, Vol. 3, No. 4, December 2011, pp. E253–E264.
- Taylor, P., L. Pezzullo, S. J. Grant, and A. Bensoussan, “Cost-Effectiveness of Acupuncture for Chronic Nonspecific Low Back Pain,” *Pain Practice*, October 21, 2013.
- Thachil, A. F., R. Mohan, and D. Bhugra, “The Evidence Base of Complementary and Alternative Therapies in Depression,” *Journal of Affective Disorders*, Vol. 97, No. 1–3, January 2007, pp. 23–35.
- Wang, H., H. Qi, B. S. Wang, Y. Y. Cui, L. Zhu, Z. X. Rong, and H. Z. Chen, “Is Acupuncture Beneficial in Depression: A Meta-Analysis of 8 Randomized Controlled Trials?” *Journal of Affective Disorders*, Vol. 111, No. 2–3, December 2008, pp. 125–134.
- Wang, J., M. Cui, H. Jiao, Y. Tong, J. Xu, Y. Zhao, M. Han, and J. Liu, “Content Analysis of Systematic Reviews on Effectiveness of Traditional Chinese Medicine,” *Journal of Traditional Chinese Medicine*, Vol. 33, No. 2, April 2013, pp. 156–163.
- Williams, J. W., J. M. Gierisch, J. McDuffie, J. L. Strauss, and A. Nagi, *An overview of Complementary and Alternative Medicine Therapies for Anxiety and Depressive Disorders: Supplement to Efficacy of Complementary and Alternative Medicine Therapies for Posttraumatic Stress Disorder*, Washington, D.C.: U.S. Department of Veterans Affairs, 2011.
- Zhang, G. C., W. B. Fu, N. G. Xu, J. H. Liu, X. P. Zhu, Z. H. Liang, Y. F. Huang, and Y. F. Chen, “Meta Analysis of the Curative Effect of Acupuncture on Post-Stroke Depression,” *Journal of Traditional Chinese Medicine*, Vol. 32, No. 1, March 2012, pp. 6–11.

Zhang, Z. J., H. Y. Chen, K. C. Yip, R. Ng, and V. T. Wong, "The Effectiveness and Safety of Acupuncture Therapy in Depressive Disorders: Systematic Review and Meta-Analysis," *Journal of Affective Disorders*, Vol. 124, No. 1–2, Jul, 2010, pp. 9–21.

***Reason Excluded: Does Not Report Data for MDD***

"Alternative Therapies: Beyond the Myths," *Consumer Reports on Health*, Vol. 19, No. 1, 2007, pp. 8–9.

"Needles to Fight Depression," *Journal of Psychosocial Nursing & Mental Health Services*, Vol. 42, No. 7, 2004, p. 12.

Arvidsdotter, T., B. Marklund, and C. Taft, "Effects of an Integrative Treatment, Therapeutic Acupuncture and Conventional Treatment in Alleviating Psychological Distress in Primary Care Patients—A Pragmatic Randomized Controlled Trial," *BMC Complementary Alternative Medicine*, Vol. 13, No. 1, November 7, 2013, p. 308.

Ashton, H., A. Nodiyal, D. Green, B. Moore, and N. Heather, "Acupuncture or Counselling: Outcomes and Predictors of Treatment Choice in a Non-Statutory Addiction Service," *Journal of Substance Use*, Vol. 14, No. 3–4, 2009, pp. 151–160.

Ay, S., D. Evcik, and B. S. Tur, "Comparison of Injection Methods in Myofascial Pain Syndrome: A Randomized Controlled Trial," *Clinical Rheumatology*, Vol. 29, No. 1, January 2010, pp. 19–23.

Balk, J., R. Day, M. Rosenzweig, and S. Beriwal, "Pilot, Randomized, Modified, Double-Blind, Placebo-Controlled Trial of Acupuncture for Cancer-Related Fatigue," *Journal of the Society for Integrative Oncology*, Vol. 7, No. 1, Winter 2009, pp. 4–11.

Barnes, J., "Are Natural Therapies Safe and Effective?" *Pharmaceutical Journal*, Vol. 258, No. 6939, 1997, pp. 561–565.

Bier, I. D., J. Wilson, P. Studt, and M. Shakleton, "Auricular Acupuncture, Education, and Smoking Cessation: A Randomized, Sham-Controlled Trial," *American Journal of Public Health*, Vol. 92, No. 10, 2002, pp. 1642–1647.

Bosch, P., G. Van Lujtelaar, M. Van Den Noort, S. Lim, J. Egger, and A. Coenen, "Sleep Ameliorating Effects of Acupuncture in a Psychiatric Population," *Evidence-Based Complementary and Alternative Medicine*, Vol. 2013, pp. 1–11.

Bullock, M. L., T. J. Kiresuk, R. E. Sherman, S. K. Lenz, P. D. Culliton, T. A. Boucher, and C. J. Nolan, "A Large Randomized Placebo Controlled Study of Auricular Acupuncture for Alcohol Dependence," *Journal of Substance Abuse Treatment*, Vol. 22, No. 2, March 2002, pp. 71–77.

- Cabioglu, M. T., N. Ergene, and U. Tan, "Electroacupuncture Treatment of Obesity with Psychological Symptoms," *International Journal of Neuroscience*, Vol. 117, No. 5, May 2007, pp. 579–590.
- Carvalho, F., K. Weires, M. Ebling, M. De Souza Rabbo Padilha, Y. A. Ferrao, and R. Vercelino, "Effects of Acupuncture on the Symptoms of Anxiety and Depression Caused by Premenstrual Dysphoric Disorder," *Acupuncture in Medicine*, Vol. 31, No. 4, December 2013, pp. 358–363.
- Ceccherelli, F., A. Lovato, E. Piana, G. Gagliardi, and A. Roveri, "Somatic Acupuncture Versus Ear Acupuncture in Migraine Therapy: A Randomized, Controlled, Blind Study," *Acupuncture & Electro-therapeutics Research*, Vol. 37, No. 4, 2012, pp. 277–293.
- Chan, J., D. Briscoomb, E. Waterhouse, and A. M. Cannaby, "An Uncontrolled Pilot Study of HT7 for 'Stress,'" *Acupuncture in Medicine*, Vol. 20, No. 2–3, August 2002, pp. 74–77.
- Chang, S. H., M. C. Fang, and Y. S. Yang, "Effectiveness of Transcutaneous Electrical Acupoint Stimulation for Improving Depressive Mood Status Among Nursing Home Elders in Taiwan: A Pilot Study," *Geriatric Nursing*, Vol. 31, No. 5, September–October 2010, pp. 324–330.
- Chen, A. S., "Sequential Electric Acupuncture or Tens in Treatment of Stress Related Mental Disorders. A Preliminary Report," *Acupuncture and Electro-Therapeutics Research*, Vol. 12, No. 3–4, 1987, pp. 254–255.
- Chen, A., "An Introduction to Sequential Electric Acupuncture (SEA) in the Treatment of Stress Related Physical and Mental Disorders," *Acupuncture & Electro-therapeutics Research*, Vol. 17, No. 4, October–December 1992, pp. 273–283.
- Chen, S. D., and X. Lu, "Experience in Clinical Application of Ligou Point," *Journal of Traditional Chinese Medicine*, Vol. 29, No. 2, 2009, pp. 104–106.
- Cherkezova, M., and S. Toteva, "Acupuncture in the Treatment of Alcoholics with a Depressive Syndrome," *Journal of Russian & East European Psychiatry*, Vol. 26, No. 1, 1993, pp. 28–30.
- Cho, S. Y., S. R. Shim, H. Y. Rhee, H. J. Park, W. S. Jung, S. K. Moon, J. M. Park, C. N. Ko, K. H. Cho, and S. U. Park, "Effectiveness of Acupuncture and Bee Venom Acupuncture in Idiopathic Parkinson's Disease," *Parkinsonism & Related Disorders*, Vol. 18, No. 8, September 2012, pp. 948–952.
- Cho, Y. C., and S. L. Tsay, "The Effect of Acupressure with Massage on Fatigue and Depression in Patients with End-Stage Renal Disease," *Journal of Nursing Research*, Vol. 12, No. 1, March 2004, pp. 51–59.
- Cho, Y. J., Y. K. Song, Y. Y. Cha, B. C. Shin, I. H. Shin, H. J. Park, H. S. Lee, K. W. Kim, J. H. Cho, W. S. Chung, J. H. Lee, and M. Y. Song, "Acupuncture for Chronic Low Back Pain: A



- Multicenter, Randomized, Patient-Assessor Blind, Sham-Controlled Clinical Trial,” *Spine (Philadelphia, Pa 1976)*, Vol. 38, No. 7, April 1, 2013, pp. 549–557.
- Chung, K.F., W.F. Yeung, C.W. Kwok, Y.M. Yu, “Risk Factors Associated with Adverse Events of Acupuncture: A Prospective Study,” *Acupuncture in Medicine* Vol. 32, No. 6, 2014, pp. 455–462.
- Courbasson, C. M., A. A. De Sorkin, B. Dullerud, and L. Van Wyk, “Acupuncture Treatment for Women with Concurrent Substance Use and Anxiety/Depression: An Effective Alternative Therapy?” *Family & Community Health*, Vol. 30, No. 2, April–June 2007, pp. 112–120.
- Creamer, P., B. B. Singh, M. C. Hochberg, and B. M. Berman, “Are Psychosocial Factors Related to Response to Acupuncture Among Patients with Knee Osteoarthritis?” *Alternative Therapies in Health and Medicine*, Vol. 5, No. 4, July 1999, pp. 72–76.
- Dean-Clower, E., A. M. Doherty-Gilman, A. Keshaviah, F. Baker, C. Kaw, W. Lu, J. Manola, R. T. Penson, U. A. Matulonis, and D. S. Rosenthal, “Acupuncture as Palliative Therapy for Physical Symptoms and Quality of Life for Advanced Cancer Patients,” *Integrative Cancer Therapies*, Vol. 9, No. 2, June 2010, pp. 158–167.
- Dias, M., D. Pagnin, V. De Queiroz Pagnin, R. L. Reis, and B. Olej, “Effects of Electroacupuncture on Stress-Related Symptoms in Medical Students: A Randomised Controlled Pilot Study,” *Acupuncture in Medicine*, Vol. 30, No. 2, June 2012, pp. 89–95.
- Dias, M., G. C. Vellarde, and B. Olej, “Effects of Electroacupuncture on Stress-Related Symptoms in Medical Students: A Randomised Placebo-Controlled Study,” *Acupuncture in Medicine*, October 10, 2013.
- Dong Jiang, T., “Research on the Reduction of Anxiety and Depression with Acupuncture,” *American Journal of Acupuncture*, Vol. 21, No. 4, 1993, pp. 327–330.
- Dormaaenen, A., M. R. Heimdal, C. E. Wang, and A. S. Grimsgaard, “Depression in Postmenopause: A Study on a Subsample of the Acupuncture on Hot Flashes Among Menopausal Women (Acuflysh) Study,” *Menopause*, Vol. 18, No. 5, May 2011, pp. 525–530.
- Duan, D. M., Y. Tu, L. P. Chen, and Z. J. Wu, “Efficacy Evaluation for Depression with Somatic Symptoms Treated by Electroacupuncture Combined with Fluoxetine,” *Journal of Traditional Chinese Medicine*, Vol. 29, No. 3, September 2009, pp. 167–173.
- Elder, C. R., C. M. Gullion, L. L. Debar, K. L. Funk, N. M. Lindberg, C. Ritenbaugh, G. Meltesen, C. Gallison, and V. J. Stevens, “Randomized Trial of Tapas Acupressure Technique for Weight Loss Maintenance,” *BMC Complementary and Alternative Medicine*, Vol. 12, 2012, p. 19.

- Eng, M. L., K. E. Lyons, M. S. Greene, and R. Pahwa, "Open-Label Trial Regarding the Use of Acupuncture and Yin Tui Na in Parkinson's Disease Outpatients: A Pilot Study on Efficacy, Tolerability, and Quality of Life," *Journal of Alternative and Complementary Medicine*, Vol. 12, No. 4, May 2006, pp. 395–399.
- Fazio, L. F., "Effects of Acupuncture Treatments upon Depressive Affect," *Dissertation Abstracts International*, Vol. 43, No. 3–4, 1982.
- Feng, B., L. Liu, X. Fangzhong, J. Chen, P. Wang, W. Chen, and E. Yu, "Thirty Cases of Obsession Treated by Point-Stimulation and with Small Dose of Chlorimipramine," *Journal of Traditional Chinese Medicine*, Vol. 27, No. 1, March 2007, pp. 3–6.
- Feng, Y., X. Y. Wang, S. D. Li, Y. Zhang, H. M. Wang, M. Li, K. Cao, Y. F. Ye, and Z. Zhang, "Clinical Research of Acupuncture on Malignant Tumor Patients for Improving Depression and Sleep Quality," *Journal of Traditional Chinese Medicine*, Vol. 31, No. 3, September 2011, pp. 199–202.
- Ferreira, M. S., and M. G. Pereira, "The Mediator Role of Psychological Morbidity in Patients with Chronic Low Back Pain in Differentiated Treatments," *Journal of Health Psychology*, July 1, 2013.
- Fink, M., "Electroacupuncture and Electroconvulsive Treatment," *Biological Psychiatry*, Vol. 20, No. 7, July 1985, pp. 817–818.
- Fogarty, S., D. Harris, C. Zaslowski, A. J. Mcainch, and L. Stojanovska, "Acupuncture as an Adjunct Therapy in the Treatment of Eating Disorders: A Randomised Cross-Over Pilot Study," *Complementary Therapies in Medicine*, Vol. 18, No. 6, December 2010, pp. 233–240.
- Fossion, J. P., "Clinical Assessment of a Model for Nervous Depression in Auriculotherapy: Proposition for New Points in the Brodmann-Representations of the Medial Prefrontal Cortex, Anterior Cingulate Cortex and Habenular Nuclei," *Deutsche Zeitschrift fur Akupunktur*, Vol. 52, No. 4, 2009, pp. 12–17.
- Fu, W. B., L. Fan, X. P. Zhu, Q. He, L. Wang, L. X. Zhuang, Y. S. Liu, C. Z. Tang, Y. W. Li, C. R. Meng, H. L. Zhang, and J. Yan, "Depressive Neurosis Treated by Acupuncture for Regulating the Liver—A Report of 176 Cases," *Journal of Traditional Chinese Medicine*, Vol. 29, No. 2, June 2009, pp. 83–86.
- Fu, W., "Observations on the Curative Effect of Acupuncture on Depressive Neurosis," *Journal of Acupuncture and Tuina Science*, Vol. 1, No. 4, 2003.
- Ga, H., J. H. Choi, C. H. Park, and H. J. Yoon, "Acupuncture Needling Versus Lidocaine Injection of Trigger Points in Myofascial Pain Syndrome in Elderly Patients—A Randomised Trial," *Acupuncture in Medicine*, Vol. 25, No. 4, December 2007, pp. 130–136.

- , “Dry Needling of Trigger Points With and Without Paraspinal Needling in Myofascial Pain Syndromes in Elderly Patients,” *Journal of Alternative and Complementary Medicine*, Vol. 13, No. 6, July–August, 2007, pp. 617–624.
- Godfrey, K., “Acupressure Helps Fatigue Management,” *Cancer Nursing Practice*, Vol. 7, No. 8, 2008, pp. 14–14.
- Han, C., X. Li, and H. Luo, “Randomized Clinical Trial Comparing the Effects of Electro-Acupuncture and Maprotiline in Treating Depression,” *International Journal of Clinical Acupuncture*, Vol. 15, No. 1, 2006.
- Han, C., X. Li, H. Luo, X. Zhao, and X. Li, “Clinical Study on Electro-Acupuncture Treatment for 30 Cases of Mental Depression,” *Journal of Traditional Chinese Medicine*, Vol. 24, No. 3, September 2004, pp. 172–176.
- Hansson, Y., C. Carlsson, and E. Olsson, “Intramuscular and Periosteal Acupuncture for Anxiety and Sleep Quality in Patients with Chronic Musculoskeletal Pain—An Evaluator Blind, Controlled Study,” *Acupuncture in Medicine*, Vol. 25, No. 4, December 2007, pp. 148–157.
- He, D., A. T. Hostmark, K. B. Veiersted, and J. I. Medbo, “Effect of Intensive Acupuncture on Pain-Related Social and Psychological Variables for Women with Chronic Neck and Shoulder Pain—An RCT with Six Month and Three Year Follow Up,” *Acupuncture in Medicine*, Vol. 23, No. 2, June 2005, pp. 52–61.
- He, Q., J. Zhang, and Y. Tang, “A Controlled Study on Treatment of Mental Depression by Acupuncture Plus TCM Medication,” *Journal of Traditional Chinese Medicine*, Vol. 27, No. 3, September 2007, pp. 166–169.
- He, Y. S., Y. S. Wu, M. F. Ouyang, G. X. Li, H. J. Li, and H. E. Xie, “Efficacy Observation of Depression in Nicotine Withdrawal Treated with Acupuncture,” *World Journal of Acupuncture - Moxibustion*, Vol. 22, No. 1, 2012, pp. 13–16.
- Hechun, L., J. Yunkui, and Z. Li, “Electro-Acupuncture vs. Amitriptyline in the Treatment of Depressive States,” *Journal of Traditional Chinese Medicine*, Vol. 3, No. 1, 1985, pp. 3–8.
- Honda, Y., A. Tsuda, and S. Horiuchi, “Four-Week Self-Administered Acupressure Improves Depressive Mood,” *Psychology*, Vol. 3, No. 9A, 2012, pp. 802–804.
- Hyun, M. K., M. S. Lee, K. Kang, and S. M. Choi, “Body Acupuncture for Nicotine Withdrawal Symptoms: A Randomized Placebo-Controlled Trial,” *Evidence-Based Complementary and Alternative Medicine*, Vol. 7, No. 2, June 2010, pp. 233–238.
- Jarzem, P. F., E. J. Harvey, N. Arcaro, and J. Kaczorowski, “Transcutaneous Electrical Nerve Stimulation Tens for Chronic Low Back Pain,” *Journal of Musculoskeletal Pain*, Vol. 13, No. 2, 2005, pp. 3–9.

- Jiahui, Z., and S. Peng, "Clinical Observation on Acupuncture Treatment of Depressive Neurosis in 30 Cases," *Journal of Traditional Chinese Medicine*, Vol. 26, No. 3, September 2006, pp. 191–192.
- Jiang, Y., "Thirty Cases of Sub-Healthy State Regulated by Acupuncture and He-Ne Laser Vascular Irradiation," *Journal of Traditional Chinese Medicine*, Vol. 26, No. 2, 2006, pp. 102–103.
- Kamanli, A., A. Kaya, O. Ardicoglu, S. Ozgocmen, F. O. Zengin, and Y. Bayik, "Comparison of Lidocaine Injection, Botulinum Toxin Injection, and Dry Needling to Trigger Points in Myofascial Pain Syndrome," *Rheumatology International*, Vol. 25, No. 8, October 2005, pp. 604–611.
- Kang, H. S., S. R. Sok, and J. S. Kang, "Effects of Meridian Acupressure for Stroke Patients in Korea," *Journal of Clinical Nursing*, Vol. 18, No. 15, August 2009, pp. 2145–2152.
- Karst, M., T. Passie, S. Friedrich, B. Wiese, and U. Schneider, "Acupuncture in the Treatment of Alcohol Withdrawal Symptoms: A Randomized, Placebo-Controlled Inpatient Study," *Addiction Biology*, Vol. 7, No. 4, October 2002, pp. 415–419.
- Kessler, R., "News from NIH/OAM. Alternative Medicine Update," *Alternative Health Practitioner*, Vol. 4, No. 3, 1998, pp. 177–178.
- Khamba, B., M. Aucoin, M. Lytle, M. Vermani, A. Maldonado, C. Iorio, C. Cameron, D. Tsirgielis, C. D'ambrosio, L. Anand, and M. A. Katzman, "Efficacy of Acupuncture Treatment of Sexual Dysfunction Secondary to Antidepressants," *Journal of Alternative and Complementary Medicine*, Vol. 19, No. 11, November 2013, pp. 862–869.
- Killeen, T. K., and K. T. Brady, "A Preliminary Study of the Effects of Auricular Acupuncture on Alcohol and Drug Withdrawal Symptoms," *Substance Abuse*, Vol. 18, No. 3, 1997, pp. 119–124.
- Knight, B., C. Mudge, S. Openshaw, A. White, and A. Hart, "Effect of Acupuncture on Nausea of Pregnancy: A Randomized, Controlled Trial," *Obstetrics & Gynecology*, Vol. 97, No. 2, February 2001, pp. 184–188.
- Kukuk, P., M. Lungenhausen, A. Molsberger, and H. G. Endres, "Long-Term Improvement in Pain Coping for cLBP and Gonarthrosis Patients Following Body Needle Acupuncture: A Prospective Cohort Study," *European Journal of Medical Research*, Vol. 10, No. 6, June 22, 2005, pp. 263–272.
- Kwak, H. Y., J. I. Kim, J. M. Park, S. H. Lee, H. S. Yu, J. D. Lee, K. H. Cho, S. Katai, H. Tsukayama, T. Kimura, and D. Y. Choi, "Acupuncture for Whiplash-Associated Disorder: A Randomized, Waiting-List Controlled, Pilot Trial," *European Journal of Integrative Medicine*, Vol. 4, No. 2, June 2012, pp. E151–E158.

- Lake, J., "The Integrative Management of Depressed Mood," *Integrative Medicine: A Clinician's Journal*, Vol. 3, No. 3, 2004, pp. 34–43.
- Latifpour, D. H., J. Grenner, and C. Sjudahl, "The Effect of a New Treatment Based on Somatosensory Stimulation in a Group of Patients with Somatically Related Tinnitus," *International Tinnitus Journal*, Vol. 15, No. 1, 2009, pp. 94–99.
- Li, C. D., Y. Huang, Y. K. Li, K. M. Hu, and Z. Y. Jiang, "Treating Post Stroke-Depression with "Mind-Refreshing Antidepressive" Acupuncture Therapy: A Clinical Study of 21 Cases," *International Journal of Clinical Acupuncture*, Vol. 5, No. 4, 1994.
- Lima, F. A., L. E. Ferreira, and F. H. Pace, "Acupuncture Effectiveness as a Complementary Therapy in Functional Dyspepsia Patients," *Arquivos de Gastroenterologia*, Vol. 50, No. 3, July–September 2013, pp. 202–207.
- Linde, K., A. Streng, A. Hoppe, W. Weidenhammer, S. Wagenpfeil, and D. Melchart, "Randomized Trial vs. Observational Study of Acupuncture for Migraine Found That Patient Characteristics Differed but Outcomes Were Similar," *Journal of Clinical Epidemiology*, Vol. 60, No. 3, March 2007, pp. 280–287.
- Litscher, G., G. Cheng, L. Wang, W. Cheng, H. Su, Q. Niu, T. Zou, Y. Wang, X. Feng, I. Gaischek, Z. Sheng, and H. Kuang, "Biomedical Teleacupuncture Between China and Austria Using Heart Rate Variability—Part 2: Patients with Depression," *Evidence-Based Complementary and Alternative Medicine*, Vol. 2012, 2012, p. 145904.
- Liu, G., Y. Jia, L. Zhan, and H. Luo, "Electroacupuncture Treatment of Presenile and Senile Depressive State," *Journal of Traditional Chinese Medicine*, Vol. 12, No. 2, June 1992, pp. 91–94.
- Lo, C., W. C. Liao, J. J. Liaw, L. W. Hang, and J. G. Lin, "The Stimulation Effect of Auricular Magnetic Press Pellets on Older Female Adults with Sleep Disturbance Undergoing Polysomnographic Evaluation," *Evidence-Based Complementary and Alternative Medicine*, 2013.
- Loh, L., P. W. Nathan, G. D. Schott, and K. J. Zilkha, "Acupuncture Versus Medical Treatment for Migraine and Muscle Tension Headaches," *Journal of Neurology, Neurosurgery, and Psychiatry*, Vol. 47, No. 4, April 1984, pp. 333–337.
- Lombardo, E. N., L. Vehvilainen, W. L. Ooi, L. Volicer, and A. Mcmanus Cet, "Acupuncture to Treat Anxiety and Depression in Alzheimer's Disease and Vascular Dementia: A Pilot Feasibility and Effectiveness Trial," *Proceedings of the World Alzheimer Congress; 2000 Jul 9–13*, Washington, D.C., 2000.
- Lombardo, N. B. E., M. V. B. Dresser, M. Malivert, C. A. Mcmanus, L. Vehvilainen, W. L. Ooi, G. Xu, E. Rosowsky, C. Drebing, P. L. Sheridan, S. Lewis, T. Imada, J. K. Hohnstein, and K.

- Perry, "Acupuncture as Treatment for Anxiety and Depression in Persons with Dementia: Results of a Feasibility and Effectiveness Study," *Alzheimer's Care Quarterly*, Vol. 2, No. 4, 2001, pp. 28–41.
- Lou, H., Y. Jia, X. Wu, and W. Dai, "Electro-Acupuncture in the Treatment of Depressive Psychosis: A Controlled Prospective Randomized Trial Using Electro-Acupuncture and Amitriptyline in 241 Patients," *International Journal of Clinical Acupuncture*, Vol. 1, No. 1, 1990.
- Lu, C. J., Y. Xiang, X. L. Xie, M. L. Xuan, and Z. H. He, "A Randomized Controlled Single-Blind Clinical Trial on 84 Outpatients with Psoriasis Vulgaris by Auricular Therapy Combined with Optimized Yinxieling Formula," *Chinese Journal of Integrative Medicine*, Vol. 18, No. 3, March 2012, pp. 186–191.
- Lu, M. J., S. T. Lin, K. M. Chen, H. Y. Tsang, and S. F. Su, "Acupressure Improves Sleep Quality of Psychogeriatric Inpatients," *Nursing Research*, Vol. 62, No. 2, March–April, 2013, pp. 130–137.
- Luo, H., F. Meng, Y. Jia, and X. Zhao, "Clinical Research on the Therapeutic Effect of the Electro-Acupuncture Treatment in Patients with Depression," *Psychiatry and Clinical Neurosciences*, Vol. 52, Suppl., December 1998, pp. S338–S340.
- Lyons, Z., G. Van Der Watt, Z. Shen, and A. Janca, "Acupuncture and Chinese Herbs as Treatments for Depression: An Australian Pilot Study," *Complementary Therapies in Clinical Practice*, Vol. 18, No. 4, November 2012, pp. 216–220.
- Ma, S. H., S. S. Qu, Y. Huang, J. Q. Chen, R. Y. Lin, C. Q. Wang, G. L. Li, C. H. Zhao, S. C. Guo, and Z. J. Zhang, "Improvement in Quality of Life in Depressed Patients Following Verum Acupuncture or Electroacupuncture Plus Paroxetine: A Randomized Controlled Study of 157 Cases," *Neural Regeneration Research*, Vol. 7, No. 27, September 2012, pp. 2123–2129.
- MacPherson, H., and R. Hammerschlag, "Acupuncture and the Emerging Evidence Base: Contrived Controversy and Rational Debate," *JAMS Journal of Acupuncture and Meridian Studies*, Vol. 5, No. 4, 2012, pp. 141–147.
- MacPherson, H., B. Elliot, A. Hopton, H. Lansdown, and S. Richmond, "Acupuncture for Depression: Patterns of Diagnosis and Treatment Within a Randomised Controlled Trial," *Evidence-Based Complementary and Alternative Medicine*, 2013.
- MacPherson, H., S. Richmond, M. Bland, S. Brealey, R. Gabe, A. Hopton, A. Keding, H. Lansdown, S. Perren, M. Sculpher, E. Spackman, D. Torgerson, and I. Watt, "Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled Trial," *PLoS Medicine*, Vol. 10, No. 9, 2013, p. e1001518.

- Man, S.-C., B. H. B. Hung, R. M. K. Ng, X.-C. Yu, H. Cheung, M. P. M. Fung, L. S. W. Li, L. S. W. Leung, K. W. Y. Tsang, E. Ziea, V. T. Wong, and Z.-J. Zhang, "A Pilot Controlled Trial of a Combination of Dense Cranial Electroacupuncture Stimulation and Body Acupuncture for Post-Stroke Depression," *BMC Complementary Alternative Medicine*, Vol. 14, No. 255, pp. 1–8.
- Margolin, A., S. K. Avants, and R. Arnold, "Acupuncture and Spirituality-Focused Group Therapy for the Treatment of HIV-Positive Drug Users: A Preliminary Study," *Journal of Psychoactive Drugs*, Vol. 37, No. 4, December 2005, pp. 385–390.
- Margolin, A., S. K. Avants, P. Change, and T. R. Kosten, "Acupuncture for the Treatment of Cocaine Dependence in Methadone-Maintained Patients," *American Journal on Addictions*, Vol. 2, No. 3, 1993, pp. 194–201.
- Mazzoni, R., E. Mannucci, S. M. Rizzello, V. Ricca, and C. M. Rotella, "Failure of Acupuncture in the Treatment of Obesity: A Pilot Study," *Eating and Weight Disorders: EWD*, Vol. 4, No. 4, December 1999, pp. 198–202.
- Mcdougall, G. J., "Research Review: The Effect of Acupressure with Massage on Fatigue and Depression in Patients with End-Stage Renal Disease," *Geriatric Nursing*, Vol. 26, No. 3, May–June 2005, pp. 164–165.
- Mehl-Madrona, L. K., B., S. Silverman, H. Lynton, and W. Merrell, "The Impact of Acupuncture and Craniosacral Therapy Interventions on Clinical Outcomes in Adults with Asthma," *Explore (NY)*, Vol. 3, No. 1, 2007, pp. 28–36.
- Mendelson, G., T. S. Selwood, H. Kranz, T. S. Loh, M. A. Kidson, and D. S. Scott, "Acupuncture Treatment of Chronic Back Pain. A Double-Blind Placebo-Controlled Trial," *American Journal of Medicine*, Vol. 74, No. 1, January 1983, pp. 49–55.
- Moffet, H. H., "Acupuncture and Oriental Medicine Update," *Alternative & Complementary Therapies*, Vol. 1, No. 1, 1994, pp. 46–47.
- Molassiotis, A., J. Bardy, J. Finnegan-John, P. Mackereth, D. W. Ryder, J. Filshie, E. Ream, and A. Richardson, "Acupuncture for Cancer-Related Fatigue in Patients with Breast Cancer: A Pragmatic Randomized Controlled Trial," *Journal of Clinical Oncology*, Vol. 30, No. 36, December 20, 2012, pp. 4470–4476.
- Mu, J. P., L. Liu, J. M. Cheng, L. Z. Zhou, J. B. Ao, J. Wang, W. Fang, and J. Hu, "Clinical Study on Electroacupuncture for Post-Withdrawal Anxiety-Depression Mood in Heroin Addicts," *Journal of Acupuncture and Tuina Science*, Vol. 7, No. 4, 2009.
- Nayak, S., S. C. Shiflett, N. E. Schoenberger, S. Agostinelli, S. Kirshblum, A. Averill, and A. C. Cotter, "Is Acupuncture Effective in Treating Chronic Pain After Spinal Cord Injury?"

- Archives of Physical Medicine and Rehabilitation*, Vol. 82, No. 11, November 2001, pp. 1578–1586.
- Painovich, J. M., C. L. Shufelt, R. Azziz, Y. Yang, M. O. Goodarzi, G. D. Braunstein, B. Y. Karlan, P. M. Stewart, and C. N. Merz, “A Pilot Randomized, Single-Blind, Placebo-Controlled Trial of Traditional Acupuncture for Vasomotor Symptoms and Mechanistic Pathways of Menopause,” *Menopause*, Vol. 19, No. 1, Jan, 2012, pp. 54–61.
- Painovich, J., and P. M. Herman, “Acupuncture in the Inpatient Acute Care Setting: A Pragmatic, Randomized Control Trial,” *Evidence-Based Complementary and Alternative Medicine*, 2012, p. 309762.
- Pavao, T. S., P. Vianna, M. M. Pillat, A. B. Machado, and M. E. Bauer, “Acupuncture Is Effective to Attenuate Stress and Stimulate Lymphocyte Proliferation in the Elderly,” *Neuroscience Letters*, Vol. 484, No. 1, October 22, 2010, pp. 47–50.
- Plank, S., J. L. Goodard, L. Pasierb, T. J. Simunich, and J. R. Croner, “Standardized Set-Point Acupuncture for Migraines,” *Alternative Therapies in Health and Medicine*, Vol. 19, No. 6, November–December, 2013, pp. 32–37.
- Rapson, L. M., “Acupuncture: A Useful Treatment Modality,” *Canadian Family Physician*, Vol. 30, January 1984, pp. 109–115.
- Rathbone, J., and J. Xia, “Acupuncture for Schizophrenia,” *Cochrane Database of Systematic Reviews*, No. 4, 2005, pp. 1–4.
- Reshef, A., B. Bloch, L. Vadas, S. Ravid, I. Kremer, and I. Haimov, “The Effects of Acupuncture Treatment on Sleep Quality and on Emotional Measures Among Individuals Living with Schizophrenia: A Pilot Study,” *Sleep Disorders*, Vol. 2013, 2013, p. 327820.
- Rinaldi, S., V. Fontani, L. Aravagli, and M. L. Margotti, “Psychological and Symptomatic Stress-Related Disorders with Radio-Electric Treatment: Psychometric Evaluation,” *Stress and Health*, Vol. 26, No. 5, December 2010, pp. 350–358.
- Rogha, M., M. Rezvani, and A. R. Khodami, “The Effects of Acupuncture on the Inner Ear Originated Tinnitus,” *Journal of Research in Medical Sciences*, Vol. 16, No. 9, September 2011, pp. 1217–1223.
- Romoli, M., and A. Giommi, “Ear Acupuncture in Psychosomatic Medicine: The Importance of the Sanjiao (Triple Heater) Area,” *Acupuncture & Electro-therapeutics Research*, Vol. 18, No. 3–4, July–December 1993, pp. 185–194.
- Salmon, J., “Evaluation of an Acupuncture Service in Oncology,” *Journal of Radiotherapy in Practice*, Vol. 12, No. 1, 2013, pp. 39–55.



- Shulman, L. M., X. Wen, W. J. Weiner, D. Bateman, A. Minagar, R. Duncan, and J. Konefal, "Acupuncture Therapy for the Symptoms of Parkinson's Disease," *Movement Disorders*, Vol. 17, No. 4, July 2002, pp. 799–802.
- Singh, B. B., W. S. Wu, S. H. Hwang, R. Khorsan, C. Der-Martirosian, S. P. Vinjamury, C. N. Wang, and S. Y. Lin, "Effectiveness of Acupuncture in the Treatment of Fibromyalgia," *Alternative Therapies in Health and Medicine*, Vol. 12, No. 2, March–April 2006, pp. 34–41.
- Solan, M., "Heal Thyself: Turning Sad into Glad," *Alternative Medicine Magazine*, No. 92, 2006, pp. 52–54.
- Song, Y., and H. Liang, "Clinical Observation of Depression Following Cerebral Apoplexy Treated by Scalp Acupuncture," *Journal of Acupuncture and Tuina Science*, Vol. 1, No. 5, 2003.
- Stener-Victorin, E., G. Holm, P. O. Janson, D. Gustafson, and M. Waern, "Acupuncture and Physical Exercise for Affective Symptoms and Health-Related Quality of Life in Polycystic Ovary Syndrome: Secondary Analysis from a Randomized Controlled Trial," *BMC Complementary and Alternative Medicine*, Vol. 13, No. 1, June 13, 2013, p. 131.
- Strauss, S., "Acupuncture for Mood and Sleep Disturbance," *Australian Family Physician*, Vol. 17, No. 4, April 1988, pp. 287–289.
- Sun, H., H. Zhao, C. Ma, F. Bao, J. Zhang, D. H. Wang, Y. X. Zhang, and W. He, "Effects of Electroacupuncture on Depression and the Production of Glial Cell Line-Derived Neurotrophic Factor Compared with Fluoxetine: A Randomized Controlled Pilot Study," *Journal of Alternative and Complementary Medicine*, Vol. 19, No. 9, September 2013, pp. 733–739.
- Sun, R., Y. Yang, Z. Li, Y. Li, S. Cheng, and F. Zeng, "Connectomics: A New Direction in Research to Understand the Mechanism of Acupuncture," *Evidence-Based Complementary and Alternative Medicine*, 2014.
- Tian, X., and S. Krishnan, "Efficacy of Auricular Acupressure as an Adjuvant Therapy in Substance Abuse Treatment: A Pilot Study," *Alternative Therapies in Health and Medicine*, Vol. 12, No. 1, January–February, 2006, pp. 66–69.
- Toomey, T. C., J. N. Ghia, W. Mao, and J. M. Gregg, "Acupuncture and Chronic Pain Mechanisms: The Moderating Effects of Affect, Personality, and Stress on Response to Treatment," *Pain*, Vol. 3, No. 2, April 1977, pp. 137–145.
- Tsay, S. L., "Acupressure and Fatigue in Patients with End-Stage Renal Disease—A Randomized Controlled Trial," *International Journal of Nursing Studies*, Vol. 41, No. 1, January 2004, pp. 99–106.

- Tsay, S.L., Y.C. Cho, and M.L. Chen, "Acupressure and Transcutaneous Electrical Acupoint Stimulation in Improving Fatigue, Sleep Quality and Depression in Hemodialysis Patients," *The American Journal of Chinese Medicine*, Vol. 32, No. 3, 2004, pp. 407–416.
- Tse, M., and J. Au, "The Effects of Acupressure in Older Adults with Chronic Knee Pain: Depression, Pain, Activities of Daily Living and Mobility," *Journal of Pain Management*, Vol. 3, No. 4, 2010, pp. 339–410.
- Venzke, L., J. F. Calvert, Jr., and B. Gilbertson, "A Randomized Trial of Acupuncture for Vasomotor Symptoms in Post-Menopausal Women," *Complementary Therapies in Medicine*, Vol. 18, No. 2, April 2010, pp. 59–66.
- Walker, E. M., A. I. Rodriguez, B. Kohn, R. M. Ball, J. Pegg, J. R. Pocock, R. Nunez, E. Peterson, S. Jakary, and R. A. Levine, "Acupuncture Versus Venlafaxine for the Management of Vasomotor Symptoms in Patients with Hormone Receptor-Positive Breast Cancer: A Randomized Controlled Trial," *Journal of Clinical Oncology*, Vol. 28, No. 4, February 1, 2010, pp. 634–640.
- Wang, Y., Y. P. Hu, W. C. Wang, R. Z. Pang, and A. R. Zhang, "Clinical Studies on Treatment of Earthquake-Caused Posttraumatic Stress Disorder Using Electroacupuncture," *Evidence-Based Complementary and Alternative Medicine*, Vol. 2012, 2012, p. 431279.
- Wasan, A. D., J. A. Kong, L. D. Pham, T. J. Kaptchuk, R. Edwards, and R. L. Gollub, "The Impact of Placebo, Psychopathology, and Expectations on the Response to Acupuncture Needling in Patients with Chronic Low Back Pain," *Journal of Pain*, Vol. 11, No. 6, June 2010, pp. 555–563.
- Wayne, P. M., D. E. Krebs, E. A. Macklin, R. Schnyer, T. J. Kaptchuk, S. W. Parker, D. M. Scarborough, C. A. McGibbon, J. D. Schaechter, J. Stein, and W. B. Stason, "Acupuncture for Upper-Extremity Rehabilitation in Chronic Stroke: A Randomized Sham-Controlled Study," *Archives of Physical Medicine & Rehabilitation*, Vol. 86, No. 12, 2005, p. 2248.
- Weiner, D. K., C. G. Moore, N. E. Morone, E. S. Lee, and C. Kent Kwok, "Efficacy of Periosteal Stimulation for Chronic Pain Associated with Advanced Knee Osteoarthritis: A Randomized, Controlled Clinical Trial," *Clinical Therapeutics*, Vol. 35, No. 11, Nov, 2013, pp. 1703–1720.
- White, A., "International Congress on Clinical Research and Quality Management in Complementary Medicine, Munich, Germany 6-8, April 2000: Evidence-Based Complementary Medicine," *Complementary Therapies in Medicine*, Vol. 8, No. 2, 2000, pp. 134–135.
- Whiting, M., G. Leavey, A. Scammell, S. Au, and M. King, "Using Acupuncture to Treat Depression: A Feasibility Study," *Complementary Therapies in Medicine*, Vol. 16, No. 2, April 2008, pp. 87–91.

- Williams, J., and C. Graham, "Acupuncture for Older Adults with Depression—A Pilot Study to Assess Acceptability and Feasibility," *International Journal of Geriatric Psychiatry*, Vol. 21, No. 6, June 2006, pp. 599–600.
- Wu, H. S., L. C. Lin, S. C. Wu, and J. G. Lin, "The Psychologic Consequences of Chronic Dyspnea in Chronic Pulmonary Obstruction Disease: The Effects of Acupressure on Depression," *Journal of Alternative and Complementary Medicine*, Vol. 13, No. 2, March 2007, pp. 253–261.
- Xue, C., P. Xue, Q. Wang, and X. Guo, "Advances in TCM Treatment of Senile Vascular Dementia," *Journal of Traditional Chinese Medicine*, Vol. 22, No. 3, 2002, pp. 228–237.
- Yang, X., X. Liu, H. Luo, and Y. Jia, "Clinical Observation on Needling Extrachannel Points in Treating Mental Depression," *Journal of Traditional Chinese Medicine*, Vol. 14, No. 1, March 1994, pp. 14–18.
- Yue, S. J., "Acupuncture for Chronic Back and Neck Pain," *Acupuncture & Electro-Therapeutics Research*, Vol. 3, No. 3–4, 1978.
- Zhang, C., "The Brain-Resuscitation Acupuncture Method for Treatment of Post Wind-Stroke Mental Depression—A Report of 45 Cases," *Journal of Traditional Chinese Medicine*, Vol. 25, No. 4, December 2005, pp. 243–246.
- Zhang, Z., R. Ng, M. S. C. Man, J. Li, W. Wong, H. K. Wong, D. Wang, M. Wong, A. Tsang, K. Yip, and C. W. Sze, "Use of Electroacupuncture to Accelerate the Antidepressant Action of Selective Serotonin Reuptake Inhibitors: A Single-Blind, Randomized, Controlled Study," *Hong Kong Medical Journal*, Vol. 19, No. 9, 2013, pp. 12–19.
- Zheng, Z., R. J. Guo, R. D. Helme, A. Muir, C. Da Costa, and C. C. Xue, "The Effect of Electroacupuncture on Opioid-Like Medication Consumption by Chronic Pain Patients: A Pilot Randomized Controlled Clinical Trial," *European Journal of Pain*, Vol. 12, No. 5, July 2008, pp. 671–676.
- Zollman, F. S., E. B. Larson, L. K. Wasek-Throm, C. M. Cyborski, and R. K. Bode, "Acupuncture for Treatment of Insomnia in Patients with Traumatic Brain Injury: A Pilot Intervention Study," *Journal of Head Trauma Rehabilitation*, Vol. 27, No. 2, March–April 2012, pp. 135–142.



## Appendix C: Evidence Tables of Included Studies

**Table C.1. Monotherapy Acupuncture Studies**

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Allen et al., 1998</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To assess the efficacy of acupuncture for major depression (SPEC) compared with nonspecific acupuncture (NONSPEC) and a waitlist control on depressive symptoms</p> <p><b>Country:</b> United States</p> <p><b>Quality rating:</b> Fair</p>	<p><b>Number of patients:</b> 38 initial, 33 final</p> <p><b>Method of identifying participants with MDD:</b> Diagnosis of current MDD according to DSM-IV assessed using the Structured Clinical Interview for DSM-III-R</p> <p><b>Baseline depressive symptom score:</b> DepHRSD (contains 19 items from HRSD<sub>31</sub>) Baseline: SPEC: 26.9 (6.7) NONSPEC: 20.5 (4.5) Waitlist: 27.7 (6.8) * Nonspecific group significantly less depressed at baseline (p&lt;0.05) than the NONSPEC and Waitlist groups, which did not differ significantly from one another.</p> <p><b>Depression severity:</b> Mild to moderate depression</p> <p><b>Average age in years (SD):</b> Not reported</p> <p><b>Gender:</b> 0% male</p> <p><b>Inclusion criteria:</b> Met the diagnostic criteria for current major depression as outlined in the DSM-IV.</p> <p><b>Exclusion criteria:</b> Dysthymia or chronic major depression (duration greater than 2 years), any current Axis I diagnosis besides MDD, history of psychosis or mania, substance abuse or dependence within the past 4 months, any current treatment, endocrine abnormalities, history of central nervous system lesions or any medical disorder or treatment that could cause depression, active suicidal potential</p>	<p><b>Type of needle acupuncture:</b> Acupuncture (SPEC): Treatment plans developed according to standardized manual developed by authors and administered by board-certified acupuncturists.</p> <p><b>Dosage:</b> 2 sessions a week for the first 4 weeks, followed by 1 session per week for total of 12 sessions (length of session not reported). Dosage the same for the SPEC and NONSPEC acupuncture groups.</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> Nonspecific acupuncture (NONSPEC): Participants received 8 weeks of acupuncture at points not associated with depression</p> <p>Waitlist: Patients waited 8 weeks before receiving depression-specific acupuncture</p> <p><b>Follow-up:</b> At end of 8-week intervention</p>	<p><b>Depressive symptoms, DepHRSD, change score:</b> SPEC: -11.7 (7.3) NONSPEC: -2.9 (7.9) Waitlist: -6.1 (10.9) ITT Sample: Significantly greater rate of decline in symptom scores for SPEC compared with NONSPEC (p&lt;0.05). Rate of decline in SPEC was not significantly different from waitlist (p&lt;0.12).</p> <p><b>Depressive symptoms, BDI, change score:</b> SPEC: -10.7 (7.8) NONSPEC: -3.4 (7.4) Waitlist: Not assessed Completers: Significantly greater reduction in symptom scores for SPEC than NONSPEC (p&lt;0.05).</p> <p><b>Depressive symptoms, Inventory of Depression Symptomology (IDS), change score:</b> SPEC: -18.5 (11.8) NONSPEC: -8.5 (9.0) Waitlist: Not assessed Completers Only: Significantly greater reduction in symptom scores for SPEC than NONSPEC (p&lt;0.05).</p> <p><b>Response</b> (at least a 50% reduction in DepHRSD score): SPEC: 50% NONSPEC: 27% Waitlist: 27% No significance test reported.</p> <p><b>Remission</b> (by DSM-IV criteria, absence of both core symptoms of depression – depressed mood and anhedonia): SPEC: 42% NONSPEC: 9% Waitlist: 20% No significance test reported</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
	necessitating immediate treatment, or pregnancy.		<b>Relapse:</b> N/A <b>Health-related quality of life:</b> N/A <b>Adverse events:</b> Not reported

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Allen et al., 2006</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To test the efficacy of acupuncture as a monotherapy for MDD, comparing (1) acupuncture specific for depression (SPEC) with an active valid acupuncture control that was not tailored to address an individual's symptoms of depression (NONSPEC) and (2) a waitlist control</p> <p><b>Country:</b> United States</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 151 initial, 131 final</p> <p><b>Method of identifying participants with MDD:</b> Current MDD diagnosed via the Structured Clinical Interview for DSM-IV</p> <p><b>Baseline depressive symptom score:</b>  <b>Baseline (HRSD<sub>17</sub>):</b>  SPEC: 22.1 (4.8)  NONSPEC: 22.0 (5.0)  Waitlist: 22.8 (4.2)  <b>Baseline (BDI):</b>  SPEC: 28.0 (6.6)  NONSPEC: 28.7 (7.5)  Waitlist: 28.7 (7.4)</p> <p><b>Depression severity:</b> Mild to moderate depression</p> <p><b>Average age in years (SD):</b> Overall: 41.2 (11.0); SPEC: 39.7 (9.9); NONSPEC: 42.2 (10.6); Waitlist: 41.6 (12.5)</p> <p><b>Gender:</b> Overall: 31% male; SPEC: 32% male; NONSPEC: 33% male; Waitlist: 29% male</p> <p><b>Inclusion criteria:</b> Aged 18–65 years; met DSM-IV criteria for current MDD (assessed by structural interview); HAMD<sub>17</sub> score ≥14.</p> <p><b>Exclusion criteria:</b> Dysthymia or chronic MDD (&gt;2 years); seasonal pattern; any current Axis I diagnosis besides MDD; any Axis II Cluster B disorder; history of psychosis or mania; substance abuse or dependence within the past 4 months; any current relevant treatment; endocrine abnormalities (e.g., hypothyroidism, unstable diabetes); history of central nervous system involvement (e.g., seizures, brain injury, neurologic illness); any medical disorder or treatment believed by the investigators to cause depression; active suicidal risk necessitating immediate intervention or suicide attempt within the past year; or pregnancy.</p>	<p><b>Type of needle acupuncture:</b>  Acupuncture (SPEC):  Acupuncture points were individualized according to principles of TCM with manual moderate stimulation and <i>de qi</i> achieved. Performed by a NCCAOM board-certified acupuncturist.</p> <p><b>Dosage:</b> SPEC AND NONSPEC: 20 minutes of needle retention 2 times a week for 4 weeks, then 1 time week for another 4 weeks (for total of 12 sessions in 8 total weeks)</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> Nonspecific acupuncture (NONSPEC): Acupuncture was conducted at meridian points associated with conditions other than depression</p> <p>Waitlist control group. Patients waited 8 weeks before receiving depression-specific acupuncture</p> <p><b>Follow-up:</b> At the end of the 8-week intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b>  <b>Baseline:</b>  SPEC: 22.1 (4.8)  NONSPEC: 22.0 (5.0)  Waitlist: 22.8 (4.2)  <b>End of intervention:</b>  Means and SDs not reported.  Random regression analysis showed significantly greater improvement in both the SPEC and NONSPEC groups compared with the waitlist (p&lt;0.001), but no significant difference in improvement between SPEC and NONSPEC (p&gt;0.2).</p> <p><b>Depressive symptoms, BDI:</b>  <b>Baseline:</b>  SPEC: 28.0 (6.6)  NSPEC: 28.7 (7.5)  Waitlist: 28.7 (7.4)  <b>End of intervention:</b>  Means and SDs not reported  Random regression analysis showed significantly greater improvement in both the SPEC and NONSPEC groups compared with the waitlist (p&lt;0.001), but no significant difference in improvement between SPEC and NONSPEC (p&gt;0.17).</p> <p><b>Response rate:</b>  (≥50% reduction in HRSD)  SPEC: 22% (11/50)  NONSPEC: 39% (19/49)  Waitlist: 17% (9/52)  Response rate in the SPEC group was not significantly different from the NONSPEC (p&lt;0.07) or waitlist groups (p=n.s.). Response rate in NONSPEC group was significantly higher than in waitlisted group (p&lt;0.05).</p> <p><b>Remission</b>  (HSRD &lt;7 and ≥50% reduction in HRSD score)  SPEC: 16% (8/50)  NONSPEC: 33% (16/49)  Waitlist: 8% (4/52)</p> <p>Remission rate in the SPEC group was not significantly different from the NONSPEC (p&lt;0.06) or</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
			<p>waitlist groups (p=n.s.). Response rate in NONSPEC group was significantly higher than in waitlisted group (p&lt;0.05).</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Assessed systematically on a weekly basis using structured form for the specific and nonspecific acupuncture groups and categorized using the Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART). Adverse reactions were not assessed in waitlist control. Five participants reported needle-related pain; one person discontinued the trial due to needle-related pain.</p> <p>SPEC: 62% (31/50) experienced at least one adverse event, including somatic symptoms (62%), pain symptoms (26%), intensification of sleep difficulties (20%), intensification of emotions/emotional reactions (18%), unusual perceptual experiences (12%), miscellaneous (4%), intervention error (2%), suicide (0%).</p> <p>NONSPEC: 65% (32/49) experienced at least one adverse event, including somatic symptoms (63%), pain symptoms (18%), intensification of sleep difficulties (20%), intensification of emotions/emotional reactions (18%), unusual perceptual experiences (4%), miscellaneous (10%), suicide (2%).</p>



Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Andreescu et al., 2011</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> No</p> <p><b>Purpose:</b> To compare the efficacy and tolerability of electroacupuncture (EA) and sham acupuncture for the treatment of mild or moderate MDD</p> <p><b>Country:</b> United States</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 57 initial, 46 final</p> <p><b>Method of identifying participants with MDD:</b> clinical diagnosis of current depression according to DSM-IV</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>17</sub> Baseline: EA: 17.7 (3.9) Sham: 18.6 (2.9)</p> <p><b>Depression severity:</b> Mild to moderate depression</p> <p><b>Average age in years (SD):</b> EA: 46.0 (11.5); Sham: 49.1 (14.0)</p> <p><b>Gender:</b> EA: 25% male, Sham: 32% male</p> <p><b>Inclusion criteria:</b> Aged 18–80 years; met criteria for mild or moderate MDD according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID), HDRS score<math>\geq</math>14.</p> <p><b>Exclusion criteria:</b> Severe MDD (as per SCID criteria); acute suicidality; seizure disorder or significant risk factors for a seizure disorder (i.e., history of brain trauma, recent stroke, brain tumor); psychosis; bipolar disorder; chronic MDD (as per SCID criteria; i.e., duration of 2 years or longer); treatment-resistant MDD, defined as having failed at least 1 adequate antidepressant trial; history of substance abuse in the 6 months prior to enrollment.</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture at <i>Du 20</i> and <i>Yingtang</i> with a current of 3-5 mA and frequency of 2 Hz for 30 minutes</p> <p><b>Dosage:</b> 30 minutes, 2 times per week for 6 weeks</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> 1 comparison group: Nonmeridian/sham electroacupuncture: Needling was conducted at two points remote from any classical meridian or extraordinary points on the scalp. No current was applied. 12 sessions, 30 minutes each, 2 sessions/week for 6 weeks</p> <p><b>Follow-up:</b> At end of intervention; 2 weeks after end of treatment</p>	<p><b>Depressive symptoms, HRSD:</b> Baseline HRSD<sub>17</sub>: EA: 17.7 (3.9) Sham: 18.6 (2.9) 2 Weeks Post Treatment (mixed-effects model): EA: Change from baseline: -6.6 (5.9) Sham: Changes from baseline: -7.6 (6.6) Mixed-effects model found no difference between groups in change from baseline to follow-up (p=0.69).</p> <p><b>Response:</b> EA: 40.0% Sham: 44% No significant difference in response rate (at least a 50% reduction and HRSD&lt;10): p=0.77.</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life, Medical Outcome Study (MOS)-SF-36 Physical Component:</b> Baseline: EA: 48.8 (9.9) Sham: 48.8 (11.8) 2 Weeks Post-Treatment : EA: Changes from baseline: 0.5 (6.9) Sham: Changes from baseline: -1.7 (8.0) Between-group comparison: t-stat= -1.00, p=0.32</p> <p><b>Health-related quality of life, MOS-SF-36 Mental Component:</b> Baseline: EA: 27.1 (9.0) Sham: 25.8 (10.9) 2 Weeks Post-Treatment: EA: Change from baseline: 6.2 (13.6) Sham: Change from baseline: 14.1 (17.5) Between-group comparison: t-stat=1.56, p =0.09</p> <p><b>Health-related quality of life, MOS-SF-36 Bodily Pain Index:</b> Baseline: EA: 62.5 (24.8) Sham: 60.3 (23.7)</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
			<p>2 Weeks Post-Treatment:  EA: Change from baseline: -1.0 (18.3)  Sham: Change from baseline: 6.8 (19.7)  Between-group comparison: t-stat=1.40, p=0.17</p> <p><b>Health-related quality of life, Global Assessment of Functioning:</b>  Baseline:  EA: 60.5 (6.1)  Sham: 59.2 (5.2)  2 Weeks Post-Treatment:  EA: Change from baseline: 10.3 (10.3)  Sham: Change from baseline: 11.4 (8.8)  Between-group comparison: t-stat=0.39, p=0.70</p> <p><b>Adverse events:</b> Systematically assessed with the UKU Side Effects Rating Scale.  No serious adverse events reported. UKU scores not significantly different between groups at end of treatment.</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Chung et al., 2012</p> <p><b>Study design:</b> Multisite (3) RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To examine the efficacy of active acupuncture versus noninvasive sham acupuncture for the treatment of postpartum depression. Feasibility and tolerability also assessed.</p> <p><b>Country:</b> Hong Kong, China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 20 initial, 14 final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of MDD according to DSM-IV</p> <p><b>Baseline depressive symptom score:</b> Hospital Anxiety and Depression Scale (HADS)-Depression Baseline: EA: 11.6 (2.4) Sham: 10.6 (3.1)</p> <p>HRSD<sub>17</sub> Baseline: EA: 14.4 (2.4) Sham: 14.6 (2.3)</p> <p>Edinburgh Postnatal Depression Scale (EPDS) Baseline: EA: 16.7 (3.9) Sham: 16.3 (3.1)</p> <p><b>Depression severity:</b> All with mild depression (HDRS<sub>17</sub> score 12–19)</p> <p><b>Average age in years (SD):</b> Total: 34.9 (3.6); EA: 35.3 (4.7); Sham: 34.4 (2.2)</p> <p><b>Gender:</b> 0% male</p> <p><b>Inclusion criteria:</b> Ethnic Chinese; permanent resident in Hong Kong; over age 18; within six months of giving birth; EPDS<math>\geq</math>12; diagnosis of MDD based on the DSM-IV criteria assessed by clinician; HDRD<sub>17</sub> between 12–19; sufficient understanding of trial protocol and willingness to give informed consent and comply with the protocol.</p> <p><b>Exclusion criteria:</b> Previous diagnosis of schizophrenia, other psychotic disorders, bipolar disorder, or alcohol or substance use disorder; significant risk of suicide or infanticide according to the clinician; any serious physical illness; (valvular heart defects or bleeding disorders); taking anticoagulant drugs; infection or abscess close to the site of selected acupoints; received acupuncture during the 12 months prior to baseline; taking herbal remedies or psychotropic drugs that were intended for</p>	<p><b>Type of needle acupuncture:</b> Cranial and body electroacupuncture: Cranial acupoints included six pairs: <i>Baihui</i>, <i>Yintang</i>, left <i>Sishencong</i> and <i>Toulingqi</i>, right <i>Sishencong</i> and <i>Toulingqi</i>, bilateral <i>Shuaigu</i>, bilateral <i>Taiyang</i>, and bilateral <i>Touwei</i>; body acupoints included bilateral <i>Sanyinjiao</i>, bilateral <i>Taichong</i>, <i>Shenmen</i> and <i>Neiguan</i>, selected according to TCM principles. Manual stimulation used to achieve <i>de qi</i>. Electrical stimulation applied with a 6-volt, biphasic triangular, brief-pulse in 2-Hz frequency.</p> <p><b>Dosage:</b> 30 minutes, 2 times per week for 4 weeks</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> 1 comparison group: Sham acupuncture: Participants were treated 2 times per week for 4 weeks at the same acupoints as the treatment group using Streitberger's placebo needles</p> <p><b>Follow-up:</b> At end of intervention; 4 weeks post-intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b> Baseline: EA: 14.4 (2.4) Sham: 14.6 (2.3) End of intervention: EA: 11.3 (4.8) Sham: 9.6 (3.4) 4 Weeks Post-Treatment EA: 9.3 (4.7) Sham: 8.6 (4.1) Difference between groups was nonsignificant (p=0.21).</p> <p><b>Depressive symptoms, HADS-Depression:</b> Baseline: EA: 11.6 (2.4) Sham: 10.6 (3.1) End of intervention: EA: 8.8 (3.8) Sham: 7.3 (1.6) 4 Weeks Post-Treatment EA: 9.2 (4.2) Sham: 7.2 (2.7) Difference between groups was nonsignificant (p=0.78).</p> <p><b>Depressive symptoms, EPDS:</b> Baseline: EA: 16.7 (3.9) Sham: 16.3 (3.1) End of intervention: EA: 11.1 (5.0) Sham: 11.4 (4.9) 4 Weeks Post-Treatment EA: 10.9 (5.8) Sham: 12.2 (6.3) Difference between groups was nonsignificant (p=0.56).</p> <p><b>Response:</b> (50% reduction in HRSD) End of intervention: EA: 12.5% (1/8) Sham: 30.0% (3/10) 4-Weeks post-intervention: EA: 33.3% (3/9)</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
	depression within the two weeks prior to baseline or during the study; receiving counseling or psychological therapies.		<p>Sham: 60.0% (9/19) Differences between the EA and sham groups were not significant at the end of intervention (p=0.59) or at follow-up (p=0.37).</p> <p><b>Remission:</b> (HRSD&lt;7) <u>End of intervention:</u> EA: 12.5% (1/8) Sham: 20.0% (3/18) <u>4-Weeks post-intervention:</u> EA: 44.4% (4/6) Sham: 50.0% (9/19) Differences between the EA and sham groups were not significant at the end of intervention (p=1.00) or at follow-up (p=1.00).</p> <p><b>Relapse:</b> NA</p> <p><b>Health-related quality of life, Sheehan Disability Scale – Work Subscale:</b> <u>Baseline:</u> EA: 4.6 (2.3) Sham: 5.3 (1.9) <u>End of intervention:</u> EA: 3.8 (3.3) Sham: 2.5 (1.7) <u>4 Weeks Post-Treatment</u> EA: 3.7 (3.4) Sham: 2.3 (2.4)</p> <p><b>Health-related quality of life, Sheehan Disability Scale – Social Subscale:</b> <u>Baseline:</u> EA: 5.4 (2.8) Sham: 4.7 (1.9) <u>End of intervention:</u> EA: 3.6 (3.0) Sham: 2.8 (1.9) <u>4 Weeks Post-Treatment</u> EA: 3.4 (3.2) Sham: 2.7 (2.3) Between group: p=0.84</p> <p><b>Health-related quality of life, Sheehan Disability Scale – Family Subscale:</b> <u>Baseline:</u></p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
			<p>EA: 4.4 (1.8)            Sham: 5.1 (2.5)  <u>End of intervention:</u>            EA: 3.1 (2.6)            Sham: 2.9 (1.7)  <u>4 Weeks Post-Treatment</u>            EA: 3.2 (2.5)            Sham: 3.2 (2.0)</p> <p>No significant differences in improvement between groups on any of the three subscales (work, social, family) at end of treatment.</p> <p><b>Adverse events:</b> Systematically assessed via open-ended question asked by research assistant.            EA group: 6 reported adverse events, including needle site pain (n=1, withdrew from study); bruises at needle site (n=1); discomfort at needle site (n=2); headache (n=2); and dizziness (n=1).            Sham: 5 reported adverse events, including rash at needle site (n=1); discomfort at needle site (n=1); headache (n=2); dizziness (n=1); and tiredness (n=1).</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Huang et al., 2005</p> <p><b>Study design:</b> Multisite (4) RCT</p> <p><b>ITT analysis:</b> Not applicable. No dropout</p> <p><b>Purpose:</b> To study the effects of electro-scalp acupuncture by clinical surveys and positron emission tomography to treat depression, compared with oral fluoxetine</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Fair</p>	<p><b>Number of patients:</b> 98 initial and final</p> <p><b>Method of identifying participants with MDD:</b> Meets the standard for depression in the Chinese Classification and Diagnostic Criteria of Mental Disorders, 3rd ed.</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>24</sub> Baseline: EA: 23.45 (4.52) Fluoxetine (FLX): 24.65 (5.24)</p> <p><b>Depression severity:</b> Mild to serious depression (by BDI scores)</p> <p><b>Average age in years (SD):</b> 36.72 (9.63)</p> <p><b>Gender:</b> 36.7% male</p> <p><b>Inclusion criteria:</b> Diagnostic criteria of the Chinese Classification and Diagnostic Criteria of Mental Disorders, 3rd ed.; HRSD<sub>24</sub> score &gt; 16.</p> <p><b>Exclusion criteria:</b> Organic psychotic disorders; depression secondary to psychotropic or nonaddictive substances; diseases such as multi-system failure, hemophilia, and acute cerebral hemorrhage, for which acupuncture were contraindicated; serious mental dysfunction preventing cooperation with the treatment; use of psychotropic medications and herbs for at least two weeks before starting the treatment; unwilling to abstain from medication for the duration of the treatment.</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture at acupoints: Middle Line of Vertex (MS5), Middle Line of Forehead (MS1), and bilateral Lateral Line 1 of Forehead (MS2). Manual manipulation used to achieve <i>de qi</i>.</p> <p>Electric stimulation was applied for 30 minutes at 50 Hz and 2 mA.</p> <p><b>Dosage:</b> 30 minutes, 6 days weekly for 6 weeks, 36 sessions</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> Medication group: oral fluoxetine 20–40 mg per day for 6 weeks</p> <p><b>Follow-up:</b> At end of intervention</p>	<p><b>Depressive symptoms, HRSD<sub>24</sub>:</b> Baseline: EA: 23.45 (4.52) FLX: 24.65 (5.24) End of intervention: EA: 9.68 (5.30) FLX: 9.32 (2.85) No significant difference between groups (<math>p &gt; 0.05</math>)</p> <p><b>Depressive symptoms, BDI:</b> Baseline: EA: 26% serious, 40% medium, 34% mild, and 0% no depression FLX: 29% serious, 42% medium, 29% mild, 0% no depression End of intervention: EA: 4% serious, 10% medium, 26% mild, and 60% no depression FLX: 0% serious, 13% medium, 21% mild, 67% no depression No significant differences in improvement between groups (<math>p &gt; 0.05</math>).</p> <p><b>Response:</b> EA: 56% experienced at least a 50% reduction in HRSD score (obviously effective); 36% experienced a 25–50% reduction in HRSD score (effective), and 8% experienced &lt;25% reduction in HRSD score (not effective) FLX: 64.58% experienced at least a 50% reduction in HRSD score (obviously effective); 27.08% experienced a 25–50% reduction in HRSD score (effective), and 8.34% experienced &lt;25% reduction in HRSD score (not effective) No significant difference between groups (<math>p &gt; 0.05</math>)</p> <p><b>Remission:</b> N/A <b>Relapse:</b> N/A <b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Systematically assessed using TESS. EA: distending pain during needling stimulation (n=3) FLX : uncomfortable feeling in the abdomen (n=1), mild insomnia (n=1)</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Manber, Schnyer, Allen, et al., 2004</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Modified ITT</p> <p><b>Purpose:</b> To evaluate the efficacy and safety of acupuncture (SPEC) as a treatment for depression during pregnancy, compared with control acupuncture (NONSPEC) and massage (MSSG).</p> <p><b>Country:</b> United States</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 61 initial, 54 at least one post-randomization evaluation (ITT sample), 47 completed follow-up</p> <p><b>Method of identifying participants with MDD:</b> Current major depressive episode according to DSM-IV assessed with the SCID-IV</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>17</sub>: 21.0 (4.2)</p> <p><b>Depression severity:</b> Not reported</p> <p><b>Average age in years (SD):</b> 33.3 (4.7)</p> <p><b>Gender:</b> 0% male</p> <p><b>Inclusion criteria:</b> 18 years or older, gestation age between 11 and 28 weeks at screening, receipt of prenatal care in the community, satisfy DSM-IV criteria for current nonpsychotic major depressive episode, HRSD<sub>17</sub> score≥14.</p> <p><b>Exclusion criteria:</b> Index major depressive episode lasting 2 years or more; psychotic features or a seasonal pattern; current active suicide potential; cluster B Axis II disorder or other Axis I disorders in the past 2 months, except for simple phobia, social phobia, or generalized anxiety disorder (determined by the SCID-IV and the SCID-II); abnormal thyroid panel; an uncontrolled medical condition; a condition that may be a medical basis for depression; current use of any medication that impacts mood; confounding treatments for depression; conditions that necessitate bed rest, massage, or acupuncture during study period other than what was provided by the study.</p>	<p><b>Type of needle acupuncture:</b> Acupuncture was individually tailored following the principles of traditional Chinese medicine</p> <p><b>Dosage (all groups):</b> Acute phase: 25–30 minutes, 12 sessions in 8 weeks. At the end of the acute phase, responders continued to receive biweekly treatment until delivery and weekly treatment until 8 weeks postpartum.</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> 2 comparison groups</p> <p>Acupuncture at nondepression points</p> <p>Massage: Provided in a standardized fashion. Same duration and frequency as acupuncture treatments</p> <p><b>Follow-up:</b> At end of intervention; 10 weeks postpartum</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b>  Baseline: Total 24.0 (4.2) with no differences across groups (p&gt;0.05)  End of intervention:  SPEC: 9.6 (7.8)  NONSPEC: 12.6 (7.5)  MSSG: 10.3 (5.6)  10 weeks postpartum (among initial responders):  SPEC: 8.6 (6.5)  NONSPEC: 9.5 (7.4)  MSSG: 9.3 (6.4)  No significant differences between groups on continuous HRSD scores.</p> <p><b>Depressive symptoms, BDI:</b>  Baseline: Not reported  End of intervention:  SPEC: 9.2 (6.1)  NONSPEC: 12.2 (5.4)  MSSG: 10.0 (4.0)  10 Weeks Postpartum (among initial responders):  SPEC: 6.9 (7.7)  NONSPEC: 10.8 (9.8)  MSSG: 10.2 (6.6)  No significant differences in improvement between groups.</p> <p><b>Response</b> (defined jointly by (a) failure to meet full criteria for MDD; (b) at least 50% reduction from baseline HRSD<sub>17</sub> score; and (c) HRSD<sub>17</sub>≤14):  SPEC: 68.8%  NONSPEC: 47.4%  MSSG: 31.6%  Significantly greater response in specific acupuncture relative to massage (p=0.031) but not relative to nonspecific acupuncture (p=0.18).</p> <p><b>In full remission</b> (among responders, HRSD≤8):  SPEC: 85.7%  NONSPEC: 50%  MSSG: 66.7%</p> <p><b>Relapse:</b> N/A  <b>Health-related quality of life:</b> N/A  <b>Adverse events:</b> Not reported</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Manber, Schnyer, Lyell, et al., 2010</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To estimate the efficacy of acupuncture for treatment of depression (SPEC) during pregnancy compared with both acupuncture nonspecific (NONSPEC) for depression and a massage group (MSSG).</p> <p><b>Country:</b> United States</p> <p><b>Quality rating:</b> Fair</p>	<p><b>Number of patients:</b> 150 initial, 108 final</p> <p><b>Method of identifying participants with MDD:</b> Diagnosis of current MDD according to DSM-IV assessed by the Structured Clinical Interview for DSM-IV</p> <p><b>Baseline depressive symptom score:</b>  HRSD<sub>17</sub> Baseline:  SPEC: 21.5 (3.8)  NONSPEC: 20.3 (3.6)  MSSG: 20.4 (3.6)</p> <p><b>Depression severity:</b> Not reported</p> <p><b>Average age in years (SD):</b> SPEC: 32.4 (4.0); NONSPEC: 33.4 (5.0); MSSG: 32.8 (5.6)</p> <p><b>Gender:</b> 0% male</p> <p><b>Inclusion criteria:</b> Between 12 to 30 weeks of gestation, 18 years or older, meet criteria for MDD according to the DSM-IV-TR determined by the Structured Clinical Interview for the DSM-IV, and HRSD<sub>17</sub> ≥14.</p> <p><b>Exclusion criteria:</b> Other current primary Axis I psychiatric disorders, except social phobia; seasonal affective disorder or psychotic features; abnormal thyroid panel or drug screen results; serious uncontrolled medical conditions or conditions that may be a medical basis of depression; cluster B personality disorders (determined by the Structured Clinical Interview for DSM-IV, Axis II disorders); current psychotherapy, herbs, or psychotropic medications; electroconvulsive therapy or vagal nerve stimulation in the past year; current active suicide potential necessitating immediate treatment; absence of prenatal care; and conditions necessitating bed rest.</p>	<p><b>Type of needle acupuncture:</b> Acupuncture for depression tailored individually to address each participant's specific symptoms according to the principles of TCM. Manual stimulation applied until <i>de qi</i> achieved.</p> <p><b>Dosage:</b> 25 minutes, 2 times per week for the first 4 weeks and weekly for the next 4 weeks (for a total of 12 sessions)</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> 2 comparison groups</p> <p>Nonspecific acupuncture: Participants received standardized acupuncture at real acupuncture points not associated with treatment for depression</p> <p>Massage group: Swedish massage was provided in a standardized fashion</p> <p><b>Follow-up:</b> At end of 8-week intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b>  <b>Baseline:</b>  SPEC: 21.5 (3.8)  NONSPEC: 20.3 (3.6)  MSSG: 20.4 (3.6)  <b>End of Intervention:</b>  Values not reported  The depression-specific acupuncture group showed more improvement than nonspecific acupuncture (p&lt;0.05, Cohen's d = 0.46) but no significant difference in improvement from the massage group (p=0.13).</p> <p><b>Response rate</b> (50%+ reduction in HSRD<sub>17</sub> score, HSRD<sub>17</sub> score between 7–14, and failure to meet full DSM-IV MDD criteria):  SPEC: 63.0% (29/46)  NONSPEC: 37.5% (15/40)  MSSG: 50% (24/48)  The response rate was significantly higher for the group receiving acupuncture specific for depression (compared with the nonspecific acupuncture group) (p&lt;0.05, number needed to treat=3.9), but was not significantly different from the massage group (p=0.20).</p> <p><b>Remission rate</b> (the absence of the core symptoms of depression and HSRD<sub>17</sub>≤7):  SPEC: 34.8% (16/46)  NONSPEC: 27.5% (11/40)  MSSG: 31.2% (15/48)  Remission was not significantly different between the group receiving acupuncture specific for depression and the nonspecific acupuncture group (p=0.47) or the massage group (p=0.72).</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Study reported both severe adverse events and milder side effects. Ten severe adverse events occurred, but the rates were not significantly different between groups. The adverse events were assessed as not related to treatment.</p>



Study Details	Patients	Intervention/Treatment	Outcomes/Results
			<p>SPEC: premature delivery of twins, with one neonatal demise and the surviving twin receiving prolonged neonatal intensive care (n=1); congenital defects among neonate (n=1); preeclampsia (n=2)</p> <p>NONSPEC: pregnancy loss (n=1); hospitalization with dehydration and low amniotic fluid (n=1)</p> <p>MSSG: congenital defects among neonate (n=1); hospitalization for esophageal spasms (n=1); hospitalization for isolated atrial fibrillation (n=1); hospitalization for premature contractions (n=1)</p> <p>Participants recorded side effects weekly. Treatment providers recorded side effects observed or reported to the provider by participants. 43 participants with side effects: massage (4), nonspecific (19), specific (20).</p> <p>Significantly fewer participants reported any side effects in the group receiving prenatal massage (8%) than in the two acupuncture groups (18%, p&lt;0.01).</p> <p>Treatment-related side effects in acupuncture groups: transient discomfort at needling sites (n=21), bleeding at needling site (n=1). None of these side effects led to discontinuation from the study.</p> <p>Treatment-related side effects in massage group: transient discomfort (n=5). None of these side effects led to discontinuation from the study.</p> <p>Other side effects not directly associated with treatment included: tiredness after treatment (SPEC=10, NONSPEC=9, massage=4), irritability or agitation after treatment (SPEC=2, NONSPEC=2), sleep disturbance (SPEC=1, NONSPEC=2), headache after treatment (SPEC=3, NONSPEC=1), nausea after treatment (SPEC=2), aggravation of depression (SPEC=1, NONSPEC=1).</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Song, Zhou, et al., 2007</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> No</p> <p><b>Purpose:</b> To evaluate and compare the therapeutic efficacy and the level of G protein in platelet membranes of electroacupuncture (EA) versus sham acupuncture + fluoxetine and sham acupuncture + placebo in depressed patients</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 90 initial, 81 final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of current depression according to DSM-IV</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>24</sub> Baseline: EA + placebo: 25.3 (3.5) Sham acupuncture + FLX: 25.1 (3.1) Sham acupuncture + placebo: 25.4 (4.2)</p> <p><b>Depression severity:</b> Not reported</p> <p><b>Average age in years (SD):</b> EA + placebo: 30.8 (10.9); Sham acupuncture + FLX: 33.9 (12.4); Sham acupuncture + placebo: 30.5 (12.0)</p> <p><b>Gender:</b> Not reported</p> <p><b>Inclusion criteria:</b> Met DSM-IV criteria for a diagnosis of MDD, HAMD score≥20</p> <p><b>Exclusion criteria:</b> Suicidal ideation and psychotic symptoms</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture plus placebo medication: Participants received electroacupuncture at <i>Yintang</i> and <i>Baihui</i> points with electrical current of 10–40 mA. Placebo capsules were given.</p> <p><b>Dosage:</b> 45 minutes, 5 days a week for 6 weeks</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> Medication plus needling at nontherapeutic points: oral fluoxetine 20 mg/day for 6 weeks; acupuncture 1 cm away from points used in the treatment group (no electric current)</p> <p>Placebo medication plus needling at nontherapeutic points: 20 mg placebo/day plus acupuncture 1 cm away from points used in the treatment group (no electric current)</p> <p><b>Follow-up:</b> At end of 6-week intervention</p>	<p><b>Depressive symptoms, HRSD<sub>24</sub>:</b> Baseline: EA + placebo: 25.3(3.5) Sham acupuncture + FLX: 25.1 (3.1) Sham acupuncture + placebo: 25.4 (4.2) End of intervention: EA + placebo: 12.0(6.7) Sham acupuncture + FLX: 12.4 (7.2) Sham acupuncture + placebo: 12.9 (7.9) No significant difference between the three groups at pretest or posttest (p=0.996)</p> <p><b>Response:</b> N/A</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not reported</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Song, Halbreich, et al., 2009</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Not applicable. No dropout.</p> <p><b>Purpose:</b> To evaluate and compare the effectiveness of electroacupuncture (EA) and fluoxetine (FLX) on pro- and anti-inflammatory cytokines</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Fair</p>	<p><b>Number of patients:</b> 95 initial and final (healthy controls recruited for immune comparison not counted here)</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of current depression according to DSM-IV</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>21</sub> Baseline: EA + placebo: 22.42 (2.93) Sham acupuncture + FLX: 22.16 (2.16) Sham acupuncture + placebo: 22.84 (3.47)</p> <p><b>Clinical Global Impression (CGI) Baseline:</b> EA + placebo: 4.03 (0.41) Sham acupuncture + FLX: 4.00 (0.00) Sham acupuncture + placebo: 4.03 (0.18)</p> <p><b>Depression severity:</b> Not reported</p> <p><b>Average age in years (SD):</b> Overall: 31.8 (12.1); EA: 30 (11); FLX: 34(13); Placebo: 30(12)</p> <p><b>Gender:</b> 41% male</p> <p><b>Inclusion criteria:</b> Diagnosed with MDD, using DSM-IV clinical interview.</p> <p><b>Exclusion criteria:</b> History of receiving acupuncture; other Axis I mental disorder/substance abuse conditions; alcohol dependence or heavy smoking; physical abnormalities revealed by exam or lab tests; physical disorders that require medical intervention; injury, acute disease, or surgery in past 4 weeks; taken fluoxetine in past 4 weeks, other antidepressant in past 3 weeks, neuroleptic drugs in past 3 years, or any drug affecting immune system; metabolic or endocrine disorder that requires treatment; pregnant, breastfeeding, or less than 6 months postpartum; suicidality; all physiological parameters were within normal limits; patient's primary care physician diagnosed any physical disorder that warranted treatment.</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture plus placebo medication. Participants received electroacupuncture at <i>Yintang</i> and <i>Baihui</i> points. Placebo capsules were given.</p> <p><b>Dosage:</b> 45 minutes, 3 times a week for 6 weeks</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> (1) Fluoxetine plus sham cranial acupuncture at nontherapeutic points for 6 weeks; (2) Placebo pills plus sham cranial acupuncture at nontherapeutic points</p> <p><b>Follow-up:</b> At end of 6-week intervention</p>	<p><b>Depressive symptoms, HRSD<sub>21</sub>:</b> <b>Baseline:</b> EA + placebo: 22.42(2.93) Sham acupuncture + FLX: 22.16(2.16) Sham acupuncture + placebo: 22.84(3.47) <b>End of intervention:</b> EA + placebo: 10.19 (5.88) Sham acupuncture + FLX: 11.34 (6.62) Sham acupuncture + placebo: 13.88 (6.29) The true acupuncture group improved more than the sham/placebo group (p&lt;0.05); no difference between sham/fluoxetine and true acupuncture.</p> <p><b>Response:</b> N/A</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not reported</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Vazquez et al., 2011</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Not applicable. No dropout</p> <p><b>Purpose:</b> To evaluate and compare the effectiveness of a low-frequency electroacupuncture versus nontherapeutic acupuncture on the clinical improvement of depressed patients and its relation to changes on salivary cortisol</p> <p><b>Country:</b> Mexico</p> <p><b>Quality rating:</b> Fair</p>	<p><b>Number of patients:</b> 42 initial and final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of current depression according to DSM-IV</p> <p><b>Baseline depressive symptom score:</b> Carroll Rating Scale for Depression Baseline: EA: 30.00 (1.48) Sham: 27.37 (1.40)</p> <p>SCL-90 Depression Baseline: EA: 2.39 (0.71) Sham: 1.74 (1.0)</p> <p><b>Depression severity:</b> Not reported</p> <p><b>Average age in years (SD):</b> EA: 42.6 (2.45); Sham: 44.9 (2.80)</p> <p><b>Gender:</b> EA: 26.1% male; Sham: 5.3% male</p> <p><b>Inclusion criteria:</b> Diagnosis of major depressive episode according to DSM-IV, a score on the Carroll Rating Scale for Depression above 18, and age above 18 years old.</p> <p><b>Exclusion criteria:</b> Suicidal tendency, organic brain syndrome, another major psychiatric disease, concomitant medication with antidepressants, psychotropic drugs (including reserpine), severe diseases, substance abuse, and pregnancy or lactation.</p>	<p><b>Type of needle acupuncture:</b> Electroacupuncture:</p> <p>Acupuncture point selection was based on TCM and included left <i>Shen Men</i>, right <i>Shen Shu</i>, right <i>Xin Shu</i>, left <i>Nei Guan</i>, left <i>San Yin Jiao</i>, and bilateral <i>Tai yang</i>. Stimulation applied with frequency of 4 Hz. Intensity was graded according to patient tolerance.</p> <p><b>Dosage:</b> 30 minutes, 2 times a week for 6 weeks</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> Sham acupuncture at two points: One point located by tracing a horizontal line that goes from the supraorbital border to the occipital and another vertical line from the anterior portion of the tragus where they join. Another point over the trapezoid bone, proximal to the articulation with the second metacarpal bone, and another over the back of the proximal epiphysis of the first metatarsal bone.</p> <p><b>Follow-up:</b> At end of 6-week intervention</p>	<p><b>Depressive symptoms, Carroll Rating Scale for Depression:</b> Baseline: EA: 30.00 (1.48) Sham: 27.37 (1.40) End of intervention: EA: 19.56 (2.28) Sham: 24.36 (1.60) Significantly larger improvement in acupuncture group than sham acupuncture group on Carroll Rating Scale for Depression (p-value not reported).</p> <p><b>Depressive symptoms, SCL-90 Depression:</b> Baseline: EA: 2.3910 (0.7099) Sham: 1.7436 (0.9978) End of intervention : EA: 1.2885 (0.8253) Sham: 1.4701 (0.8289) Between-group comparison not reported.</p> <p><b>Response:</b> N/A</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not reported</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Wang, Lu, et al., 2013</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> No</p> <p><b>Purpose:</b> To explore the personality-adjusting effect of electroacupuncture treatment for depression compared with paroxetine treatment</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 60 initial, 48 final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of current depression according to DSM-IV</p> <p><b>Baseline depressive symptom score: SDS</b> EA: 64.60 (9.25) Paroxetine: 52.17 (11.52)</p> <p><b>Depression severity:</b></p> <p><b>Average age in years (SD):</b> EA: 48.10 (13.4); Paroxetine: 47.10 (10.6)</p> <p><b>Gender:</b> Overall: 33.3% male; EA: 29.2% male; Paroxetine: 33.3% male</p> <p><b>Inclusion criteria:</b> Diagnosed with MDD (single episode) as assessed by Structured Clinical Interview for DSM-IV; 18 to 60 years old; not on antidepressants or other psychotropic medications for at least 2 weeks before the treatment; able to understand the questionnaires.</p> <p><b>Exclusion criteria:</b> Suicidality; breast-feeding; pregnant; history of comorbid mental disorders or substance abuse; unwilling to commit to study treatment regime for 6 months.</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture was applied at <i>Baihui</i>; <i>Yintang</i>; <i>Sishencong</i>, <i>Neiguan</i> bilateral; Shenmen bilateral; and <i>Sanyinjiao</i> bilateral. The <i>de qi</i> sensation was obtained. Electrical current (125 ms intermittent pulses at 40 Hz) was applied to <i>Sishencong</i> and <i>Neiguan</i> acupuncture points, with intensity dependent upon patients' tolerance.</p> <p><b>Dosage:</b> 20 minutes, 3 times per week for 24 weeks</p> <p><b>Co-interventions:</b> None</p> <p><b>Comparator:</b> Medication group: oral paroxetine 20 mg per day for two weeks, then adjusted in 10 mg increments according to the response of patients, with maximum dosage of 60 mg per day for 24 weeks</p> <p><b>Follow-up:</b> At end of 24-week intervention</p>	<p><b>Depressive symptoms, SDS:</b> <u>Baseline:</u> EA: 64.60 (9.25) Paroxetine: 59.30 (12.40) <u>End of intervention:</u> EA: 52.17 (11.52) Paroxetine: 44.17 (10.75) No statistical tests for between-group differences reported.</p> <p><b>Depressive symptoms, Montgomery-Åsberg Depression Rating Scale (MADRS):</b> <u>Baseline:</u> EA: 24.70 (5.92) Paroxetine: 22.80 (7.86) <u>End of intervention:</u> EA: 13.75 (6.23) Paroxetine: 11.38 (7.16) No statistical tests for between-group differences reported.</p> <p><b>Depressive symptoms, MMPI – Depression:</b> <u>Baseline:</u> EA: 68.80 (8.19) Paroxetine: 66.80 (12.34) <u>End of intervention:</u> EA: 60.25 (11.16) Paroxetine: 54.75 (11.80) No significant between-group differences in improvement</p> <p><b>Response:</b> N/A <b>Remission:</b> N/A <b>Relapse:</b> N/A <b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not systematically assessed. Reasons for dropouts due to adverse events: Treatment group: 1 subject suffered from pain in arm, 1 subject stopped treatment because of worry about unspecified hypertension. Paroxetine: 2 subjects stopped treatment because of pain in stomach, 1 subject stopped because of palpitations, 1 subject stopped treatment because of blurred vision.</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
---------------	----------	------------------------	------------------

NOTES: Unless otherwise noted, numbers in parentheses are standard errors. CGI = Clinical Global Impression; EA = electroacupuncture; FLX = fluoxetine; MOS = Medical Outcome Study; MSSG = massage; N/A = not available; NONSPEC = acupuncture not specific to depression; SPEC = acupuncture specific to depression.

**Table C.2. Adjunctive Acupuncture Studies**

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Chen et al., 2014</p> <p><b>Study design:</b> Multisite (4) RCT</p> <p><b>ITT analysis:</b> Modified ITT</p> <p><b>Purpose:</b> To compare the clinical efficacy of acupuncture/ electroacupuncture combined with an antidepressant drug with that of an antidepressant drug alone, using the Symptom Checklist-90</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> Seroxat: 33, Acupuncture: 31; EA: 31</p> <p><b>Method of identifying participants with MDD:</b> clinical diagnosis</p> <p><b>Baseline depressive symptom score: SCL-90</b> Seroxat: 2.74 (0.71) Acupuncture: 3.48 (0.63) EA: 3.07 (0.59)</p> <p><b>Average age in years (SD):</b> Seroxat: 35.37 (11.37); Acupuncture: 32.11 (9.38); EA: 31.89 (8.81)</p> <p><b>Gender:</b> Seroxat: 40% male; Acupuncture: 40% male; EA: 42.9% male</p> <p><b>Inclusion criteria:</b> Age 18–60 years; meet diagnostic criteria of ICD-10 for mild or moderate depressive episodes, HRSD score ≥ 17 points at acute phase of depression.</p> <p><b>Exclusion criteria:</b> Participation in other clinical trials within 4 weeks of experiment; taking antidepressants or in the elution period of antidepressant pharmacological action; suicidal plans or behavior; comorbid systemic diseases; brain diseases; thrombocytopenia; hemophilia; pregnancy, potential pregnancy or lactation; postpartal and menopausal women; unable to cooperate with the treatment schedule or evaluation owing to psychosis or illiteracy.</p>	<p><b>Type of needle acupuncture:</b> Acupuncture: Acupuncture with acupoints selected according to the World Federation of Acupuncture-Moxibustion Societies. The main points were <i>Baihui</i>, <i>Yintang</i>, <i>Dazhui</i>, <i>Fengfu</i>, <i>Fengchi</i> (bilateral), <i>Neiguan</i> (bilateral), <i>Sanyinjiao</i> (bilateral); coordinate points were <i>Zusanli</i> for poor appetite or fatigue, <i>Shenmen</i> for poor sleep, <i>Shuaigu</i> for headache, <i>Zhigou</i> for constipation. Needles were in place for 30 minutes and twisted once at 15 minutes for 5–10 seconds.</p> <p>EA: Same acupoints as acupuncture group, with electrical stimulation at <i>Baihui</i> and <i>Yintang</i> using disperse-dense wave at 2 or 15 Hz frequency, with strength based on patient's tolerance. Needles were in place for 30 minutes and twisted once at 15 minutes for 5–10 seconds.</p> <p><b>Dosage:</b> 30 minutes, 3 times a week for 6 weeks</p> <p><b>Co-interventions:</b> Oral Seroxat, which was continued for four weeks after acupuncture ended</p> <p><b>Comparator:</b> Oral Seroxat, 10mg per day on days 1 and 2, then 20 mg per day for 10 weeks</p> <p><b>Follow-up:</b> At end of 6-week intervention; 4 weeks post-treatment (participants remained on Seroxat for those 4 weeks)</p>	<p><b>Depressive symptoms dimension on SCL-90:</b></p> <p><b>Baseline</b> Seroxat: 2.74 (0.71) Acupuncture: 3.48 (0.63) EA: 3.07 (0.59)</p> <p><b>End of intervention</b> Seroxat: 2.23 (0.53) Acupuncture: 2.16 (0.68) EA: 2.04 (0.52)</p> <p><b>4 weeks post intervention</b> Seroxat: 2.09 (0.51) Acupuncture: 1.95 (0.59) EA: 2.07 (0.62)</p> <p>An analysis of variance showed that baseline depression symptoms were significantly different (<math>p &lt; 0.05</math>). An analysis of covariance revealed significant differences in depression scores among the three groups postintervention (<math>p &lt; 0.05</math>). Degree of improvement at the end of intervention in the acupuncture and EA groups was significantly better than that in the drug group (<math>p &lt; 0.05</math>). Comparison between acupuncture and EA groups was not reported. At 4 weeks postintervention, no difference was observed between depression scores in the three groups (<math>p &gt; 0.05</math>).</p> <p><b>Response:</b> N/A</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not systematically assessed. Seroxat: 3 participants had mild insomnia, nausea, and headaches. Acupuncture: 1 subject had moderate loss of appetite. EA: 2 participants had mild insomnia and dry mouth. No other participants presented with adverse reactions.</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Duan, Tu, Jiao, and Chen, 2010; Duan, Tu, Jiao, and Qin, 2011</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> No</p> <p><b>Purpose:</b> To compare the effectiveness of combined electroacupuncture and fluoxetine (FLX) relative to fluoxetine alone in reducing depressive symptoms, and observe pathological changes</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 75 initial, 70 final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of depression with ICD-10 criteria</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>17</sub> Baseline: EA + FLX: 23.8 (4.0) FLX: 25.1 (3.7)</p> <p><b>Depression severity:</b> EA + FLX: 18 mild; 20 moderate FLX: 17 mild; 20 moderate</p> <p><b>Average age in years (SD):</b> Treatment: 49.72 (5.47); FLX: 48.93 (7.60)</p> <p><b>Gender:</b> Overall: 17.6% male; Treatment: 16% male; FLX: 20% male</p> <p><b>Inclusion Criteria:</b> Mild and moderate depression according to ICD-10, free of psychosis or bipolar depression symptoms, 19–49 years old, HRSD scores &gt;20 and &lt;35, primary depression, course of disease ≤2 weeks, no history of severe brain organic disease or psychiatric disorders.</p> <p><b>Exclusion Criteria:</b> Schizophrenia or other psychiatric disorders; tumor, central nervous system disease, or other organic disease; pregnant or lactating; possibility of pregnancy; recurrent major depression; severe depression; HRSD scores &gt;35; suicidal tendency; not tolerant to fluoxetine adverse reactions; or hypersensitive to fluoxetine.</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture: <i>Baihui</i> (needle inserted to depth of 13–20 mm) and <i>Yintang</i> (needle inserted to depth of 7–13 mm) were stimulated with continuous wave at 2 Hz and comfortable intensity for 30–40 minutes, with the needle maintained for 1 hour. Patients who complained of discomfort received acupuncture at different acupoints. Conventional acupuncture was adopted with acupoints selected based on symptoms, including <i>Anmian</i>, <i>Sanyinjiao</i>, <i>Shenting Fengchi</i>, <i>Zhongwan</i>, <i>Zusanli</i>, <i>Shenmen</i>, <i>Neiguan</i>, and back <i>shu</i> points.</p> <p><b>Dosage:</b> 5 days per week (once a day) followed by 2 days of rest for 6 weeks</p> <p><b>Co-interventions:</b> Oral fluoxetine 20 mg per day for 6 weeks</p> <p><b>Comparator:</b> Oral fluoxetine 20 mg per day for 6 weeks</p> <p><b>Follow-up:</b> End of 6-week intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b></p> <p><b>Baseline:</b> EA + FLX: 23.8 (4.0) FLX: 25.1 (3.7)</p> <p><b>End of intervention:</b> EA + FLX: 10.1 (5.1) FLX: 12.7 (5.5)</p> <p>The electroacupuncture plus fluoxetine group had greater improvement than fluoxetine alone group (p&lt;0.01).</p> <p><b>Response:</b> Clinically controlled (&gt;75% improvement) EA + FLX: 17% FLX: 9% Favorable (50–75% improvement) EA + FLX: 44% FLX: 38% Effective (25–49% improvement): EA + FLX: 22% FLX: 26% Noneffective (&lt;25% improvement): EA + FLX: 17% FLX: 26% Effective rate (at least 25% improvement): EA + FLX: 83% FLX: 74% Not significantly different (p=0.17)</p> <p><b>Remission:</b> N/A <b>Relapse:</b> N/A <b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not systematically assessed. EA + FLX: 2 withdrew because of adverse reactions, including heart attack (n=1) and deterioration and hospitalization following death of mother (n=1). FLX: 3 withdrew because of adverse reactions, including dizziness and postural hypotension occurring after two weeks of treatment (n=1), panic and pyknosphygmia detected by electrocardiogram (EKG) after four weeks of treatment (n=1), and dysuria (n=1). No statistical analyses performed</p>



Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Qu et al., 2013</p> <p><b>Study design:</b> Multisite (3) RCT</p> <p><b>ITT analysis:</b> Modified ITT</p> <p><b>Purpose:</b> To evaluate whether electroacupuncture enhances the efficacy of SSRIs</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 160 initial, 143 at post-treatment, 91 at 4 weeks follow-up</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis with ICD-10 criteria</p> <p><b>Baseline depressive symptom score:</b> CGI Baseline: EA + paroxetine (PRX): 4.3 (1.2) Manual manipulation (MA) + PRX: 4.5 (1.0) PRX: 4.1 (0.8)</p> <p>HRSD Baseline: EA + PRX: 25.0 (5.2) MA + PRX: 25.1 (5.6) PRX: 23.3 (4.6)</p> <p><u>Chinese-version SDS Baseline:</u> EA + PRX: 51.1 (7.0) MA + PRX: 51.8 (9.0) PRX: 48.3 (7.1)</p> <p><b>Depression severity, HRSD<sub>17</sub>:</b> moderate or severe depression</p> <p><b>Average age in years (SD):</b> EA + PRX: 33.2 (9.0); MA + PRX: 32.3 (9.6); PRX: 34.4 (10.8)</p> <p><b>Gender:</b> EA + PRX: 39.7 % male; MA + PRX: 42.6% male; PRX: 39.6% male</p> <p><b>Inclusion criteria:</b> Aged 18–60 years; diagnosis of MDD with ICD-10; moderate or severe illness, with HRSD<sub>17</sub>≥17, CGI<sub>17</sub>≥4, current PRX or other antidepressant treatment not exceeding 1 month.</p> <p><b>Exclusion criteria:</b> Unstable medical conditions; history of brain injury or surgery; suicidal attempts; aggressive behavior; history of manic, hypomanic, or mixed episode illness; comorbid with other neuropsychiatric disorders; family</p>	<p><b>Type of needle acupuncture:</b> 2 interventions</p> <p>Cranial electroacupuncture (alternating frequency) using acupoints commonly used in the treatment of depression (<i>Baihui</i>, <i>Yintang</i>, <i>Fengfu</i>, <i>Dazhui</i>, bilateral <i>Fengchi</i>, bilateral <i>Neiguan</i>, and bilateral <i>Sanyinjiao</i>). Manual manipulation performed to achieve needling sensation. Electrical stimulation applied for 30 minutes between <i>Baihui</i> and <i>Yintang</i> and between bilateral <i>Fengchi</i> with continuous waves at alternating low (2 Hz) and high (100 Hz) frequency. Noted as EA.</p> <p>Acupuncture using acupoints commonly used in the treatment of depression (same as listed above). Manual manipulation performed to achieve needling sensation and then needles were retained for 30 minutes. Noted as MA.</p> <p><b>Dosage:</b> 18 sessions, 30 minutes, 3 times weekly for 6 weeks</p> <p><b>Co-interventions:</b> Paroxetine</p> <p><b>Comparator:</b> Medication group: Paroxetine treatment: dose escalated to 20–40mg/day, based on individual patient response</p> <p><b>Follow-up:</b> End of 6-week intervention; 4 weeks post-treatment</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b> Baseline: EA + PRX: 25.0 (5.2) MA + PRX: 25.1 (5.6) PRX: 23.3 (4.6) <u>End of intervention (change in score from baseline):</u> EA + PRX: -15.7 (5.1) MA + PRX: -14.1 (6.8) PRX: -11.3 (4.6) One-way analysis of variance: F=7.708, p=0.000. Post-hoc comparisons show significantly greater reduction both between EA + PRX and PRX and between MA + PRX and PRX post-treatment (p=0.000), but no significant differences in reductions between EA + PRX and MA + PRX <u>1 Month Post-Treatment (change in score from baseline):</u> EA + PRX: -17.1 (6.1) MA + PRX: -14.8 (5.5) PRX: -13.1 (3.8) Comparison across all 3 groups: F=4.553, p=0.013.</p> <p><b>Depressive symptoms, Chinese-version SDS:</b> Baseline: EA + PRX: 51.1 (7.0) MA + PRX: 51.8 (9.0) PRX: 48.3 (7.1) <u>End of intervention (change in score from baseline):</u> EA + PRX: -17.8 (10.3) MA + PRX: -15.4 (13.1) PRX: -11.2 (6.6) One-way analysis of variance: F=4.720, p=0.009. Post-hoc comparisons show significantly greater reductions in SDS scores both between EA + PRX and PRX and between MA + PRX and PRX post-treatment (p&lt;0.012). <u>1 Month Post-Treatment (change in score from baseline):</u> EA + PRX: -21.0 (12.7) MA + PRX: -15.0 (10.3) PRX: -13.9 (6.6) Comparison across all 3 groups: F=4.255, p=0.017.</p> <p><b>Response (at least 50% reduction in HRSD):</b> EA + PRX: 69.6% MA + PRX: 69.8% PRX: 41.7% Significantly greater response rate in EA + PRX and MA +</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
	<p>history of mental illnesses; investigational drug treatment within the previous 6 months; history of alcohol or drug abuse within the previous 12 months; pregnancy or lactation; currently receiving cognitive behavioral therapy or other behavioral therapies.</p>		<p>PRX than PRX, <math>p=0.004</math>.</p> <p><b>Remission (HRSD score &lt;8):</b>  EA + PRX: 28.6%  MA + PRX: 22.6%  PRX: 22.9%  EA + PRX and MA + PRX not significantly different from PRX, <math>p=0.723</math>.</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Systematically Assessed using SERS.  EA + PRX: 58  MA + PRX: 54  PRX: 48  Adverse events occurred in at least 5 percent of patients in each group. No significant differences in specific adverse events across groups.  EA + PRX: Adverse events included physical tiredness (n=27), headache (n=5), sleep disturbance (n=21), vertigo (n=2), palpitations (n=4), dry mouth (n=3), constipation (n=4), somnolence (n=0), and sexual problems (n=6). 2 subjects did not complete the first session and dropped out because of fainting due to needling.  MA + PRX: Adverse events included physical tiredness (n=28), headache (n=11), sleep disturbance (n=28), vertigo (n=5), palpitations (n=2), dry mouth (n=1), constipation (n=4), somnolence (n=3), and sexual problems (n=4). 1 subject did not complete the first session and dropped out because of fainting due to needling.  PRX: Adverse events included physical tiredness (n=19), headache (n=11), sleep disturbance (n=18), vertigo (n=3), palpitations (n=4), dry mouth (n=5), constipation (n=5), somnolence (n=3), and sexual problems (n=1).</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Roschke et al., 2000</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To evaluate the efficacy of acupuncture combined with mianserin, sham acupuncture combined with mianserin, and mianserin alone on depression symptoms among patients with MDD</p> <p><b>Country:</b> Germany</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 70 initial, 69 final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis with DSM-III-R criteria</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>21</sub> mean (SD) Verum acupuncture: 28 (5) Placebo acupuncture: 29 (5) Mianserin: 28 (7)</p> <p><b>Depression severity:</b> N/A</p> <p><b>Average age in years (SD):</b> Verum acupuncture: 49 (13), Placebo acupuncture: 47 (9), Mianserin: 49 (11)</p> <p><b>Gender:</b> Overall: 31.4% male; Verum acupuncture: 14% male; Placebo acupuncture: 38% male; Mianserin: 42% male</p> <p><b>Inclusion criteria:</b> Diagnosis of a major depressive episode according to DSM-III-R; HRSD score <math>\geq 18</math>; age between 20 and 70 years.</p> <p><b>Exclusion criteria:</b> Acute suicidality, history of schizoaffective or bipolar disorder; delusions; coagulation disease; wound-healing disease; emphysematous thorax; abnormal blood cell count; serious liver or kidney disease; epilepsy.</p>	<p><b>Type of needle acupuncture:</b> Verum acupuncture: Standardized body acupuncture treatment at the following points: U.B.15, U.B.17, U.B.18 (back), H7 (wrist), P6 (forearm), St40 (lower leg), Sp5, Sp6 (foot), Lu1 (upper part of the body)</p> <p><b>Dosage:</b> 30-minute sessions, 3 times weekly for 4 weeks, for total of 12 sessions</p> <p><b>Co-interventions:</b> Mianserin (90–120 mg/day)</p> <p><b>Comparator:</b> 2 comparison groups  Medication plus placebo acupuncture: Mianserin treatment (90–120 mg/day) plus minimal acupuncture—pricking skin at nonspecific locations near the points used in the treatment condition  Medication alone: Mianserin treatment (90–120 mg/day) plus clinical management</p> <p><b>Follow-up:</b> Twice weekly after treatment for one month</p>	<p><b>Depressive symptoms, GAS:</b> Greater improvement in the two acupuncture plus mianserin groups separately than the mianserin alone group (F=2.16, p=0.052). No significant difference between the verum acupuncture and sham acupuncture groups (F-test not reported).</p> <p><b>Depressive symptoms, BRMS:</b> No differences in improvement in the two acupuncture plus mianserin groups than the mianserin alone group (F=1.39, p=0.226). No significant difference between the verum acupuncture and sham acupuncture groups (F-test not reported).</p> <p><b>Response</b> (defined as &gt;25 point improvement on GAS): Verum acupuncture: 18% Placebo acupuncture: 33% Mianserin: 4% No statistical difference between verum acupuncture and placebo acupuncture. Verum and placebo acupuncture combined had greater response than mianserin (p=0.025).</p> <p><b>Remission:</b> None of the patients experienced a full remission.</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Not reported</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Wang, Lee, et al., 2014</p> <p><b>Study design:</b> Single-site RTC</p> <p><b>ITT analysis:</b> No</p> <p><b>Purpose:</b> To assess the effectiveness of acupuncture combined with an SSRI compared with SSRI alone for patients with depression in the hospital</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> Initial 76, final 71</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis with ICD-9 criteria</p> <p><b>Baseline depressive symptom score:</b> HDRS<sub>17</sub> Acupuncture: 22.0(0.60); SSRI: 22.07(0.33)</p> <p><b>Depression severity:</b> Not reported</p> <p><b>Average age in years (SD):</b> &gt;50 years: Acupuncture: 22; SSRI: 12; 31–50 years: Acupuncture: 18; SSRI: 10; ≤30 years: Acupuncture: 5; SSRI: 4</p> <p><b>Gender:</b> Acupuncture: 25.5% male; SSRI: 31.0% male</p> <p><b>Inclusion criteria:</b> Adults diagnosed with MDD by a qualified psychiatrist using the ICD-9 criteria, current at the time of the research; HDRS-17 total score ≥18.</p> <p><b>Exclusion criteria:</b> Receipt of SSRIs or acupuncture treatment for depression in the past 3 months; severe medical disease; brain stroke; other mental health disorders; pregnant or breast feeding.</p>	<p><b>Type of needle acupuncture:</b> Acupuncture points used for all patients were <i>Shenting</i>, <i>Baihui</i>, <i>Dazhui</i>, and <i>Mingmen</i>. Additional points were used according to TCM differentiation for depression. After achieving <i>de qi</i> needling sensation, <i>Dao qi</i> technique acupuncture was applied at the four key acupuncture points.</p> <p><b>Dosage:</b> 35 minutes, 5 days a week for 6 weeks</p> <p><b>Co-interventions:</b> SSRI (varied – fluoxetine, paroxetine, duloxetine)</p> <p><b>Comparator:</b> SSRI only</p> <p><b>Follow-up:</b> At end of 6-week intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub></b></p> <p><b>Baseline</b> Acupuncture: 22.0 (0.60) SSRI: 22.07 (0.33)</p> <p><b>End of intervention</b> Acupuncture: 6.3 (0.49) SSRI: 8.2 (0.35)</p> <p>A statistically significant reduction in mean HDRS score was found for the treatment group (acupuncture) compared with the SSRI group receiving SSRIs only (p&lt;0.05).</p> <p>Difference in average scale improvements across the two groups: -1.83 (95% CI -2.07, -1.58); p &lt;0.05.</p> <p><b>Response:</b> N/A</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Reported that there were no adverse events but did not describe a systematic assessment.</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Yeung et al., 2011</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To assess the efficacy of electroacupuncture, minimal acupuncture, and placebo acupuncture for residual insomnia in patients with a previous diagnosis of MDD after remission or partial response compared with a stable dosage of antidepressants</p> <p><b>Country:</b> China</p> <p><b>Quality rating:</b> Good</p>	<p><b>Number of patients:</b> 78 initial, 68 final</p> <p><b>Method of identifying participants with MDD:</b> Clinical diagnosis of MDD based on DSM-IV criteria</p> <p><b>Baseline depressive symptom score:</b> HRSD<sub>17</sub> Baseline: EA: 10.4 (3.9) Minimal: 11.2 (3.9) Placebo: 11.8 (3.9)</p> <p><b>Depression severity:</b> N/A</p> <p><b>Average age in years (SD):</b> 48.1 (9.1)</p> <p><b>Gender:</b> 25.8% male</p> <p><b>Inclusion criteria:</b> Ethnic Chinese; age 18 to 65 years; chief complaint of insomnia; previous diagnosis of MDD based on DSM-IV criteria, as assessed by a clinician; HRSD score <math>\leq 18</math> at screening and baseline; taking the same antidepressants at a fixed dose for 12 weeks prior to baseline.</p> <p><b>Exclusion criteria:</b> Any symptoms suggestive of specific sleep disorders, as assessed by the Insomnia Interview Schedule, a semistructured face-to-face interview; significant risk of suicide; previous diagnosis of schizophrenia, other psychotic disorders, bipolar disorder, or alcohol or substance use disorder; pregnant, breast-feeding, or a woman of childbearing potential not using adequate contraception; valvular heart defects, bleeding disorders, or taking anticoagulant drugs; infection or abscess close to the site of selected acupoints; any serious physical illness; taking Chinese herbal medicine or over-the-counter drugs intended for insomnia.</p>	<p><b>Type of needle acupuncture:</b> Cranial electroacupuncture with acupoints selected based on the literature and expert opinion (<i>Yintang</i>, <i>Baihui</i>, bilateral Ear <i>Shenmen</i>, <i>Sishencong</i>, and <i>Anmian</i>); sought to achieve <i>de qi</i></p> <p><b>Dosage:</b> 9 sessions, 3 times a week for 3 weeks</p> <p><b>Co-interventions:</b> Treatment as usual</p> <p><b>Comparator:</b> 2 comparison groups</p> <p>Minimal nontherapeutic acupuncture: superficial needling at nontherapeutic points. <i>De qi</i> was avoided.</p> <p>Placebo acupuncture: Participants were treated at the same acupoints as in the electroacupuncture group, using placebo needles placed 1 inch beside the acupoints. Needles were connected to electric stimulator, which was set at zero frequency and amplitude.</p> <p><b>Follow-up:</b> 1 week after end of intervention; 4 weeks after end of intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b></p> <p><b>Baseline:</b> EA: 10.4 (3.9) Minimal: 11.2 (3.9) Placebo: 11.8 (3.9)</p> <p><b>1 Week Post-Treatment:</b> EA: 9.9 (4.5) Minimal: 9.7 (2.6) Placebo: 11.9 (5.3) No difference between groups 1-week after treatment.</p> <p><b>4 Weeks Post-Treatment:</b> EA: 9.6 (5.1) Minimal: 9.0 (3.8) Placebo: 11.1 (5.3) Omnibus test of group x time interaction over multiple time points was not significant.</p> <p><b>Response:</b> N/A</p> <p><b>Remission:</b> N/A</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life, Sheehan Disability Scale – Work:</b></p> <p><b>Baseline:</b> EA: 4.6 (3.6) Minimal: 5.1 (2.3) Placebo: 5.7 (3.4)</p> <p><b>1 Week Post-Treatment:</b> EA: 3.5 (3.0) Minimal: 4.4 (2.7) Placebo: 4.4 (3.8) Linear mixed-effects models showed no significant between-group differences over time.</p> <p><b>Health-related quality of life, Sheehan Disability Scale – Social:</b></p> <p><b>Baseline:</b> EA: 5.6 (2.8) Minimal: 4.5 (2.3) Placebo: 5.9 (2.6)</p> <p><b>1 Week Post-Treatment:</b> EA: 4.1 (2.9) Minimal: 4.2 (2.4) Placebo: 5.7 (3.1)</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
			<p>Linear mixed-effects models showed no significant between-group differences over time.</p> <p><b>Health-related quality of life, Sheehan Disability Scale – Family:</b>  <b>Baseline:</b>  EA: 5.6 (2.9)  Minimal: 4.8 (2.6)  Placebo: 6.0 (2.1)  <b>1 Week Post-Treatment:</b>  EA: 3.4 (2.7)  Minimal: 4.3 (2.7)  Placebo: 5.7 (3.3)</p> <p>Linear mixed-effects models showed no significant between-group differences over time.</p> <p><b>Adverse events:</b> Not systematically assessed.  EA: headache (n=2), dizziness (n=1).  Minimal: worsening of insomnia (n=1), hand numbness (n=2), hematoma (n=1), palpitation (n=1), and pain at acupoints (n=1).  Placebo: headache (n=2), dizziness (n=2), and hand numbness (n=1).  Most adverse events were mild.</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
<p><b>Reference:</b> Zhang, Ng, et al., 2012; Zhang, Ng, et al., 2013</p> <p><b>Study design:</b> Single-site RCT</p> <p><b>ITT analysis:</b> Yes</p> <p><b>Purpose:</b> To compare the effectiveness of dense cranial electroacupuncture stimulation (DCEAS) combined with fluoxetine relative to noninvasive electroacupuncture (n-EA) combined with fluoxetine in the early-phase treatment of MDD patients</p> <p><b>Country:</b> Hong Kong, China</p> <p><b>Quality rating:</b> Poor</p>	<p><b>Number of patients:</b> 73 initial, 63 final</p> <p><b>Method of identifying participants with MDD:</b> DSM-IV diagnosis of MDD</p> <p><b>Baseline depressive symptom score:</b> CGI Baseline: DCEAS: 4.4 (0.5) n-EA: 4.3 (0.5)</p> <p>HRSD<sub>17</sub> Baseline: DCEAS: 23.9 (3.8) n-EA: 23.1 (3.6)</p> <p>SDS Baseline: DCEAS: 41.9 (4.0) n-EA: 40.6 (14.5)</p> <p><b>Depression severity:</b> N/A</p> <p><b>Average age in years (SD):</b> DCEAS: 46.3 (9.9); n-EA: 48.2 (9.8)</p> <p><b>Gender:</b> DCEAS: 30.6% male; n-EA: 2.9% male</p> <p><b>Inclusion criteria:</b> Age 25–65 years; DSM-IV diagnosis of MDD; HRSD score ≥18; CGI-Severity score ≥4.</p> <p><b>Exclusion criteria:</b> Unstable medical conditions; suicidal attempts; aggressive behavior; history of manic, hypomanic, or mixed episode; family history of bipolar or psychotic disorders; history of substance abuse within the previous 12 months; investigational drug treatment in the previous 6 months; current psychotropic treatment exceeding one week; needle phobia.</p>	<p><b>Type of needle acupuncture:</b> Dense cranial electroacupuncture with electrical stimulation, with continuous waves delivered at 2 Hz on 6 pairs of forehead acupoints <i>Baihui</i> and <i>Yintang</i>, left <i>Sishencong</i> and <i>Toulingqi</i>, right <i>Sishencong</i> and <i>Toulingqi</i>, bilateral <i>Shuaigu</i>, bilateral <i>Taiyang</i>, and bilateral <i>Touwei</i>.</p> <p><b>Dosage:</b> 9 sessions, 30 minutes, 3 times per week for 3 weeks</p> <p><b>Co-interventions:</b> Fluoxetine (for unmedicated patients); dosage was initiated at 10 mg/day and escalated to an optimal dose within 1 week, based on patient response; the maximum dose was 40 mg/day.</p> <p><b>Comparator:</b> Sham electroacupuncture plus fluoxetine: Streitberger's noninvasive acupuncture needles were used on the same acupoints used in DCEAS without inserting into the skin. Needles were then affixed with plastic O-rings and adhesive tapes. Electrical stimulation was delivered with the same parameters as DCEAS.</p> <p><b>Follow-up:</b> At end of intervention</p>	<p><b>Depressive symptoms, HRSD<sub>17</sub>:</b> Baseline: DCEAS: 23.9 (3.8) n-EA: 23.1 (3.6) Change score at end of intervention: DCEAS: -8.66 (95% CI -9.39, -7.91) n-EA: -6.27 (95% CI -6.90, -5.62) HRSD showed greater improvement in the EA plus fluoxetine group (between-group difference = 2.39, 95% CI 1.41, 3.37); p=0.000.</p> <p><b>Depressive symptoms, SDS:</b> Baseline: DCEAS: 41.9 (4.0) n-EA: 40.6 (14.5) Change score at end of intervention: DCEAS: -13.06 (95% CI -15.33, -10.79) n-EA: -8.38 (95% CI -10.42, -6.34) SDS showed greater improvement in the EA plus fluoxetine group (between-group difference = 4.68, 95% CI 1.62, 7.74); p=0.004.</p> <p><b>Response rate</b> (at least 50% reduction in HRSD): DCEAS: 19.4%; n-EA: 8.8% Not significantly different</p> <p><b>Remission rate</b> (HRSD ≤ 7): DCEAS: 2.7%; n-EA: 2.9% Not significantly different.</p> <p><b>Relapse:</b> N/A</p> <p><b>Health-related quality of life:</b> N/A</p> <p><b>Adverse events:</b> Systematically assessed using TESS. At least 5% of patients in each group experienced adverse events. DCEAS: 14 patients (38.9%) felt uncomfortable. Side effects included dizziness (n=11), tiredness (n=15), nausea (10), excessive sweating (n=6), headache (n=10), transient tachycardia (n=9), insomnia (n=9), discomfort during needling sensation (n=14), vomiting (n=3), unsteadiness (n=6), and somnolence (n=6). 2 patients discontinued because of intolerance to acupuncture stimulation.</p>

Study Details	Patients	Intervention/Treatment	Outcomes/Results
			n-EA: 7 patients (20.6%) felt uncomfortable. Side effects included dizziness (n=15), tiredness (n=10), nausea (n=10), excessive sweating (n=9), headache (n=8), transient tachycardia (n=8), insomnia (n=7), uncomfortable needling sensation (n=7), vomiting (n=4), unsteadiness (n=2), and somnolence (n=2). No significant differences in the incidence of any adverse events were found between the two groups.

NOTES: Unless otherwise noted, numbers in parentheses are standard errors. CGI = Clinical Global Impression; DCEAS = dense cranial electroacupuncture stimulation; FLX = fluoxetine; MA = manual manipulation; N/A = not available; n-EA = noninvasive electroacupuncture; PRX = paroxetine.



## References

---

- Allen, J. J. B., R. N. Schnyer, A. S. Chambers, S. K. Hitt, F. A. Moreno, and R. Manber, "Acupuncture for Depression: A Randomized Controlled Trial," *Journal of Clinical Psychiatry*, Vol. 67, No. 11, November 2006, pp. 1665–1673.
- Allen, J. J. B., R. N. Schnyer, and S. K. Hitt, "The Efficacy of Acupuncture in the Treatment of Major Depression in Women," *Psychological Science*, Vol. 9, No. 5, September 1998, pp. 397–401.
- Andreescu, C., R. M. Glick, C. A. Emeremni, P. R. Houck, and B. H. Mulsant, "Acupuncture for the Treatment of Major Depressive Disorder: A Randomized Controlled Trial," *Journal of Clinical Psychiatry*, Vol. 72, No. 8, August 2011, pp. 1129–1135.
- Ben-Zeev, D., P. W. Corrigan, T. W. Britt, and L. Langford, "Stigma of Mental Illness and Service Use in the Military," *Journal of Mental Health*, Vol. 21, No. 3, 2012, pp. 264–273.
- Brozek, J. L., E. A. Akl, P. Alonso-Coello, D. Lang, R. Jaeschke, J. W. Williams, B. Phillips, M. Lelgemann, A. Lethaby, J. Bousquet, G. H. Guyatt, and H. J. Schünemann, "Grading Quality of Evidence and Strength of Recommendations in Clinical Practice Guidelines. Part 1 of 3. An Overview of the GRADE Approach and Grading Quality of Evidence About Interventions," *Allergy*, Vol. 64, No. 5, 2009, pp. 669–677. As of October 13, 2015: <http://web.b.ebscohost.com/ehost/pdfviewer/pdfviewer?sid=40f6e108-dea5-43af-8e82-e5b87d9b97e5%40sessionmgr111&vid=1&hid=118>
- Canfield, S. E., and P. Dahm, "Rating the Quality of Evidence and the Strength of Recommendations Using GRADE," *World Journal of Urology*, Vol. 29, No. 3, 2011, pp. 311–317.
- Chan, Y.-Y., W.-Y. Lo, N. Yang, Y.-H. Chen, and J.-G. Lin, "The Benefit of Combined Acupuncture and Antidepressant Medication for Depression: A Systematic Review and Meta-Analysis," *Journal of Affective Disorders*, Vol. 176, 2015, pp. 106–117.
- Chen, J., W. Lin, S. Wang, C. Wang, G. Li, S. Qu, Y. Huang, Z. Zhang, and W. Xiao, "Acupuncture/Electroacupuncture Enhances Antidepressant Effect of Seroxat: The Symptom Checklist-90 Scores," *Neural Regeneration Research*, Vol. 9, No. 2, 2014, pp. 213–222.
- Chung, K. F., W. F. Yeung, Z. J. Zhang, K. P. Yung, S. C. Man, C. P. Lee, S. K. Lam, T. W. Leung, K. Y. Leung, E. T. Ziea, and V. Taam Wong, "Randomized Non-Invasive Sham-Controlled Pilot Trial of Electroacupuncture for Postpartum Depression," *Journal of Affective Disorders*, Vol. 142, No. 1–3, December 15, 2012, pp. 115–121.

- Colagiuri, B., and C. A. Smith, "A Systematic Review of the Effect of Expectancy on Treatment Responses to Acupuncture," *Evidence-Based Complementary and Alternative Medicine*, 2012.
- Coryell, W., H. S. Akishal, A. C. Leon, G. Winokur, J. D. Maser, T. I. Mueller, and M. B. Keller, "The Time Course of Nonchronic Major Depressive Disorder: Uniformity Across Episodes and Samples," *Archives of General Psychiatry*, Vol. 51, May 1994, pp. 405–410.
- Donohue, J. M., and H. A. Pincus, "Reducing the Societal Burden of Depression: A Review of Economic Costs, Quality of Care and Effects of Treatment," *Pharmacoeconomics*, Vol. 25, No. 1, 2007, pp. 7–24.
- Duan, D. M., Y. Tu, L. P. Chen, and Z. J. Wu, "Efficacy Evaluation for Depression with Somatic Symptoms Treated by Electroacupuncture Combined with Fluoxetine," *Journal of Traditional Chinese Medicine*, Vol. 29, No. 3, September 2009, pp. 167–173.
- Duan, D. M., Y. Tu, S. Jiao, and W. Qin, "The Relevance Between Symptoms and Magnetic Resonance Imaging Analysis of the Hippocampus of Depressed Patients Given Electro-Acupuncture Combined with Fluoxetine Intervention—A Randomized, Controlled Trial," *Chinese Journal of Integrative Medicine*, Vol. 17, No. 3, March 2011, pp. 190–199.
- Duan, D. M., Y. Tu, S. A. Jiao, and L. P. Chen, "Combined Effects of Electroacupuncture and Anti-Depression Drugs on the Hippocampus and Frontal Lobe," *Neural Regeneration Research*, Vol. 5, No. 22, November 2010, pp. 1723–1727.
- Egger, M., G. D. Smith, M. Schneider, and C. Minder, "Bias in Meta-Analysis Detected by a Simple, Graphical Test," *BMJ: British Medical Journal*, Vol. 315, No. 7109, 1997, pp. 629–634.
- Ernst, E., M. S. Lee, and T. Y. Choi, "Acupuncture for Depression? A Systematic Review of Systematic Reviews," *Evaluation & the Health Professions*, Vol. 34, No. 4, December 2011, pp. 403–412.
- Feng, Y., X. Y. Wang, S. D. Li, Y. Zhang, H. M. Wang, M. Li, K. Cao, Y. F. Ye, and Z. Zhang, "Clinical Research of Acupuncture on Malignant Tumor Patients for Improving Depression and Sleep Quality," *Journal of Traditional Chinese Medicine*, Vol. 31, No. 3, September 2011, pp. 199–202.
- Freeman, M. P., M. Fava, J. Lake, M. H. Trivedi, K. L. Wisner, and M. David, "Complementary and Alternative Medicine in Major Depressive Disorder: The American Psychiatric Association Task Force Report," *Journal of Clinical Psychiatry*, Vol. 71, No. 6, June 2010, pp. 669–681.
- Guyatt, G. H., A. D. Oxman, G. E. Vist, R. Kunz, Y. Falck-Ytter, P. Alonso-Coello, and H. J. Schünemann, "GRADE: An Emerging Consensus on Rating Quality of Evidence and

- Strength of Recommendations,” *BMJ (Clinical Research Ed.)*, Vol. 336, No. 7650, 2008, pp. 924–926.
- Han, C., X. Li, and H. Luo, “Randomized Clinical Trial Comparing the Effects of Electro-Acupuncture and Maprotiline in Treating Depression,” *International Journal of Clinical Acupuncture*, Vol. 15, No. 1, 2006.
- Hasin, D. S., R. D. Goodwin, F. S. Stinson, and B. F. Grant, “Epidemiology of Major Depressive Disorder: Results from the National Epidemiologic Survey on Alcoholism and Related Conditions,” *Archives of General Psychiatry*, Vol. 62, October 2005, pp. 1097–1106.
- He, Y. S., Y. S. Wu, M. F. Ouyang, G. X. Li, H. J. Li, and H. E. Xie, “Efficacy Observation of Depression in Nicotine Withdrawal Treated with Acupuncture,” *World Journal of Acupuncture - Moxibustion*, Vol. 22, No. 1, 2012, pp. 13–16. As of October 13, 2015: [http://dx.doi.org/10.1016/S1003-5257\(12\)60003-8](http://dx.doi.org/10.1016/S1003-5257(12)60003-8)
- Higgins, J., D. G. Altman, P. C. Gøtzsche, P. Jüni, D. Moher, A. D. Oxman, J. Savović, K. F. Schulz, L. Weeks, and J. A. Sterne, “The Cochrane Collaboration’s Tool for Assessing Risk of Bias in Randomised Trials,” *BMJ: British Medical Journal*, Vol. 343, 2011.
- Hoge, C. W., C. A. Castro, S. C. Messer, D. Mcgurk, D. I. Cotting, and R. L. Koffman, “Combat Duty in Iraq and Afghanistan, Mental Health Problems, Barriers to Care,” *The New England Journal of Medicine*, Vol. 351, No. 1, 2004, pp. 13–22.
- Huang, Y., W. M. Htut, D. Li, A. Tang, Q. Li, N. Shi, D. Xia, C. Zhao, J. Zou, and W. Gong, “Studies on the Clinical Observation and Cerebral Glucose Metabolism in Depression Treated by Electro-Scalp Acupuncture Compared to Fluoxetine,” *International Journal of Clinical Acupuncture*, Vol. 14, No. 1, 2005.
- Jiahui, Z., and S. Peng, “Clinical Observation on Acupuncture Treatment of Depressive Neurosis in 30 Cases,” *Journal of Traditional Chinese Medicine*, Vol. 26, No. 3, September 2006, pp. 191–192.
- Judd, L. L., “The Clinical Course of Unipolar Major Depressive Disorders,” *Archives of General Psychiatry*, Vol. 54, November 1997, pp. 989–991.
- Kessler, R. C., “The Costs of Depression,” *Psychiatric Clinics North America*, Vol. 35, No. 1, 2012, pp. 1–14.
- Kessler, R. C., P. Berglund, O. Demler, R. Jin, D. Koretz, K. R. Merikangas, A. J. Rush, E. E. Walters, and P. S. Wang, “The Epidemiology of Major Depressive Disorder: Results from the National Comorbidity Survey Replication (NCS-R),” *Journal of American Medical Association*, Vol. 289, No. 23, June 2003, pp. 3095–3105.
- Kessler, R. C., J. Soukup, R. B. Davis, D. F. Foster, S. A. Wilkey, M. I. Van Rompay, and D. M. Eisenberg, “The Use of Complementary and Alternative Therapies to Treat Anxiety and

- Depression in the United States,” *American Journal of Psychiatry*, Vol. 158, No. 2, February 2001, pp. 289–294.
- Leo, R. J., and J. S. A. Ligot Jr, “A Systematic Review of Randomized Controlled Trials of Acupuncture in the Treatment of Depression,” *Journal of Affective Disorders*, Vol. 97, 2007, pp. 13–22.
- Lewin Group and ECRI Institute, *Management of Dyslipidemia: Evidence Synthesis Report. Clinical Practice Guideline*, Washington, D.C.: Veterans Health Administration, U.S. Department of Veterans Affairs and U.S. Department of Defense, 2014.
- Lund, I., and T. Lundeberg, “Are Minimal, Superficial or Sham acupuncture Procedures Acceptable as Inert Placebo Controls?” *Acupuncture in Medicine*, Vol. 24, No. 1, 2006, pp. 13–15.
- Luo, H. C., Y. K. Jia, and Z. Li, “Electro-Acupuncture vs. Amitriptyline in the Treatment of Depressive States,” *Journal of Traditional Chinese Medicine*, Vol. 5, No. 1, March 1985, pp. 3–8.
- Ma, S. H., S. S. Qu, Y. Huang, J. Q. Chen, R. Y. Lin, C. Q. Wang, G. L. Li, C. H. Zhao, S. C. Guo, and Z. J. Zhang, “Improvement in Quality of Life in Depressed Patients Following Verum Acupuncture or Electroacupuncture Plus Paroxetine—A Randomized Controlled Study of 157 Cases,” *Neural Regeneration Research*, Vol. 7, No. 27, September 2012, pp. 2123–2129.
- MacPherson, H., S. Richmond, M. Bland, S. Brealey, R. Gabe, A. Hopton, A. Keding, H. Lansdown, S. Perren, M. Sculpher, E. Spackman, D. Torgerson, and I. Watt, “Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled Trial,” *PLoS Med*, Vol. 10, No. 9, 2013, p. e1001518.
- Man, S.-C., B. H. B. Hung, R. M. K. Ng, X.-C. Yu, H. Cheung, M. P. M. Fung, L. S. W. Li, K.-P. Leung, K.-P. Leung, K. W. Y. Tsang, E. Ziea, V. T. Wong, and Z.-J. Zhang, “A Pilot Controlled Trial of a Combination of Dense Cranial Electroacupuncture Stimulation and Body Acupuncture for Post-Stroke Depression,” *BMC Complementary and Alternative Medicine*, Vol. 14, No. 255, 2014, pp. 1–8.
- Management of Major Depressive Disorder Working Group, *VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder*, Washington, D.C.: Department of Veterans Affairs, May 2009. As of October 15, 2015:  
[http://www.healthquality.va.gov/mdd/mdd\\_full09\\_c.pdf](http://www.healthquality.va.gov/mdd/mdd_full09_c.pdf)
- Manber, R., R. N. Schnyer, J. J. Allen, A. J. Rush, and C. M. Blasey, “Acupuncture: A Promising Treatment for Depression During Pregnancy,” *Journal of Affective Disorders*, Vol. 83, No. 1, November 15, 2004, pp. 89–95.

- Manber, R., R. N. Schnyer, D. Lyell, A. S. Chambers, A. B. Caughey, M. Druzin, E. Carlyle, C. Celio, J. L. Gress, M. I. Huang, T. Kalista, R. Martin-Okada, and J. J. Allen, "Acupuncture for Depression During Pregnancy: A Randomized Controlled Trial," *Obstetrics & Gynecology*, Vol. 115, No. 3, March 2010, pp. 511–520.
- Nahas, R., and O. Sheikh, "Complementary and Alternative Medicine for the Treatment of Major Depressive Disorder," *Canadian Family Physician*, Vol. 57, No. 6, June 2011, pp. 659–663.
- Qu, S. S., Y. Huang, Z. J. Zhang, J. Q. Chen, R. Y. Lin, C. Q. Wang, G. L. Li, H. K. Wong, C. H. Zhao, J. Y. Pan, S. C. Guo, and Y. C. Zhang, "A 6-Week Randomized Controlled Trial with 4-Week Follow-Up of Acupuncture Combined with Paroxetine in Patients with Major Depressive Disorder," *Journal of Psychiatric Research*, Vol. 47, No. 6, June 2013, pp. 726–732.
- Roschke, J., C. Wolf, M. J. Muller, P. Wagner, K. Mann, M. Grozinger, and S. Bech, "The Benefit from Whole Body Acupuncture in Major Depression," *Journal of Affective Disorders*, Vol. 57, No. 1–3, January–March 2000, pp. 73–81.
- Schell, T. L., and G. N. Marshall, "Survey of Individuals Previously Deployed for OEF/OIF," in Terri Tanielian and Lisa H. Jaycox, eds., *Invisible Wounds of War: Psychological and Cognitive Injuries, Their Consequences, and Services to Assist Recovery*, Santa Monica, Calif.: RAND Corporation, MG-720-CCF, 2008. As of October 15, 2015: <http://www.rand.org/pubs/monographs/MG720z1.html>
- Smith, C. A., P. P. Hay, and H. MacPherson, "Acupuncture for Depression," *The Cochrane Library: Cochrane Database of Systematic Reviews*, Vol. 1, No. CD004046 (pub 3), January 20, 2010.
- Snizek, D. P., and I. J. Siddiqui, "Acupuncture for Treating Anxiety and Depression in Women: A Clinical Systematic Review," *Medical Acupuncture*, Vol. 25, No. 3, 2013, pp. 164–172.
- Song, C., U. Halbreich, C. Han, B. E. Leonard, and H. Luo, "Imbalance Between Pro- and Anti-Inflammatory Cytokines, and Between Th1 and Th2 Cytokines in Depressed Patients: The Effect of Electroacupuncture or Fluoxetine Treatment," *Pharmacopsychiatry*, Vol. 42, No. 5, September 2009, pp. 182–188.
- Song, Y., and H. Liang, "Clinical Observation of Depression Following Cerebral Apoplexy Treated by Scalp Acupuncture," *Journal of Acupuncture and Tuina Science*, Vol. 1, No. 5, 2003.
- Song, Y., D. Zhou, J. Fan, H. Luo, and U. Halbreich, "Effects of Electroacupuncture and Fluoxetine on the Density of GTP-Binding-Proteins in Platelet Membrane in Patients with Major Depressive Disorder," *Journal of Affective Disorders*, Vol. 98, No. 3, March 2007, pp. 253–257.

- Spijker, J., R. De Graaf, R. V. Bijl, A. T. F. Beekman, J. Ormel, and W. A. Nolen, "Duration of Major Depressive Episodes in the General Population: Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS)," *British Journal of Psychiatry*, Vol. 181, No. 3, 2002, pp. 208–213.
- Sun, H., H. Zhao, C. Ma, F. Bao, J. Zhang, D. H. Wang, Y. X. Zhang, and W. He, "Effects of Electroacupuncture on Depression and the Production of Glial Cell Line-Derived Neurotrophic Factor Compared with Fluoxetine: A Randomized Controlled Pilot Study," *Journal of Alternative and Complementary Medicine*, Vol. 19, No. 9, 2013, pp. 733–739.
- Tylee, A., and R. Jones, "Managing Depression in Primary Care: Public Confidence Needs to Be Restored After Concerns over the Safety of SSRIs," *BMJ: British Medical Journal*, Vol. 330, No. 7495, 2005, pp. 800–801.
- U.S. Preventive Services Task Force, *U.S. Preventive Services Task Force Procedure Manual*, Rockville, Md.: Agency for Healthcare Research and Quality, 2008.
- Vaughan, C. A., T. L. Schell, L. H. Jaycox, G. N. Marshall, and T. Tanielian, "Quantitative Needs Assessment of New York State Veterans and Their Spouses," in Terry L. Schell and Terri Tanielian, eds., *A Needs Assessment of New York State Veterans: Final Report to the New York State Health Foundation*, Santa Monica, Calif.: RAND Corporation, TR-920-NYSHF, 2011. As of October 15, 2015:  
[http://www.rand.org/pubs/technical\\_reports/TR920.html.html](http://www.rand.org/pubs/technical_reports/TR920.html.html)
- Vazquez, R. D., L. Gonzalez-Macias, C. Berlanga, and F. J. Aedo, "Effect of Acupuncture Treatment on Depression: Correlation Between Psychological Outcomes and Salivary Cortisol Levels," *Salud Mental*, Vol. 34, No. 1, January–February 2011, pp. 21–26.
- Vickers, A., N. Goyal, R. Harland, and R. Rees, "Do Certain Countries Produce Only Positive Results? A Systematic Review of Controlled Trials," *Controlled Clinical Trials*, Vol. 19, No. 2, 1998, pp. 159–166.
- Vogt, D., "Mental Health-Related Beliefs as a Barrier to Service Use for Military Personnel and Veterans: A Review," *Psychiatric Services*, Vol. 62, No. 2, 2011, pp. 135–142.
- Wang, F., E.-K. O. Lee, T. Wu, H. Benson, G. Fricchione, W. Wang, and A. S. Yeung, "The Effects of Tai Chi on Depression, Anxiety, and Psychological Well-Being: A Systematic Review and Meta-Analysis," *International Journal of Behavioral Medicine*, Vol. 21, No. 605, 2014, pp. 605–617.
- Wang, H., H. Qi, B.-S. Wang, Y.-Y. Cui, L. Zhu, Z.-X. Rong, and H.-Z. Chen, "Is Acupuncture Beneficial in Depression: A Meta-Analysis of 8 Randomized Controlled Trials?" *Journal of Affective Disorders*, Vol. 111, No. 2, 2008, pp. 125–134.

- Wang, W. D., X. Y. Lu, S. M. Ng, L. Hong, Y. Zhao, Y. N. Lin, and F. Wang, "Effects of Electro-Acupuncture on Personality Traits in Depression: A Randomized Controlled Study," *Chinese Journal of Integrative Medicine*, Vol. 19, No. 10, October 2013, pp. 777–782.
- Wells, T., C. L. Mann, S. Fortuna, B. Smith, T. C. Smith, M. a. K. Ryan, E. J. Boyko, and D. Blazer, "A Prospective Study of Depression Following Combat Deployment in Support of the Wars in Iraq and Afghanistan," *American Journal of Public Health*, Vol. 100, No. 1, 2010, pp. 90–99.
- Whiting, M., G. Leavey, A. Scammell, S. Au, and M. King, "Using Acupuncture to Treat Depression: A Feasibility Study," *Complementary Therapies in Medicine*, Vol. 16, No. 2, April 2008, pp. 87–91.
- Yeung, W. F., K. F. Chung, K. C. Tso, S. P. Zhang, Z. J. Zhang, and L. M. Ho, "Electroacupuncture for Residual Insomnia Associated with Major Depressive Disorder: A Randomized Controlled Trial," *Sleep*, Vol. 34, No. 6, June 2011, pp. 807–815.
- Zhang, C., "The Brain-Resuscitation Acupuncture Method for Treatment of Post Wind-Stroke Mental Depression—A Report of 45 Cases," *Journal of Traditional Chinese Medicine*, Vol. 25, No. 4, December 2005, pp. 243–246.
- Zhang, G. J., Z. Y. Shi, S. Liu, S. H. Gong, J. Q. Liu, and J. S. Liu, "Clinical Observation on Treatment of Depression by Electro-Acupuncture Combined with Paroxetine," *Chinese Journal of Integrative Medicine*, Vol. 13, No. 3, September 2007, pp. 228–230.
- Zhang, Z.-J., R. M. K. Ng, S. C. Man, T. Y. J. Li, W. Wong, Q.-R. Tan, H. K. Wong, K.-F. Chung, M.-T. Wong, W.-K. A. Tsang, K.-C. Yip, E. Ziea, and V. T. Wong, "Dense Cranial Electroacupuncture Stimulation for Major Depressive Disorder—A Single-Blind, Randomized, Controlled Study," *PloS One*, Vol. 7, No. 1, 2012, p. e29651.
- Zhang, Z., R. Ng, M. S. C. Man, J. Li, W. Wong, H. K. Wong, D. Wang, M. Wong, A. Tsang, K. Yip, and C. W. Sze, "Use of Electroacupuncture to Accelerate the Antidepressant Action of Selective Serotonin Reuptake Inhibitors: A Single-Blind, Randomized, Controlled Study," *Hong Kong Medical Journal*, Vol. 19, No. 9, 2013, pp. 12-19.
- Zhang, Z. J., H. Y. Chen, K. C. Yip, R. Ng, and V. T. Wong, "The Effectiveness and Safety of Acupuncture Therapy in Depressive Disorders: Systematic Review and Meta-Analysis," *Journal of Affective Disorders*, Vol. 124, No. 1–2, July 2010, pp. 9–21.
- Zinzow, H. M., T. W. Britt, A. C. Mcfadden, C. M. Burnette, and S. Gillispie, "Connecting Active Duty and Returning Veterans to Mental Health Treatment: Interventions and Treatment Adaptations That May Reduce Barriers to Care," *Clinical Psychology Review*, Vol. 32, No. 8, 2012, pp. 741–753.