Master Thesis in Public Health
(Folkehelsevitenskap)
ISM, UiTø

(HEL-3950)

Acupuncture Treatment for Depression – An Overview of Systematic Reviews

Tromsø 10.06.2009

Student
Trine Stub

Supervisor
Jianping Liu

TABLE OF CONTENTS

ABSTRACT……..... 3
BACKGROUND……..... 4
OBJECTIVES……..... 9
CRITERIA FOR CONSIDERING STUDIES FOR THIS OVERVIEW…….... 9
METHODS OF THE OVERVIEW…… 11
SEARCH METHODS FOR IDENTIFICATION OF STUDIES……... 12
SEARCH RESULTS…….. 13
METHODOLOGICAL QUALITY OF SYSTEMATIC REVIEWS……. 15
COMMENTS OF CONSISTENCY AND DIFFERENCES AMONG THE REVIEWS…….. 20
NEW INCLUDED STUDIES……..... 23
METHODOLOGICAL QUALITY OF RANDOMIZED CONTROLLED TRIALS... 24
COMMENTS ON THE METHODOLOGICAL QUALITY OF NEW TRIALS……. 29
ANALYSIS OF TRIALS ACCORDING TO THE STRICTA GUIDELINES……. 30
ADVERSE EFFECTS OF ACUPUNCTURE…… 32
RESULTS……... 33
DISCUSSION……. 38
AUTHOR'S CONCLUSION…… 44
NOTE…….. 45
REFERENCES……... 45
APPENDIX I…….. 54
APPENDIX II……. 61

TABLES…….. 14

Number of RCTs in Systematic Reviews with Overlapping and Different trials…… 14
Methodological Quality of Included Systematic Reviews…….. 15
Description of New Included RCTs…… 25
Search Result from January 2009 with Time and Time range…… 54
Primary Outcome measures of RCTs, Data used in the Meta Analysis…….. 56
Intervention Details according to the STRICTA Checklist……. 58
Methodological quality of New Included RCTs……... 61
Outcome Data from Chinese Trials extracted by Jianping Liu……..... 72

ANALYSIS WITH GRAPHS AND OTHER TABLES……. 33

Analysis 01. Comparison 1.1.2. Classical Acupuncture versus placebo
Outcome 01 Reduction in severity of depression…… 33
Analysis 02. Comparison 1.2.2. Classical Acupuncture versus placebo
Outcome 02 Improvement in depression……. 34
Analysis 03. Comparison 2.1.1. Electro-acupuncture versus medication
Comparison 2.1.2. Classical acupuncture versus medication
Outcome 03 Reduction in severity of depression……. 35
Analysis 04. Comparison 3.1.2. Acupuncture versus waiting list
Outcome 04 Reduction in severity of depression……. 37

ABSTRACT

Background: For more than 2000 years acupuncture has been used to treat depression, and randomized controlled trials have been conducted to investigate their efficacy.

Objective: The objective of this overview is to assess the effects and adverse effects of acupuncture in patients with depression, and to evaluate the report quality of acupuncture treatment for depression in Randomized Controlled Trials (RCTs) and Systematic Reviews (SRs).

Search Strategy: The following electronic databases were searched: Cochrane Central Register for Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE, EMBASE, AMED, PsycINFO and PUBMED, combined with manual searches in journals of interest and reference lists. The searches were limited from the year 1966 to January 2009, and the filters used were systematic reviews and randomized controlled trials.

Selection Criteria: Systematic Reviews and Randomized Controlled Trials of acupuncture for depression compared to medication, waiting lists, non-specific acupuncture/sham and placebo were included.

Data Collection and Analyses: The methodological quality of the RCTs was assessed using the criteria in the Cochrane Handbook describing the relationship between allocation concealment and bias. The methodological quality of the systematic reviews were evaluated using the QUAROM statement checklist (1). To evaluate the impact on clinical practice, the trials were analyzed according to the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA)-guidelines.

Main Result: Four systematic reviews and eighteen RCTs including 1,587 participants with depression were analyzed. In addition, six new identified Chinese trials (781 participants) were included in the meta-analyses. The methodological quality of trial reports was generally low in terms of generation of the allocation sequence, allocation concealment, blinding and intention to treat. Ten trials (1,063 participants) included a comparison between acupuncture and medication. A significant reduction in depression was found by electro-acupuncture compared to antidepressant medication (WMD – 0, 91, 95 % CI – 1.43 to – 0.40, P=0.0006). Two subgroup analyses included 676 participants, compared classical acupuncture with placebo. A significant beneficial effect was found for classical acupuncture in improving and reducing depression compared to placebo (WMD – 3.77, 95% CI – 7.11 to – 0.42, P=0.03) and (WMD – 4.44, 95 % CI – 5.84 to – 3.04, P = 0.00001) respectively. There was insufficient data to demonstrate whether classical acupuncture was more effective in reducing depression than a waiting list control.

Author's Conclusion: Current evidence shows beneficial effects of acupuncture in reducing depression compared to medication. Classical acupuncture is also beneficial for improving and reducing depression compared to placebo. More rigorous trials are needed and long-term effects should be investigated if acupuncture is to be recommended as one of the alternative treatments for depression.

BACKGROUND

Western medicine classifies depression as a mood disorder that manifests itself across a wide range of severity. The severity of depression can be classified as mild, moderate or

severe (2). Clinically significant depression is called Major Depressive Disorder (MDD). It is a state of mind that is characterized by significantly lowered mood and loss of interest or pleasure in activities that are normally enjoyable. Thus, depression has a great impact on the quality of life (3). Other symptoms may include changes in sleep and/or appetite, decreased libido, thoughts of death or suicide, fatigue, feeling worthless or guilty, and difficulty concentrating (4). Symptoms must have been persistent for at least two weeks and not be related to other medical or psychiatric diagnoses, or be due to substances (4). The World Health Organization ranks the social costs of depression as the 4th highest of all diseases (5). Furthermore, current trends indicate that by 2020 depression will represent the highest cost to society of any disease (5). Clearly prevention, early diagnosis and intervention of depression have a huge social significance.

Management of Depression

Currently supported treatment for depression is medication and different psychological interventions, such as Cognitive Behavioral Therapy (CBT), psychotherapy and counseling (3). However, most people with depression are only being treated by their primary care provider (6). Patients often report intolerable side effects of antidepressant medications, and this may be a reason for them to explore alternative medicines such as acupuncture. Others recognize the body-mind relationship and want to approach depression holistically rather than symptomatically (7).

Traditional Chinese Medicine (TCM)

TCM is a 3000-year old holistic system of medicine which combines medicinal herbs, acupuncture, nutrition therapy, massage and therapeutic exercises for treatment and prevention of diseases (8). Acupuncture is a translation of the Chinese term 'zhen jiu' which means needle and moxa. The practice of moxibustion refers to burning of small pieces of punk of dried Artemisia Vulgaris (mugvort) plant. The term acupuncture comes from the late seventeenth century Europe and is often referred to as both needle and moxa (8). TCM has a unique concept of aetiology, system of diagnoses and treatment which are essential to its practice. These theories include the concept of *Yin-Yang* which represents the opposite principles and balance between the positive and negative system in the body. The Five Elements of *Earth, Water, Fire, Metal* and *Wood* are another important diagnostic tool in this medical kit together with *Qi* and *Blood. Qi* is the force that animates all living things. *Qi* is constantly in flux so that nothing ever stays the same. This opens up for the possibility of change. *Qi* circulates in the body in regular patterns in a system of channels or meridians. It is disturbance in *Qi* that causes health problems. *Zhang-Fu* is the Chinese concept of internal organs which consist of five Viscera and six Bowels. Diseases are considered to result from external or internal causes which are defined as a disturbance and an imbalance between *Yin* and *Yang*.

Acupuncture has been widely used for more than 2000 years to treat depression. The classical category *Bèi Dìe* demonstrates the complex pathology behind this disease. It is defined in the Chinese language as an illness wherein the sufferer has "apologies in the Heart/centre of the chest, prefers to be in a dark room, and is afraid to the point of

wanting to hide upon seeing others" (9). The physical symptoms associated with *Bèi Dìe* include inability to consume food or drink and a globules blockage in the chest. This syndrome presents a picture of someone overwhelmed with shame and fear, someone that withdraws from others and whose physical status suggests a fundamental lack of strength. We recall here insufficiencies on many levels including *Wei* and *Ying, Yin* and *Yang, Blood* and *Qi,* inside and outside. A fundamental thinning and lowering of the Reflective Ability (*Yi*) and the Will (*Zhi*) are present. A falling of the Spirit (*Shen*) felt in the Lung as a blockage, in the Stomach as a lack of appetite, and in the Heart as the inability of *Qi* and *Blood* to hold it up. TCM does not separate physiological and psychological events. The *Shen* is made by both *Qi* and *Blood,* which in turn are generated by the *Zhang-Fu* (10). Emotions are considered to be a manifestation of *Qi* that if not expressed or transformed, becomes stagnant. They become a cause of disease only when they are experienced excessively or for a prolonged period of time, or a combination of these. Therefore, TCM-practitioners believe that all depressive patterns have a degree of Liver pathology (11, 12). There is also an interrelationship between the Heart, Kidney, Essence, Brain and Spirit in the aetiology of psycho-emotional disorders in TCM. The relationship between the Brain and the Heart reflects the vital relationship between the Kidney and the Heart as the Kidney stores Essence that comes from the parents. This Essence nourishes the Brain and the Spinal Cord and is the source of the Spirit. This explains why points on the head, such as DU20, DU24, DU16 and Sishencong are efficient in the treatment of depression (13, 14). To be true to the TCM-philosophy, it is essential that the treatment schedule in depression is individualized and based on these complex patterns.

Conventional science suggests that acupuncture works by neurological, neurohormonal and psychological mechanisms. In relation to depression, acupuncture may affect many structures and neurotransmitters in the central nervous system including serotonin, norepinephrine, dopamine and GABA; as well as the hypothalamus, pituitary, thyroid and adrenal glands (12, 15-18). A westernized medical application of acupuncture involves the use of trigger points, segmental points and commonly used formula points. It may involve the application of acupuncture based on neurohormonal theories, anatomy and the exclusion of TCM-principles and philosophy.

Auricular Therapy (AT) involves the use of the ear to make a diagnosis and subsequent needling to the point on the ear. Electro-acupuncture involves passing a pulsed current through body tissues via acupuncture needles.

It is proposed that the therapeutic relationship may be a significant component in TCM-treatment of depression (2, 19). Flaws and Lake (12) quote that needling efficacy is due to a combination of the psychological relationship between practitioner and patient, concentration and point stimulation. However, analyses of data released by pharmaceutical companies demonstrate that antidepressant drug treatment may account for only 25% of the improvement in depression (2, 20). 50% appear to be due to placebo, and 25% to the natural course of disease. This suggests that the use of acupuncture or pharmaceutical treatment only account for part of the healing process. Therefore, the therapeutic relationship and the patient's intent to achieve health may be significant factors in both acupuncture and pharmaceutical therapy.

Systematic reviews of RCTs are considered to provide the highest level of evidence about the effectiveness of interventions. Although systematic reviews summarize the effects of a specific intervention for a specific condition, an overview of reviews (sometimes called "umbrella review" in the science of research synthesis) typically summarizes evidence for many interventions for the same condition or evidence on the same intervention for different or similar conditions, in order to provide users with easily available information. Clinicians and policy makers need evidence from overviews to improve clinical practice and policy. Patients and researchers also need such information to support shared decisions to set priorities for research.

OBJECTIVES FOR THIS OVERVIEW

- To assess the effects and adverse effects of acupuncture in patients with depression from systematic reviews and RCTs
- To evaluate the report quality of acupuncture treatment for depression in systematic reviews
- To evaluate the report quality of acupuncture treatment for depression in RCTs

CRITERIA FOR CONSIDERING STUDIES FOR THIS OVERVIEW

Types of Studies: All published and unpublished systematic reviews and the RCTs included which fulfilled the inclusion criteria were eligible for this overview. All new RCTs found in the literature searches have been considered, ideally people who

administered the treatment, trial participants and outcome assessors should all have been blinded. However, single blinded trials were also considered.

Types of participants: Adults with depression defined by clinical state description or diagnosed by the Diagnostic and Statistical manual, DSM-IV (21) or the Research Diagnostic Criteria, RCD (22) or the International Classification of Disease, ICD (23).

Types of Intervention: Treatment group: classical-acupuncture, electro-acupuncture and laser–acupuncture versus control group: Placebo control (sham-acupuncture, minimal-acupuncture, non-invasive control, electro-acupuncture), no treatment (waiting list, treatment as usual) or pharmacological treatment (standard medication to treat depression) or structured psychotherapies (cognitive behavioral therapy, psychotherapy, counseling) or other standard care as defined by the country-specific health care setting.

Types of Outcome Measures: For inclusion data at least one primary outcome needed to be included:

Primary Outcome:

- Reduction in severity of depression, patient reported and/or clinician evaluated.
- Improvement in depression symptom, measured as a dichotomous outcome, remission versus no remission. Patient reported and/or clinician evaluated.

Secondary Outcome:

- Quality of life (such as short Form 36 Health Status questionnaire).
- Change in use of medication.
- Adverse side effects.

- Acceptability of acupuncture, electro-acupuncture or laser-acupuncture (patient reported).

METHODS OF THE OVERVIEW

Statistical Methods: The effect estimate will be presented according to the categories of data, i.e. dichotomous and continuous data. Dichotomous data have only two possible values, for example male or female or survival or death. Continuous data measure values on a continuous scale. Furthermore, I will use Weight Mean Difference (WMD), Standard Deviation (SD) and their 95 % Confidence Interval (CI) were used to present the effect estimate. Mean Difference (MD) is the average value usually represented by the arithmetic mean, and SD is a measure on the variability or dispersion of a data set and the most frequently reported measure of spread. 95 % CI is an interval likely to include a population parameter, and in 95 % of the cases the interval will contain the true parameter value. Heterogeneity will be tested and different statistical models will be used depending on the significance, which is defined as $P < 0.10$ as significant with heterogeneity. Studies brought together in a systematic review may differ. Any kind of variability among studies in an review may be termed heterogeneity (24). A P-value is defined as the probability of the occurrence of a particular event which equals the proportion of times that the event would (or does) occur in a large number of similar repeated trials. It has a value between 0 and 1 (equaling 0, the event can never occur, and 1, it is certain to occur).

Pre-specified subgroup analysis examined the effect of different styles of acupuncture, for example classical-acupuncture versus electro-acupuncture.

To perform a meta–analysis, data were entered directly from the data sheets into the Review Manager Software 5 (RevMan 5) see appendix I, **Table 2**: *Primary Outcome Measures of RCTs, data used in the Meta Analysis*

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

The focused question was:

Does acupuncture relieve symptoms in adults with depression?

This question was analyzed according to PICO

Population: Adults with depression

Intervention: Acupuncture

Comparison: Medication, waiting lists, non-specific acupuncture/sham and placebo

Outcome: Reduction in the severity of depression or improvement of depression

The following electronic databases were searched: Cochrane Central Register for Controlled Trials (Central) in the Cochrane library, MEDLINE, EMBASE, AMED, PsycINFO and PUBMED. See Appendix 1, **Table 1:** *Search Results from their inception date until January 2009 with Time and Time Range.*

Manual Search: Journals of interest: *Journal of Chinese Medicine*, *Complementary Therapies in Medicine*, *The Journal of Alternative and Complementary Medicine* and, if possible, Chinese Acupuncture Journals.

Additional Search: Reference lists of identified systematic reviews and RCTs were checked in order to find additional studies not found by the electronic or manual searches. Ongoing trials were searched through the National Research Register.

SEARCH RESULTS

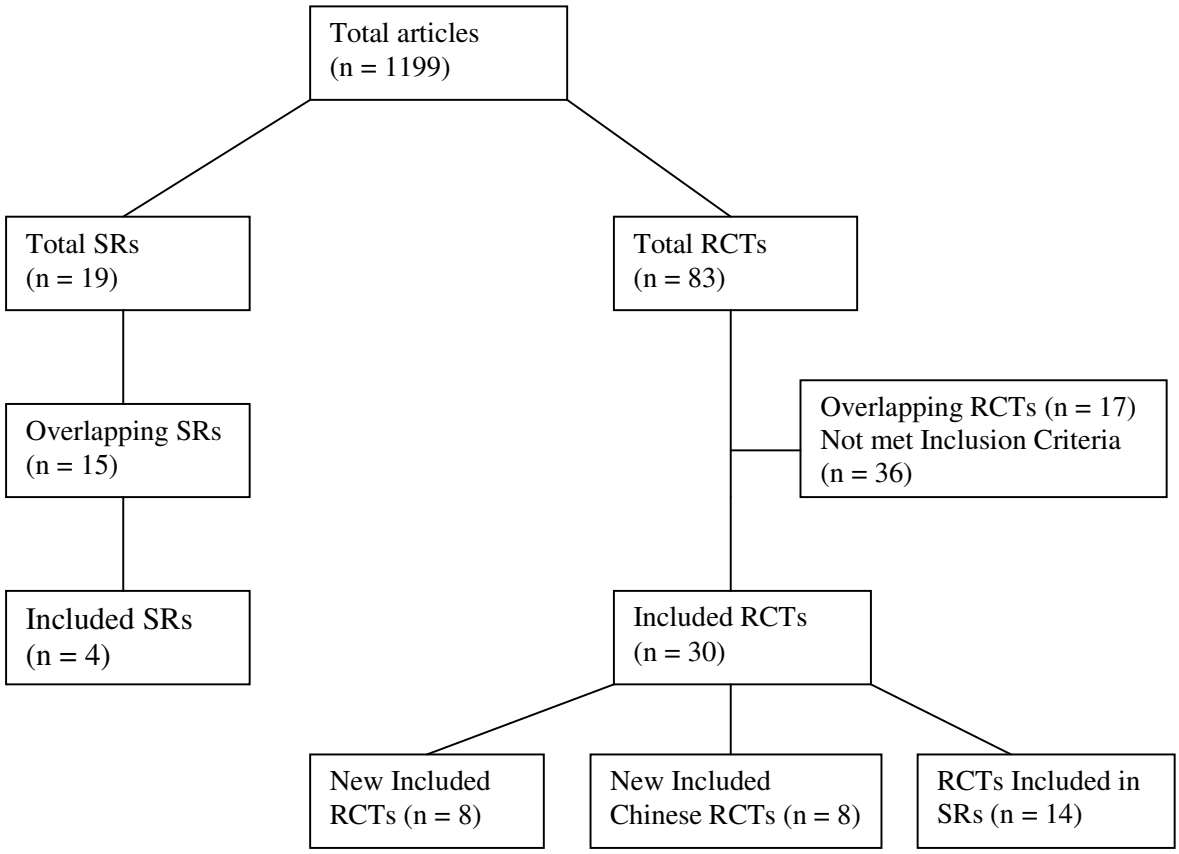


Figure 1. *Flow Chart of the selection process of SRs and RCTs for this overview*

A total of 1199 articles of interest were identified from searches performed in January 2009. 19 of these were systematic reviews. 15 publications were overlapping reviews, which left 4 reviews for this overview (25-28). 83 publications were RCTs, 36 did not meet the inclusion criteria and 17 were overlapping RCTs, leaving a total of 30 trials included for this overview. 14 different RCTs (19, 29-41) were included in 4 systematic reviews and 8 new RCTs (42-49) were identified and included. Another 8 new Chinese RCTs (50-57) which were not translated into English were identified. The Chinese trials were evaluated for eligibility, data extracted, translated and analyzed by a PhD candidate, Xing Liao, from Beijing University of Chinese Medicine. Jianping Liu extracted the outcome data for the meta-analyses for these eight Chinese trials. See Appendix II **Table 4:** *Methodological quality of New Included RCTs,* and **Table 5:** *Outcome Data from Chinese Trials extracted by Jianping Liu*

Table 1. *Number of RCTs in Systematic Reviews, with Overlapping and Different trials*

Systematic Reviews	RCTs included in SRs	Overlapping Trials compared to Smith (2005)	Different Trials compared to Smith (2005)
Smith (2004)	**7**		
Leo (2007)	**9**	**7 (78 %)**	**2**
Mukaino (2005)	**7**	**6 (86 %)**	**1**
Wang (2008)	**8**	**2 (25 %)**	**6**
Average Trial	**7.75**		

The average trials in each review were 7.75. 47 % (14/30) of the trials were overlapping. using Smith (2004) as a standard, 78 % of the included trials in Leo (2007) were also included in Smith (2004). 86 % of the trials included in Mukaino (2005) were included in Smith (2004) as well. Moreover, Mukaino (2005) had included the exact same trials as Leo (2007). Further, Wang (2008) included 2 trials (25 %) which were included in Smith (2004) and 6 trials that were published more recently. Based on this, Smith (2004) and Wang (2008) have performed good and independent searches and included relevant trials. Leo (2007) and Mukaino (2005) have copied 78 % and 86 % respectively of Smith's (2004) trials.

METHODOLOGICAL QUALITY OF SYSTEMATIC REVIEWS (1)

Four systematic reviews were analyzed according to the following criteria included in the QUORUM- statement checklist for improving the quality of reports of meta-analyses of RCTs: inclusion criteria, participants, objectives, search strategy, main findings, conclusion and recommendation for clinical practice, see the Tables below.

TABLES

Table 2. *Methodological Quality of Included Systematic Reviews*

Study	**Smith 2005**
Inclusion criteria	All published and unpublished Randomized Controlled Trials comparing acupuncture with sham acupuncture, no treatment, pharmacological treatment, structured psychotherapies or standard care. The following models of treatment were included: acupuncture, electro-acupuncture and laser-acupuncture.

Participants	517 adults with depression defined by clinical state description or diagnosed by The Diagnostic and Statistical Manual (DSM-IV), Research Diagnostic Criteria (RDC) or The International Classification of Disease (ICD).
Objectives	To examine the efficacy and adverse effects of acupuncture for depression.
Search strategy	The following databases were searched: Cochrane Central Register of Controlled Trial (CENTRAL and DARE), MEDLINE (1966 to Sept 2003), EMBASE (1980 to Sept 2003), PsycINFO (1874 to Sept 2003), CISCOM, CINAHL (1980 to Sept 2003). The following terms were used: depression, depressive disorder, dysthymic disorder and acupuncture. Keywords: Depressi* or Dysthymi* and Acupuncture*
Main findings	This review included seven RCTs that found no evidence that medication was better than acupuncture in reducing the severity of depression or in improving depression, defined as remission versus no remission.
Conclusion	There is insufficient evidence to determine the efficacy of acupuncture compared to medication, to waiting list control or sham acupuncture, in the management of depression. The RCTs evaluated in this review had a poor study design and the number of people studied was small. Further RCTs are required to evaluate the effectiveness of acupuncture in the treatment of depression.
Clinical practice	Recommendations for practice cannot be made until further high quality research has been undertaken.
Study	**Leo 2007**
Inclusion criteria	More recent clinical trials with the diagnosis of depression based on Clinical Interview and Hamilton Rating Scale for Depression (HRSD)
Participants	Hospitalized stroke patients, pregnant depressed patients, people with bipolar

	disorder and general anxiety. People recruited from advertising and outpatient setting.
Objectives	To assess the efficacy of acupuncture in treating depression.
Search strategy	The Following databases were searched: MEDLINE (1966-2004), Allied and Complementary Medicine (1985-2004), Cochrane Central Register of Controlled Trials. The terms used were: acupuncture, electroacupuncture, depressive disorder, depression and dysthymic disorder.
Main findings	This review included nine RCTs that found some evidence for the utility of acupuncture in depression. Acupuncture treatment was as effective as antidepressants. Sham acupuncture was often no different from acupuncture.
Conclusion	The evidence for the efficacy of acupuncture in treating clinical depression is inconclusive. The evidence was limited by the varied methodology and study design in the RCTs evaluated in this paper. Further research with scientific rigor is needed.
Clinical practice	The number of treatment needed to elicit antidepressant effect is between 10-18 sessions. Caution is required when treating pregnant women to avoid stimulation of pelvic organs or contractibility. The administration of acupuncture treatment in depression requires appropriate training skills.
Study	**Mukaino 2005**
Inclusion criteria	RCTs in which either manual acupuncture or electro-acupuncture was compared with any control procedure in subjects with depression.
Participants	509 subjects with major or minor depression. Recruited from hospital care and a newspaper advertisement. Patients were diagnosed for depression based on DSM-III or DSM-IV, ICD and Hamilton Rating Scale for Depression.
Objectives	To summarize the existing evidence for or against the hypothesis that

	acupuncture is an efficacious therapy for depression.
Search strategy	The following databases were searched: MEDLINE (1969 to May 2003), The Cochrane Library (Issue 2, 2003), EMBASE, PsycINFO and the Centralized Information Service for Complementary Medicine (1988 to May 2003), Japana Centra Revuo Medicina (1981-May 2003), manual search in The Journal of Korean Acupuncture Society and Kyung-Hee University Oriental Medicine Journal, the website of Chinese Medical Psychiatry and personal files of all reviewers. Reference lists of included papers were searched for further relevant trials. The search terms were as follows: acupuncture, electro-acupuncture or laser acupuncture and depression or depressive state or mental disorder or Dysthymia.
Main findings	Seven RCTs found inconsistent evidence on whether manual acupuncture was superior to sham and waiting list control. The effect of electro-acupuncture may not be significantly different from antidepressant medication, and there was inconclusive evidence on whether acupuncture has an addictive effect when given as an adjunct to antidepressant medication.
Conclusion	The evidence from RCTs is insufficient to conclude whether or not acupuncture treatment is an effective treatment for depression. As some trials generated promising result, large-scale RCTs are warranted.
Clinical practice	No data was reported.

Study	**Wang 2008**
Inclusion criteria	RCTs published or unpublished, comparing acupuncture with sham acupuncture in subjects with major depression.
Participants	477 patients with depression or depressive neurosis classified by DSM, ICD, and HRSD.
Objectives	To assess the beneficial effect of acupuncture in depression.
Search strategy	The following databases were searched in March 2007: MEDLINE, EMBASE, BIOSIS, Cochrane Central Register of Controlled Trials and Chinese Medical Literature Database. The following terms were used: acupuncture, acupressure, depression, depressive disorder, clinical trials and randomized controlled trials. No restriction due to language and year of publication. Manual search was done in secondary sources and reference lists.
Main findings	Eight RCTs found that acupuncture was an effective treatment that could significantly reduce the severity of disease in patients with depression.
Conclusion	This meta-analysis might be discounted due to the low quality of individual trials. It supported that acupuncture was an effective treatment that could reduce the severity of diseases in patients with major depression and depressive neurosis. More full-scale RCTs with reliable designs are recommended. Moreover, a study that compares the efficacy of acupuncture with placebo and pharmacotherapy in the same study would be desirable.
Clinical practice	The main side effect of acupuncture treatment in depression was fatigue that was transient and persisted for less than 24 hours. These effects were better tolerated than side effects from pharmacotherapy.

COMMENTS ON CONSISTENCY AND DIFFERENCES AMONG THE REVIEWS

Inclusion Criteria

Consistency and Differences: All four SRs included randomized controlled trials. Smith (2004) compared acupuncture with sham, no treatment, pharmacological treatment, psychotherapy and standard care. Wang (2008) compared acupuncture with sham acupuncture. Mukaino (2005) compared acupuncture to any control and Leo (2007) had no written information on included control interventions. The following acupuncture models were included: In Smith (2004) acupuncture, electro-acupuncture and laser-acupuncture, in Mukaino (2005) electro-acupuncture. Leo (2007) and Wang (2008) did not specify the acupuncture intervention. Three reviews (25, 26, 28) used DSM III or IV and ICD as diagnostic tools to diagnose depression. In addition, Smith (2005) included research diagnostic criteria (RCD). Leo (2007) used clinical interviews as a diagnostic tool without specifying which criteria that was included in the review. All reviews used HRSD to measure self-reporting and clinician evaluated outcome. In addition, Smith (2004) included Beck Depression Inventory Scale for self-reporting measure.

Participants

Consistency: 517 and 509 male and female patients with depression were included in Smith and Mukaino.

Differences: Wang included 477 patients with depression and depressive neurosis. Leo included hospitalized stroke patients, pregnant depressed patients, subjects with bipolar disorder and general anxiety.

Summary: Three of the reviews had a strong consistency regarding participants, as they included men and women with diagnosed depression according to valid medical criteria and scales (25, 26, 28). However, Leo (2007) included patients with so different medical diagnosis that it seems problematic to compare the different groups of participants. This inconsistency in the application of diagnostic criteria may bias the evaluation of the acupuncture treatment due to the heterogeneous mix of participants in the included trials.

Objectives

Consistency and Differences: All four SRs assessed the efficacy of acupuncture for depression. Smith (2004) assessed the adverse effects as well.

Search Strategy

Consistency: Smith (2004) searched for literature in six different Western databases. Mukaino (2005) and Wang (2008) used the same databases as Smith (2004). Keyword and MESH-terms were the same for all of them. They also stated when the searches were performed.

Differences: In addition, Wang (2008) searched for literature in a Chinese medical literature database and Mukaino (2005) in a Japanese database plus a manual search through two leading Korean acupuncture journals. Leo (2007) searched in three Western databases.

Summary: There was consistency regarding databases used for search in three Reviews (25, 26, 28). Mukaino (2007) and Wang (2008) got a better rating for their additional search in Japanese, Korean and Chinese databases. Leo (2005) got a poor rating, as he

just used three databases for his literature search. None of the reviews had a table for search strategy in the appendix.

Main Findings

Consistency: Two reviews (25, 27) found that acupuncture was as effective as antidepressant medication for treating depression. Three reviews (25-27) found no evidence that acupuncture was superior to sham acupuncture and a waiting list control. Two systematic reviews (27, 28) found that acupuncture was an effective treatment for depression.

Differences: One review (26) found insufficient evidence to determine the efficacy of acupuncture compared to medication.

Conclusion

Consistency: Three reviews (25-27) found that the evidence for the efficacy of acupuncture in treating depression was inclusive. They found no evidence for acupuncture to be superior to sham and waiting list controls. Two reviews (25, 27) found that acupuncture was as effective as antidepressant medication in treating depression. All reviews found that there was poor methodological quality (study design and number of people treated) in the included trials. They also stated that more research is required; especially RCTs with more rigorous design are needed.

Differences: One review (58) found that acupuncture was an effective treatment for depression.

Summary: Even though previous research found no evidence for the efficacy of acupuncture in treating depression, it is interesting that the most updated review (Wang 2008) found a positive result in favor of acupuncture for treating depression, and that acupuncture was as effective as medication in treating depression. However, one should be cautious in interpreting the findings due to low methodological quality, generally small sample size and a limited number of trials identified.

Clinical Practice

Consistency: Two systematic reviews (25, 26) had no recommendation for practice.

Differences: One review (27) recommended that 10-18 sessions of acupuncture treatment were needed to treat depression, and that causation was required when treating depressive pregnant women to avoid stimulation of pelvic organs and contractibility. Another review (58) reported that fatigue was a common side-effect after acupuncture treatment, but that patients tolerated this better than side-effects from pharmacotherapy.

Summary: There is a weak consistency between the reviewers regarding recommendation for clinical practice.

NEW INCLUDED STUDIES

After a closer look at the data, four studies were excluded (42, 43, 48, 49). Han C (2004 and 2006) were the same trials as Han C (2002) which was included in Smith (2004). All of Han C's trials were published in different journals. In Gallagher (2001) data for outcome measures for each arm in the trial were missing. I contacted the author, but he had stored the data in the long term archive and it was therefore difficult to find. Da Silva

(2007) had no data for depression alone, but mixed with anxiety and irritability, which allowed four RCTs for further analyses (44-47).

METHODOLOGICAL QUALITY OF RANDOMIZED CONTROLLED TRIALS

The methodological quality of the RCTs was assessed using the criteria in the Cochrane Reviewers Handbook (24), describing the relationship between Allocation Concealment and Bias. Criteria for assessing bias are:

A Low risk of bias (adequate allocation concealment). A was used to indicate an RCT with a high level of quality in which all the criteria were met. Adequate measures to conceal allocation such as central randomization was serial numbered, opaque, sealed envelopes or other description that contained convincing elements of concealment.

B Moderate risk of bias (some doubt about the results). B was used when the authors either did not report allocation concealment at all, or reported an approach that did not fall into one of the categories in A.

C High risk bias (inadequate allocation concealment). C was used when the method of allocation was not concealed, such as alternation methods or the use of case record numbers. Such trials were excluded.

The double blinding method was described. Further, whether the randomized clinical trials reported to have used intention to treat analysis or not were reported.

Table 4: *Description of New Included RCTs*

Study	**Fu 2003**
Methods	Acupuncture versus standard medication. No details were provided on how the allocation sequence and the method of concealment were generated. No details were reported on blinding. There was no loss to follow up reported, and an intention to treat analysis was performed.
Participants	Sixty-two in and out patients were recruited to the trial from The Second Clinical Medical College in Guangzhou in China. The inclusion criteria were CCMD-2 R more than 2, and a score greater than 20 on the Hamilton Rating Scale for Depression. Exclusion criteria were not specified.
Interventions	Subjects were randomly allocated to receive acupuncture or standard medication care using Fluoxetine 20 mg daily for eight weeks. The acupuncture points Liv3, Co4, Du20 and Yintang were used in all subjects and in addition, points according to the Chinese medical diagnosis. For palpitations Bl15 and Bl14 were used. For insomnia the ear points Heart, Gallbladder and Shenmen were used. For deficiency of Heart and Spleen Ht7 and Sp6 were used. For deficiency of Heart with Timidity He7 and Gb40 were used. For stagnation of Liver Qi with Sp Deficiency Sp6 was used. For disharmony between Heart and Kidney with Phlegm Kid3, P7 and Sp1 were used. For Spleen and Kidney Yang Xu, Kid1 and Sp1 were used. For disharmony between Chong and Ren, Sp4 and Lu7 were used. The needle retention time was 30 minutes, and daily treatment was given for eight weeks.

Outcome	The Hamilton Rating Scale for Depression was completed at the start and end of the study with curative effects evaluated at the end of the study.
Notes	No Power Calculation was performed. No loss to follow up was reported. An intention to treat analysis was performed.
Allocation Concealment	B - unclear
Study	**Zhang 2003**
Methods	Electro-acupuncture versus standard medication. No details were provided on randomization. The study participants and therapist were not blinded, and it was unclear if the outcome assessor and analyst were blinded to the study group. No loss to follow up was reported.
Participants	Four hundred and sixty men and women were recruited to the trial from the Third People's Hospital of Mianyang in China. The inclusion criteria were CCMD-2, and a score greater than 20 on the Hamilton Rating Scale for Depression. Exclusion criteria were not specified.
Interventions	Subjects were randomly allocated to receive either electro-acupuncture or Amitriptyline. In addition both groups received psychotherapy. The main acupuncture points in group 1 were: Du20 and P8. In group 2 they were: Kid1, Du26, Co4 and Liv3. These two groups of points were needled alternately with electronic stimulation. Additional points for palpitation, insomnia and vexation Bl15, P6 and He7 were needled. For stomachache, poor appetite and abdominal distention, St36, Bl20 and Bl21 were needled. The needle retention time was 30-60 minutes, six times a week. Subjects on medication

	received an initial dose of 25mg three times a day for one week. The treatment dose was then modified according to effects, average 150mg daily.
Outcome	The Hamilton Rating Scale was completed at the start and end of the trial.
Notes	No Power Calculation was performed. An intention to treat analysis was performed.
Allocation Concealment	B - Unclear

Study	**Zhao 2006**
Methods	Electro-acupuncture versus standard treatment Fluoxine. No details were provided on randomization and blinding. No loss to follow up was reported, and an intention to treat analysis was performed.
Participants	Sixty out patients were recruited to the trial from the Hilongjiang University of Traditional Chinese Medicine in China. Subjects who scored 20 or more on the Hamilton Rating Scale for Depression were included. Subjects with organic diseases, drug abuse or systematic antidepressant users were excluded.
Interventions	Subjects were randomized to receive acupuncture or standard medical care using Fluoxine. The acupuncture points Taiyang, Du24, Bl4, Du20 P6, He7, Sp6 and Liv3 were used. The needles were stimulated for two minutes using electro-acupuncture, and the retention time was 30 minutes. Treatment was given once a day for 30 days. The medical group used Fluoxine for 30 days, but the dose was not specified.
Outcome	The Hamilton Rating Scale for Depression was completed at the start and end of the trial.

Notes	No Power Calculation was reported. A complete follow up was obtained. An intention to treat analysis was performed.
Allocation Concealment	B - Unclear
Study	**Zhang 2007**
Method	Acupuncture and standard medication versus standard medication alone. No details were provided on how the allocation sequence and the method of concealment were generated. The study participants and therapist were not blinded, and it was unclear if the outcome assessor and analyst were blinded to the study group.
Participants	Forty-two men and women aged 18-65 years were recruited to the trial from the Hospital of Traditional Chinese Medicine of Shiyan City in China. The inclusion criteria were the Chinese Standard for Sorting and Diagnosis of Mental Disorder and a score of 18 or more on Hamilton Rating Scale for Depression. The exclusion criteria were severe organ diseases, drug and alcohol dependence, pregnancy, breastfeeding and suicidal attempts.
Interventions	Both groups were treated orally with Paroxetine 10-40 mg daily for six weeks. The intervention group received electro-acupuncture on the points Du 20 and Yintang. In addition, these points were used: P6, Sj5, He7, Co4, Liv3, St36, St40, Sp6 and Lu9. Treatment was given once a day six days a week for six weeks. The needles were retained for 30 minutes.
Outcome	Subjects completed the Hamilton Depression Rating Scale for Depression and Treatment Emergent Symptoms Scale (TESS) for side effects. Outcome measures were collated at baseline and at the

	end of the 2nd, 4th and 6th week.
Notes	No Power Calculation was reported. A complete follow up was obtained. An intention to treat analysis was performed.
Allocation Concealment	B - Unclear

COMMENTS ON THE METHODOLOGICAL QULITY OF NEW TRIALS

Allocation Concealment: Fu (2003), Zhang (2003), Zhao (2006) and Zhang (2007) were given a score of B, as the allocation concealment was unclear.

Method of Concealment: The method of concealment was not mentioned in any of the trials.

Blinding: Fu (2003), Zhang (2003), Zhao (2006) and Zhang (2007) had no details reported on blinding. The participants and therapist were probably not blinded since the treatment groups received acupuncture and the control groups received medication. Whether or not the outcome assessor and analyst were blinded to study group were not reported.

Intention to treat analysis: None of the trials reported a sample size calculation or stated that intention to treat analysis was used**.** However, one must assume that this has been done as they used all the numbers of randomization in the data analyses.

Losses to follow up: There were no losses to follow up reported in Fu (2003), Zhao (2003), Zhao (2006) and Zhang (2007).

Accordingly, these trials have generally low methodological quality. All trials provided baseline data for the comparability among groups. The average sample size of the RCTs was 156, ranging from 22 to 250 participants per trial.

ANALYSIS OF TRIALS ACCORDING TO THE STRICTA-GUIDELINES (59)

A lot of poorly reported studies in acupuncture have been conducted. In the need for more precise standards of reporting interventions, the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) guidelines have been developed. If researchers follow these guidelines, acupuncture trials will be more adequately reported and thereby facilitate an improvement in critical appraisal, analyses and replication of trials. One of the trials (Fu 2003), that was included in Wang (2008), only the abstract was translated into English; therefore seventeen RCTs were analyzed according to the Revised Standard of STRICTA 2, see Appendix I **Table 3:** *Analysis of Intervention Details according to the STRICTA-Checklist for 17 Included RCTs, whether or not each item was reported.*

How many trials reported according to the STRICTA?

Only 24 % (4/17) of the trials reported every STRICTA-item, except for needle type under needling details. These four trials were Allen (1998 and 2006), Manber (2004) and Quah-Smith (2005). 76 % (13/17) of the trials had major problems reporting every STRICTA-item.

However, 50 % of the STRICTA-items were well reported across the trials, and these items were acupuncture rationale, needle details and treatment regimen. Acupuncture rationale and treatment regimen were reported in every trial. Only two trials (Yang 1994 and Eich 2000) had no information about duration of session under treatment regimen. Under needling details two details (number and name) were reported in every trial. Stimulation and retention time were reported in 14 and 15 trials respectively. The major

reporting problems under this item were depth, response and needle type, which were reported in 10, 11 and 6 trials respectively.

50 % of the STRICTA-items were poorly reported. These items were practitioner background, other components of treatment and control or comparator intervention. Regarding practitioner background only one trial (Fu 2003) reported every detail under this theme. 65 % (11/17) of the trials had no information on practitioner qualification. 76 % (13/17) of the trials had no information about years of practice, and 94 % (16/17) had no information about relevant experience. Under other components of treatment it was especially instruction given to practitioner/information to patients that were poorly reported. 76 % (13/17) of the trials did not report these details. Furthermore, under control or comparator interventions, 76 % (13/17) of the trials had no information about rationale and source to justify choice. Precise description of control was not reported by 35 % (6/17) of the trials.

Conclusion

Based on this analysis, it seems reasonable to conclude that researchers still have a job to do writing appropriate reports. When designing a trial, it is important to have these questions in mind so when the time comes, it is easy to answer and incorporate them in the writing process. This will ensure good report quality of the trials as well as help clinical practitioners to improve and change their treatment schedule or state the fact that their practice is in line with the best evidence available.

ADVERSE EFFECTS OF ACUPUNCTURE

Adverse effects of acupuncture are classified into three categories: mechanical organ injuries, infections and other adverse effects (60). Pneumothorax is the dominant mechanical organ injury but was not reported in this overview. Acupuncture inducted infections were not reported in this paper but seem nearly always due to lack of hygienic procedures. Other adverse effects may be asthmatic death, contact dermatitis and increased pain.

In this overview limited data was reported on adverse effects from acupuncture treatment. Lou (1988) reported 138 adverse events in the acupuncture group with headaches (n=26), palpitations (n=16) and dryness of the mouth (n=16) as the most common adverse effects. Lou (1998) reported 138 adverse events in the acupuncture group with physical tiredness (n=26), sleep disturbance (n=18), palpitation (n=16) and headaches (n=14) as the most common adverse effects. Quah-Smith (2005) reported that 29 % in the laser-acupuncture group experienced adverse effects and 60 % of these were fatigue. The effects were transient and persisted for less than 24 hours. Allen (2006) reported that 62 % in the intervention group experienced somatic symptoms, 26 % pain symptoms, 20 % intensification of sleep difficulties and 18 % intensification of emotions/emotional reactions. In this paper headache, palpitation, tiredness and sleep disturbance were most frequently reported. Minor adverse effects such as small hematoma and discomfort during treatment (insertion pain) are probably much more common than serious adverse consequences of acupuncture (60, 61). Adequate acupuncture education and practical use of basic medical knowledge should prevent most of these adverse effects.

RESULTS

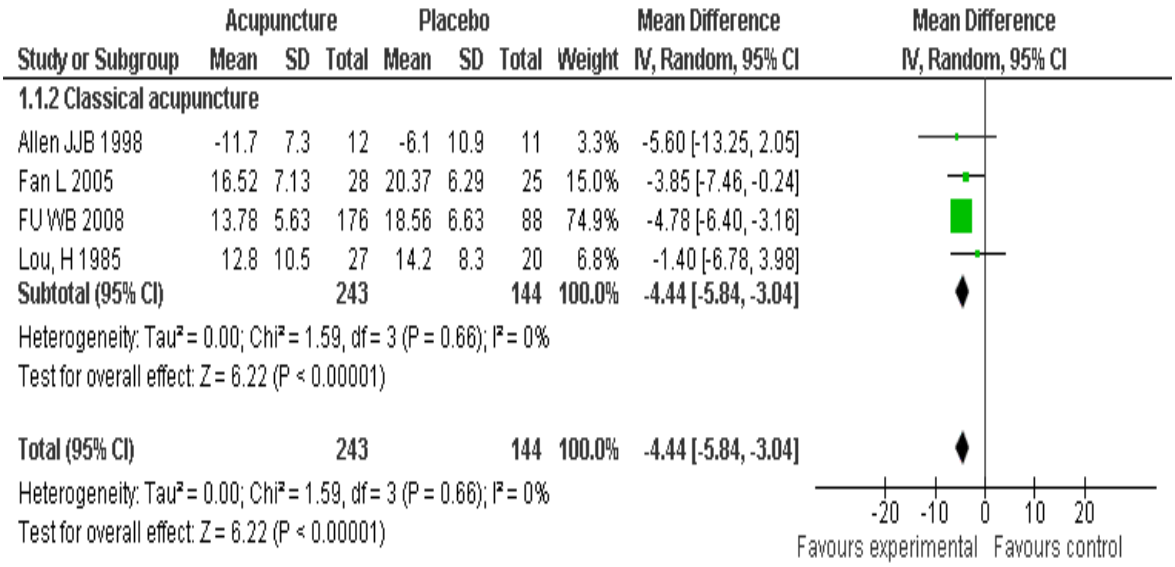
A total of twenty-one different trials were included in the Meta Analysis which contained a total of 2, 102 subjects.

Acupuncture versus placebo

1.1.2. Classical acupuncture

01. Outcome: Reduction in severity of depression

Four studies (387 participants) made this comparison and reported reduction in severity of depression using the Hamilton Depression Rating Scale for Depression (Allen 1998, Fan 2005, Fu 2008 and Lou 1985). Significant difference was found between classical acupuncture and placebo (WMD -4.44, 95 % Confidence Interval (CI) -5.53 to – 3.04, P = 0.00001).

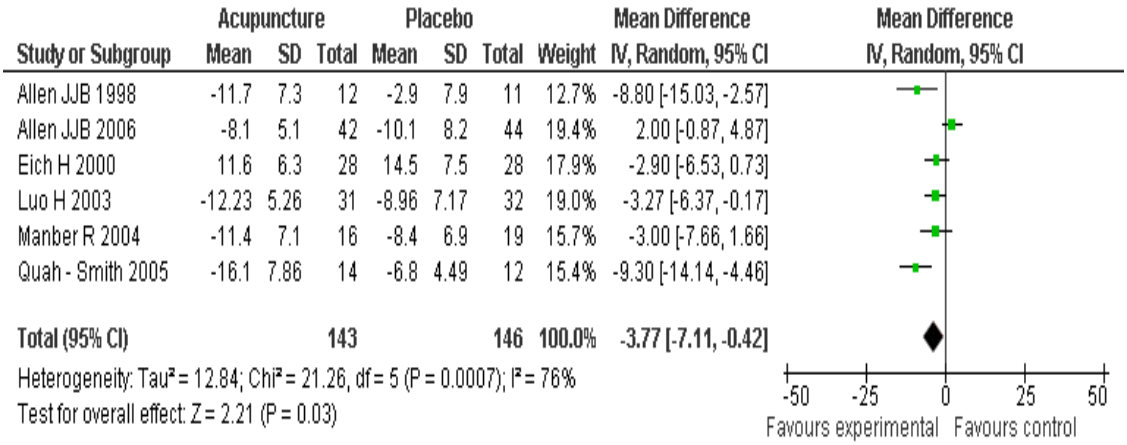


Acupuncture versus placebo

1.2.2. Classical Acupuncture

02. Outcome: Improvement in depression

Six studies (289 participants) investigated this comparison and reported improvement in depression using Hamilton Rating Scale for Depression (Allen 1998, Allen 2006, Eich 2000, Lou 2003, Manber 2004 and Quah-Smith 2005). A significant difference was detected between the acupuncture and placebo groups at the end of the intervention (WMD – 3.77, 95 % CI – 7.11 to - 0.42, P = 0.03). Heterogeneity was 76 %, which is quite high and makes comparison somewhat difficult. When there is an I-square over 50 %, a random effects' model for the meta-analysis is to be chosen. In this comparison I-square was 76 %, therefore a random model was used for the analysis.



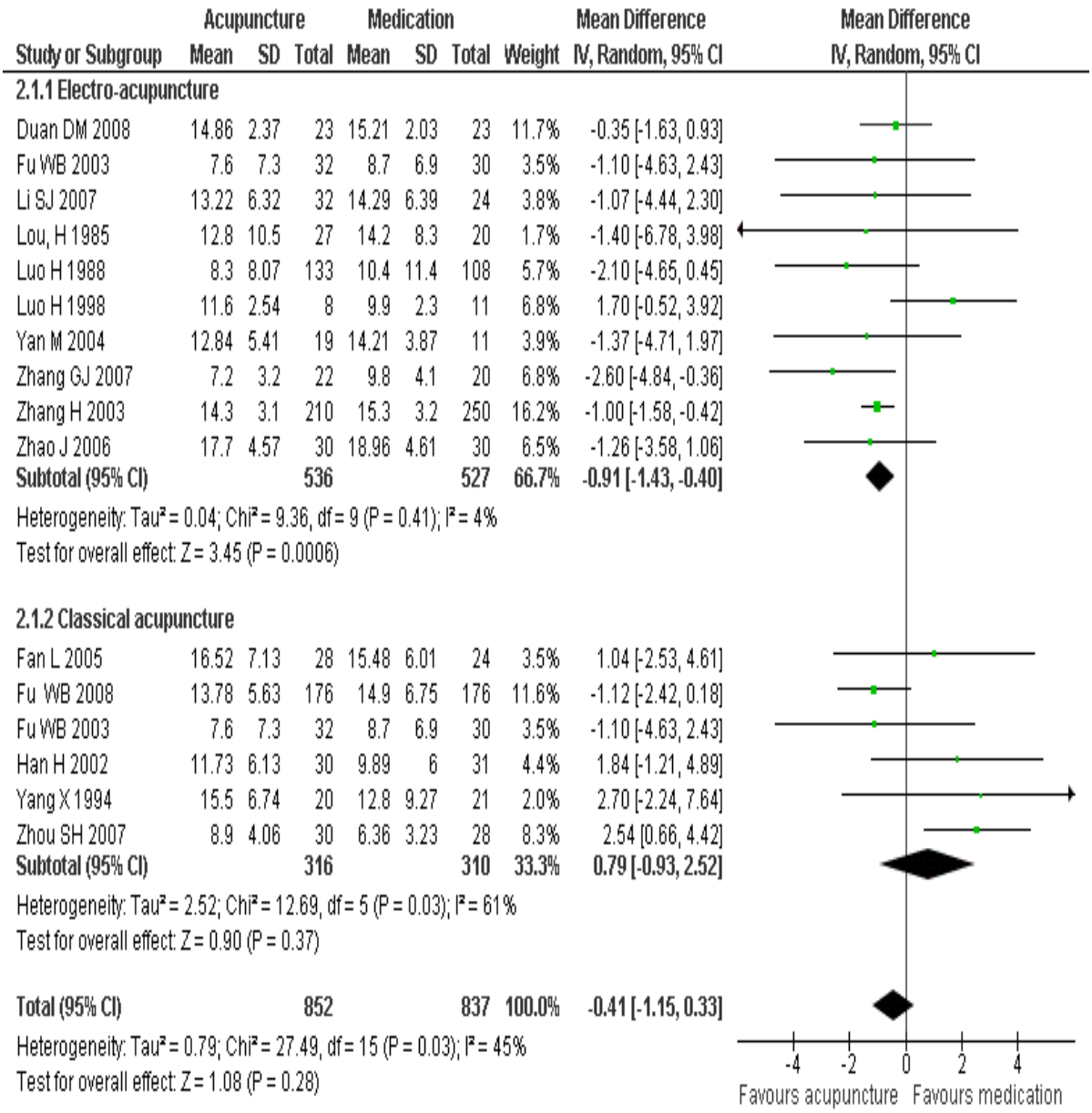
Acupuncture versus medication

2.1.1. Electro-acupuncture

2.1.2. Classical acupuncture

03. Outcome: Reduction in severity of depression

Fifteen studies (1,689 participants) investigated this comparison and reported reduction in severity of depression using the Hamilton Depression Rating Scale for Depression (Duan 2008, Fu 2008, Li 2007, Lou 1988, Lou 1998, Lou 1985, Yan 2004, Zhao 2006, Zhang 2003, Zhang 2007, Fan 2005, Fu 2003, Yang 1994 and Han 2002 and Zhou 2007). No significant difference was found between the two acupuncture groups and medication group at the end of the intervention (WMD – 0, 41 95 % CI – 1.15 to 0.33, P = 0.28). A comparison was made between electro-acupuncture (Duan 2008, Fu 2003 Li 2007, Lou1985, Lou 1988, Lou1998, Yan 2004, Zhang 2007, Zhang 2003 and Zhao 2006) and a classical acupuncture approach (Fan 2005, Fu 2003, Fu 2008, Han 2002, Yang 1994 and Zhou 2007). A difference was found between these two styles. A significant reduction in the severity of depression was found by electro-acupuncture (WMD – 0.91, 95 % CI -1.43 to - 0.40, P = 0.0006) but not in the classical acupuncture approach (WMD 0.79, 95 % CI – 1.93 to 2.52, P = 0.37).

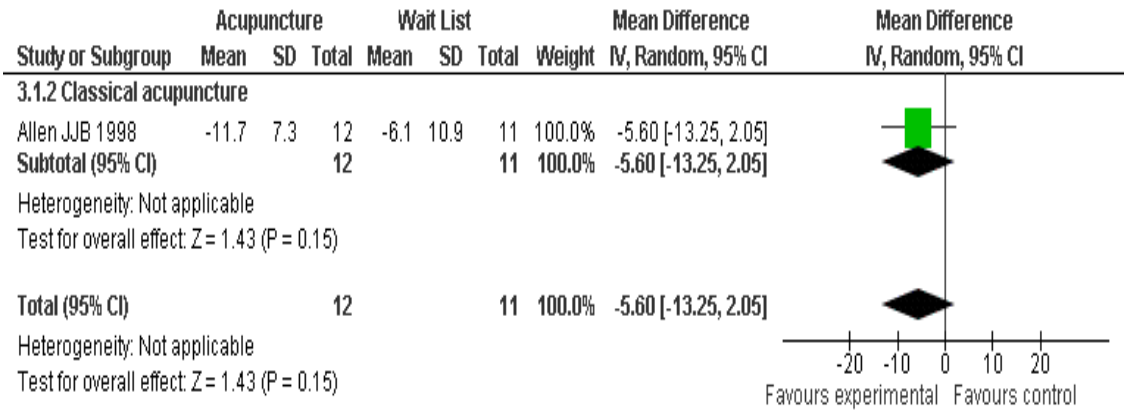

Acupuncture
Medication
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
2.1.1 Electro-acupuncture
Duan DM 2008 14.86 2.37 23 15.21 2.03 23 11.7% -0.35 [-1.63, 0.93]
Fu WB 2003 7.6 7.3 32 8.7 6.9 30 3.5% -1.10 [-4.63, 2.43]
Li SJ 2007 13.22 6.32 32 14.29 6.39 24 3.8% -1.07 [-4.44, 2.30]
Lou, H 1985 12.8 10.5 27 14.2 8.3 20 1.7% -1.40 [-6.78, 3.98]
Luo H 1988 8.3 8.07 133 10.4 11.4 108 5.7% -2.10 [-4.65, 0.45]
Luo H 1998 11.6 2.54 8 9.9 2.3 11 6.8% 1.70 [-0.52, 3.92]
Yan M 2004 12.84 5.41 19 14.21 3.87 11 3.9% -1.37 [-4.71, 1.97]
Zhang GJ 2007 7.2 3.2 22 9.8 4.1 20 6.8% -2.60 [-4.84, -0.36]
Zhang H 2003 14.3 3.1 210 15.3 3.2 250 16.2% -1.00 [-1.58, -0.42]
Zhao J 2006 17.7 4.57 30 18.96 4.61 30 6.5% -1.26 [-3.58, 1.06]
Subtotal (95% CI) 536 527 66.7% -0.91 [-1.43, -0.40]
Heterogeneity: Tau² = 0.04; Chi² = 9.36, df = 9 (P = 0.41); I² = 4%
Test for overall effect: Z = 3.45 (P = 0.0006)
2.1.2 Classical acupuncture
Fan L 2005 16.52 7.13 28 15.48 6.01 24 3.5% 1.04 [-2.53, 4.61]
Fu WB 2008 13.78 5.63 176 14.9 6.75 176 11.6% -1.12 [-2.42, 0.18]
Fu WB 2003 7.6 7.3 32 8.7 6.9 30 3.5% -1.10 [-4.63, 2.43]
Han H 2002 11.73 6.13 30 9.89 6 31 4.4% 1.84 [-1.21, 4.89]
Yang X 1994 15.5 6.74 20 12.8 9.27 21 2.0% 2.70 [-2.24, 7.64]
Zhou SH 2007 8.9 4.06 30 6.36 3.23 28 8.3% 2.54 [0.66, 4.42]
Subtotal (95% CI) 316 310 33.3% 0.79 [-0.93, 2.52]
Heterogeneity: Tau² = 2.52; Chi² = 12.69, df = 5 (P = 0.03); I² = 61%
Test for overall effect: Z = 0.90 (P = 0.37)
Total (95% CI) 852 837 100.0% -0.41 [-1.15, 0.33]
Heterogeneity: Tau² = 0.79; Chi² = 27.49, df = 15 (P = 0.03); I² = 45%
Test for overall effect: Z = 1.08 (P = 0.28)
-4
-2
0
2
4
Favours acupuncture
Favours medication

Acupuncture versus waiting list

3.1.2. Classical acupuncture

04. Outcome: Reduction in severity of depression

Allen (1998) reported on the mean change in Hamilton Depression Rating scores from baseline to eight weeks. No significant differences was found between the groups (MWD – 5.60, 95 % CI – 13.25 to 2.05, P = 0.15). Two trials should have undertaken this comparison (Allen1998 and 2006), but data from Allen (2006) was reported in an inappropriate way, and it was impossible to transfer data into mean and standard deviation. Therefore it could not be incorporated into the meta- analysis. However, data from Allen demonstrates that patients receiving acupuncture demonstrated significantly greater improvement than patients assigned to waiting lists. However, there was no evidence to support differential efficacy between depression-specific and non-specific acupuncture intervention in his study.



DISCUSSION

Four systematic reviews and eighteen randomized controlled trials were included in this overview. Four randomized trials were excluded; two of these trials were identical but published in different journals. One trial had no data for outcome measures, and one trial had depression data mixed with other psychological data. Eight Chinese trials were evaluated and translated by Xing Liao and data outcome was extracted by Jianping Liu and I transferred the data into Revman 5. In that way, they were included in the meta-analyses but not analyzed further in this overview. Four systematic reviews and eighteen RCTs compared acupuncture with pharmacotherapy, sham acupuncture, placebo and waiting list control. The present overview found no positive effect in reduction of depression by classical acupuncture compared to a waiting list control. But this overview suggests significant beneficial effects for classical acupuncture in both improving and reducing depression compared to placebo. Further, it suggests that electro-acupuncture may have positive effects in reduction of depression compared to medication. A comparison made between electro-acupuncture and classical acupuncture suggested that the latter approach has no significant effect in reducing depression. This may emphasize the importance of using electro-acupuncture on head points when treating depression.

It is difficult to find a satisfactory control intervention for acupuncture, as needles inserted into the skin avoiding acupuncture points and meridians (sham acupuncture) are likely to have some effect (62, 63). In Allen (1998 and 2006) valid acupuncture points not designed to treat individuals' depression were used as control intervention (NONSPEC acupuncture) which was compared to specific acupuncture points (SPEC

acupuncture). The trials found no evidence to support differential efficacy of the two types of acupuncture intervention. Such results could reflect that the specific acupuncture intervention was not particularly effective, or that the intended control was somewhat more effective than predicted, or both. On this basis, the positive effect of acupuncture compared to placebo found in this overview is therefore interesting and justifies further research.

Before accepting the findings of this overview to form a basis for clinical practice, the following weaknesses have to be considered. First of all the randomized controlled trials in this overview had several methodological flaws in terms of insufficient reporting of generating methods of the allocation sequence, allocation concealment and double blinding. Ten trials (30-34, 38, 44-47) provided limited description of study design, and most trials stated only that patients were randomly assigned. Such information does not allow a judgment of whether or not it was conducted properly. However, five trials reported how the randomization was performed in detail. One study used stratified randomization (41). Two studies used utilized block randomization (36, 39) and two studies reported simple randomization procedure (29, 40). In addition, two studies referred to a manual (10) in which the study design and randomization were described (19, 37). These seven trials also used double-blinded design, including subject, acupuncturist and evaluator blinding. In addition, one trial (35) reported single-blinded design, involving patient but not therapist-blinding. If a double-blinded design is impossible, outcome assessment should be done by an investigator blinded to the treatment receiver. Lack of this may introduce a source of bias (64). These eight trials, six

conducted in Western countries (19, 35-37, 40, 41) and two in China (29, 39), were of high quality in terms of generation of allocation sequence, concealment of allocation, double blinding and application of intention to treat analyses. They also received a high score (3-5 points) on the Jadad Scale (65), which included the following criteria: method of randomization, double blinding and reporting of withdrawal and dropout. However, this scale has limitations as it gives more weight to the quality of reporting than to the actual methodological quality (64). This scale addresses randomization but does not assess allocation concealment. The use of an open random-number table would thus be considered equivalent to concealed randomization using a telephone or computer system and earn the maximum points foreseen for randomization. Therefore, relevant methodological aspects should be assessed individually and always include the key domains of concealment of treatment allocation, blinding of outcome assessment or double blinding and handling of withdrawals and dropouts (64).

Methodological issues such as poor quality in terms of randomization and blinding may be associated with exaggerated effects of acupuncture interventions due to subjected systematic bias. Potential bias may be found in selection of participants, administration of treatment and assessment of outcomes. In addition, less rigorous methodological trials demonstrate significantly larger intervention effects than trials with more rigor (66, 67).

Secondly, in an intention to treat analysis participants are analyzed according to their original group assignment, whether or not this is the intervention they actually received, or whether or not they accepted or adhered to the intervention (68). The primary analysis

of an RCT should always be an intention to treat analysis, since it avoids the possibility of any bias associated with loss, miss-allocation or non-adherence of participants. Even though not reported, we must assume that most of the trials in this Overview performed an intention to treat analysis, since they used all the numbers of randomization in their data analyses.

Ten trials (56 %) had no information on missing or drop-out of participants. In Zhang (2003) (46) for example, there were 210 participants in the intervention group and 250 in the control group. Since an important principle in research is to get the two groups as equal as possible, it is tempting to ask what happened to the 40 participants that were missing in the intervention group. The insufficient report of loss to follow up makes it impossible to explore potential bias on an intention to treat basis. This may be associated with exaggerated effects for the acupuncture intervention due to systematic error (bias) (68). Although improved reporting practice should facilitate the assessment of methodological quality in the future, incomplete reporting continues to be an important problem when assessing trial quality.

Thirdly, six trials (33 %) had well defined diagnostic criteria for participants whereas twelve trials (67 %) had unclear diagnostic criteria. This inconsistency in the application of diagnostic criteria may bias the evaluation of the acupuncture treatment due to the heterogeneous mix of participants in the included trials. The included trials may have included patients with other psychiatric diseases with symptoms that overlap depression.

Fourthly, most of the included trials were small. Although some data analyses did not demonstrate a statistically significant difference between acupuncture and control intervention, the results are likely to have been underpowered. Therefore, the analyses from the small trials may not establish with confidence that two interventions have equivalent effects (69).

Fifthly, many of the studies included in this overview come from China, a country that traditionally never publishes negative acupuncture studies (70). Publication bias is the tendency for individuals to submit or publish trials depending on the direction or strength of the findings. Clinical trials are much more likely to be published if there is statistically significant difference among treatment groups (24, 66). This may vary across countries and cultures, but one will expect that the overall proportion of positive trials would tend to be higher in countries with the greatest publication bias. Accordingly, when interpreting the present findings, publication bias should be taken into consideration.

Sixthly, another possible explanation for positive results in favor of acupuncture could be that acupuncture is more effective in countries where it is traditionally practiced. In addition, Chinese doctors may be more skilled at acupuncture or more enabled to predict which patients may benefit from the treatment. It is possible that studies published in English and designed correctly with a Western scientific approach, do not have the correct TCM approach in terms of appropriate dose/intensity and duration of acupuncture treatment and use practitioners with insufficient acupuncture skills to carry out the intervention in research programs, both regarding appropriate needle insertion and

manipulation techniques. Data from this overview demonstrates that Chinese trials give an average of thirty-three treatment sessions for treating depression, with vigorous electro-stimulation on head points (DU20) and (Yintang), in contrast to Western trials that give an average of twelve treatment sessions and no electro-stimulation on head points at all. This may be a contributor to the positive results in favor of acupuncture in Chinese studies.

Seventhly, there are many styles of acupuncture, such as individual tailored acupuncture as used in Allen (2006), or standard/formula acupuncture as used in Lou (1988). As illustrated in this overview, there is a wide variation in the mode of stimulation, duration, needle depth and number of needles used in these trials. Only 24 % of the trials in this Overview reported every STRICTA-item. It is important that future acupuncture trials report every item and detail that is asked in the STRICTA- guidelines both to ensure good report quality in trials, but also for clinical practice; so as to enable acupuncturists to treat the patients according to the best evidence available.

Eighthly, although strong efforts have been made to retrieve all RCTs on the subject, one cannot be absolutely certain that one have succeeded. However, findings from overviews should primarily be used as a compass for deciding what type of intervention to use for certain conditions and it is important for clinicians and policy makers not to interpret low-quality evidence of no effect. Low-quality evidence means unclear evidence and findings should initiate more research and reviews.

AUTHOR'S CONCLUSIONS

Implication for Practice

Current evidence from systematic reviews and randomized trials shows beneficial effects of electro-acupuncture in reduction of depression compared to antidepressant medication. A beneficial effect was also found for classical acupuncture in improving and reducing depression compared to placebo. However, there was insufficient data to demonstrate whether classical acupuncture was more effective in reducing depression than a waiting list control. More rigorous trials are needed and long-term effects should be investigated if acupuncture is to be recommended as one of the alternative treatments for depression.

Implication for Research

Further randomized trials are required to evaluate the effectiveness of acupuncture in treating depression. The methodological quality of clinical trials needs to be improved. The following aspects concerning methodological quality are important: (a) reporting of the generation of the allocation sequence and allocation concealment, (b) blinding of practitioner (where appropriate), outcome assessor and analyst, (c) clear description of withdrawals/dropouts during trials, (d) improving the quality of reporting and particular attention should be given to reporting practitioner background, other components of treatment and control or comparator interventions.

Future studies may need to consider the use of comparative designs using medication, standard care or psychotherapy due to the ethics of administering this intervention to the study population. Long term evaluation of effectiveness and adverse effects should also be considered in future trials.

NOTE

I have got permission from Ragnar Hotvedt (Institute leader); to include the translation of the Chinese trials into this thesis. All new identified trials could then be included in the meta-analyses, even though the page limit was consequently exceeded. The figures and graphs from RevMan 5 were directly transferred into the thesis so that no manipulation with the numbers was possible.

References

1. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of mata - analyses of randomised controlled trials: the QUORUM statement.Quality of Reporting of Meta - Analyses Lancet1999;354(9193):1896-900.

2. MacPherson H, Thorpe L, Thomas K, Geddes D. Acupuncture for Depression: First Step Toward a Clinical Evaluation. The Journal of Alternative and Complementary Medicine2004;10(6):1083-91.

3. World Health Organization. Management of Mental Disorders. 4th ed. Sydney: WHO Collaborating Centre for Evidence in Mental Health Policy; 2004.

4. Dozois DJA, Westra HA. The nature of anxiety and depression: Implication for prevention. The prevention of anxiety and depression: Theory, research, and practice. Washington: American Psychological Association; 2004. p. 9-41.

5. Murthy RS, Bertolote JM, Epping-Jordan J, Funk M, Prentice T, Saraoeno B. Mental Health: New understanding, new hope2001 [cited 2009 14.01.]: Available from: http://www.who.int/whr/2001/en/index.html.

6. Beardslee WR, Gladstone TRG, Wright EJ, Cooper AB. A Family-Based Approach to the Prevention of Depressive Symptoms in Children at Risk: Evidence of Parental and Child Change. Pediatrics2003 August 1, 2003;112(2):e119-31.

7. MacPherson H, Hammerschlag R, Lewith G, Schnyer R. Acupuncture Research Strategies for Establishing an Evidence Base London: Churchill Livingstone; 2007.

8. Birch S, Kaptchuk T. History, nature and current practice of acupuncture: an East Asian perspective. Oxford: Butterworth-Heinmann; 1999.

9. Bing Y, Pritzer S. The Apologetic Heart, Shame, Depression and Bèi Dìe in Chinese Culture & Medicine. Journal of Chinese Medicine2004;76:9-14.

10. Schnyer R, Allen JJB. Acupuncture in the Treatment of Depression. A Manual for Practice and Research. Edinburgh: Churchill Livingstone; 2001.

11. Maciocia G. The Practice of Chinese Medicine. Edinburgh: Churcill Livingstone; 1994.

12. Flaws B, Lake J. Chinese Medical Psychiatry, A Textbook and Clinical Manual. Boulder: Blue Poppy Press; 2001.

13. Yang N. Health protection of Essence - Spirit (Brain Aspects) in TCM. Master study in Acupuncture, Mental Health in Chinese Medicine; 09.07.05.; Sydney - Australia: University of Western Sydney; 2005. p. 1-8.

14. Deadman P, Al-Khafaji M. Emotional Disturbance by Acupuncture with particular reference to the Du Mai. Journal of Chinese Medicine1995;47:30-4.

15. Dahr HL, Vasanti T. Endogenous depression, thyroid function and acupuncture. Indian Journal of Physiology & Pharmacology2001;45(1):125-26.

16. Sadock BJ, Sadock VA. Other pharmacological and biological therapies. Comprehensive textbook of psychiatry: Lippincott Williams & Wilkins; 2004.

17. Spence DW, Kayumov L, Chen A, Lowe A, Jain U, Katzman MA, et al. Acupuncture Increases Nocturnal Melatonin Secretion and Reduces Insomnia and Anxiety: A Preliminary Report. J Neuropsychiatry Clin Neurosci2004 February 1, 2004;16(1):19-28.

18. Xu X. Acupuncture in an Outpatient Clinic in China: A Comparison With the Use of Acupuncture in North America. Southern Medical Journal: Lippincott Williams & Wilkins; 2001. p. 813-6.

19. Allen JJB, Schnyler RN, Hitt SK. The efficacy of acupuncture in the treatment of major depression in women. American Psychological Society1998;9(5):397-401.

20. Kirsch I. St John's wort, conventional medication, and placebo: an egregious double standard. Complementary Therapies in Medicine2003;11(3):193-5.

21. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington, DC: American Psychiatric Association; 1994.

22. Spitzer RL, Kroenke K, Linzer M, Hahn SR, Williams JB, deGruy FV. Health-related quality of life in primary care patients with mental disorders. Results from the PRIME-MD 1000 Study. JAMA1995;275:1511-7.

23. World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders. Diagnostic Criteria for Research. Geneva: World Health Organization; 1993.

24. Higgins JPT. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5.(Updated May 2005). Green S, editor. Chichester U.K: John Wiley & Sons, Ltd; 2005.

25. Mukaino Y, Park J, White A, Ernst E. The effectiveness of acupuncture for depression - a systematic review of randomised controlled trials. Acupuncture in Medicine2005;23(2):70-6.

26. Smith CA, Hay PPJ. Acupuncture for depression. Cochrane Database of Systematic Reviews [serial on the Internet]. 2004; (3): Available from: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004046/frame.html.

27. Leo RJ, Ligot JR, Salvador JA. A systematic review of randomized controlled trials of acupuncture in the treatment of depression. Journal of Affective Disorders2007;97(1-3):13-22.

28. Wang H, Qi H, Wang B, Cui YY, Zhu L, Rong ZX, et al. Is acupuncture beneficial in depression: A meta-analysis of 8 randomized controlled trials? Journal of Affective Disorders2008;111(2-3):125-34.

29. Fu WB, Fan L, Zhu XP, He Q, Wang L, Zhuang LX, et al. Clinical research on acupuncture treatment of depressive neurosis by using liver-function-regulating method. Acupunct Res2006;31:355-8.

30. Han C, Li XW, Luo HC. Comparative study of electro-acupuncture and maprotiline in treating depression. Zhongguo Zhong Xi Yi He Za Zhi2002;22(7):512-4.

31. Luo H, Yunkui J, Li Z. Electro-Acupuncture vs.amitriptyline in the treatment of depressive states. Journal of Traditional Chinese Medicine1985;5(1):3-8.

32. Luo HC, Shen YC, Jia YK, Zhou D. Clinical study of electro-acupuncture on 133 patients with depression in comparison with tricyclic amitriptyline. Chinese Journal of Modern Development in Traditional Medicine1988;8(2):77-80.

33. Lou H, Meng F, Jia Y, Zhao X. Clinical research on the therapeutic effect of the electro-acupuncture treatment in patients with depression. Psychiatry and Clinical Neurosciences1998;52:338-40.

34. Yang X, Liu X, Luo H, Jia Y. Clinical observation on needling extrachannel points in treating mental depression. Journal of Traditional Chinese Medicine1994;14(1):14-8.

35. Roschke J, Wolf CH, Muller MJ, Wagner P, Mann K, Grozinger M, et al. The benefit from whole body acupuncture in major depression. Journal of Affective Disorders2000;57:73-81.

36. Eich H, Agelink MW, Lehmann E, Lemmer W, Klieser E. Acupuncture in patients with minor depressive episodes and generalized anxiety. Results of an experimental study. Fortschritte der Neurologie-Psychiatrie2000;68(3):137-44.

37. Manber R, Schnyer RN, Allen JJB, Rush AJ, Blasely CM. Acupuncture: a promising treatment for depression during pregnancy. Journal of Affective Disorders2004;83:89-95.

38. Li C, Huang Y, Li Y, Hu K, Jiang Z. Treating post-stroke depression with mind-refreshing antidepressive acupuncture therapy. Int J Clin Acupunct1994;5(4):389-93.

39. Luo HC, Ureil H, Shen YC, Meng FQ, Zhao XY, Liang W, et al. Comparative study of electroacupuncture and fiuoxetine for treatment of depression. Chin J Psychiatry2003;36:215-9.

40. Quah-Smith JL, Tang WM, Russell J. Laser acupuncture for mild to moderate depression in a primary care setting - a randomized controlled trial. Acupuncture In Medicine2005;23(3):103-11.

41. Allen JJB, Schnyer RN, Chambers AS, Hitt SK, Moreno FA, Manber R. Acupuncture for Depression: A Randomized Controlled Trial. J Clin Psychiatry 2006;67(11):1665-73.

42. Han C, Li X, Luo H. Randomized Clinical Trial Comparing the Effects of Electro-acupuncture and Maprotiline in Treating Depression. International Journal of Clinical Acupuncture2006;15(1):7-13.

43. Han C, Li X, Luo H. Clinical Study on Electro-acupuncture Treatment for 30 Cases of Mental Depression. Journal of Chinese Medicine2004;24(3):172-76.

44. Fu W. Observations on the curative effect of acupuncture on depressive neurosis. Journal of Acupuncture and Tuina Science [serial on the Internet]. 2003; (4): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/385/CN-00595385/frame.html.

45. Zhang GJ, Shi ZY, Liu S, Gong SH, Liu JQ, Liu JS. Clinical observation on treatment of depression by electro-acupuncture combined with Paroxetine. Chinese journal of integrative medicine [serial on the Internet]. 2007; (3): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/670/CN-00619670/frame.html.

46. Zhang H HJ. Clinical observation of electroacupuncture in treating depression. Journal of Acupuncture and Tuina Science [serial on the Internet]. 2003; (4): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/328/CN-00596328/frame.html.

47. Zhao J, Peng S. Clinical observation on acupuncture treatment of depressive nevrosis in 30 cases. J Tradit Chin Med2006;26(3):191-2.

48. Gallagher SM, Allen JJB, Hitt SK, Schnyer RN, Manber R. Six-month depression relapse rates among women treated with acupuncture. Complementary Therapies in Medicine2001;2:216-8.

49. Da Silva JBG. Acupuncture for mild to moderate emotional complains in pregnancy. Acupuncture in Medicine2007;25(3):65-71.

50. Yan M, Mao X, Wu JL. [Comparison of electroacupuncture and amitriptyline in treating depression]. Zhongguo Linchuang Kangfu [serial on the Internet]. 2004; (18): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/321/CN-00497321/frame.html.

51. Fan L, Fu WB, CR; M, Zhu XP, Mi JP, Li WX, et al. [Effect of acupuncture at routine acupoint and non-acupoint on depressive neurosis evaluated with Hamilton depression scale]. Zhongguo Linchuang Kangfu [serial on the Internet]. 2005; (28): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/474/CN-00557474/frame.html.

52. Duan DM, Tu Y, Chen LP. [Assessment of effectiveness of electroacupuncture and fluoxetine for treatment of depression with physical symptoms]. Zhongguo zhen jiu = Chinese acupuncture & moxibustion [serial on the Internet]. 2008; (3): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/432/CN-00631432/frame.html.

53. Zhou SH. [Acupuncture in the treatment of female climacteric depression in 60 cases]. Journal of Clinical Rehabilitative Tissue Engineering Research [serial on the Internet]. 2007; (39): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/102/CN-00641102/frame.html.

54. Li SJ, Liu T. [Clinical observation on treatment of melancholia by acupuncture following principle of relieving depression and regulating mentality]. Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi = Chinese journal of integrated traditional and Western medicine / Zhongguo Zhong xi yi jie he xue hui, Zhongguo Zhong yi yan jiu yuan zhu ban [serial on the Internet]. 2007; (2): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/094/CN-00627094/frame.html.

55. Fu WB, Fan L, Zhu XP, He Q, Wang L, Zhuang LX, et al. Acupuncture for treatment of depressive neurosis: a multi-center randomized controlled study. Zhongguo Zhen Jiu = Chinese acupuncture & moxibustion2008;28(1):3-6.

56. Hou Q, Yan L, Fu L, Du YH. [Tiaoshen shugan acupuncture versus routine acupuncture for intervention of depression and anxiety]. Zhongguo Linchuang Kangfu [serial on the Internet]. 2005; (28): Available from: http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/473/CN-00557473/frame.html.

57. Huang Y, Xia DB. Clinical observation on treatment of depression with scalp electro-acupuncture: a report of 30 cases. Zhong Xi Yi Jie He Xue Bao2004;2(2):151.

58. Wang H, Qi H, Wang B-S, Cui Y-Y, Zhu L, Rong Z-X, et al. Is acupuncture beneficial in depression: A meta-analysis of 8 randomized controlled trials? Journal of Affective Disorders2008;111:125-34.

59. MacPherson H, White A, Cummings M, Jobst KA, Niemtzow RC. Standards For Reporting Interventions In Controlled Trials Of Acupuncture: The STRICTA Recommendations. The Journal of Alternative and Complementary Medicine2002;8(1):85-90.

60. Norheim A. Adverse Effects of Acupuncture: A Study of the Literature for the Years 1981 - 1994. The Journal of Alternative and Complementary medicine1996;2(2):291-7.

61. Ernst E, White AR. Prospective studies of the safety of acupuncture: a systematic review. The American Journal of Medicine2001;110(6):481-5.

62. Kaptchuk TJ, Stason WB, Davis RB, Legedza ART, Schnyer RN, Kerr CH, et al. Sham device v inert pill: randomised controlled trial of two placebo treatments. BMJ2006 February 18, 2006;332(7538):391-7.

63. Birch S. A Review and Analysis of Placebo Treatments, Placebo Effects, and Placebo Controls in Trials of Medical Procedures When Sham Is Not Inert. The Journal of Alternative and Complementary Medicine2006;12(3):303-10.

64. Juni P, Witschi A, Bloch R, Egger M. The Hazards of Scoring the Quality of Clinical Trials for Meta-analysis. JAMA1999 September 15, 1999;282(11):1054-60.

65. Jadad AR, Moore AR, Carroll D, Jenkinson C, Reynolds JMD, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? Controlled Clinical Trials1996;17(1):1-12.

66. Kjaergard LL, Villumsen J, Gluud C. Reported Methodological Quality and Discrepancies between Large and Small Randomized Trials in Meta-Analyses. Ann Intern Med2001 December 4, 2001;135(11):982-9.

67. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? The Lancet1998;352(9128):609-13.

68. Kirkwood BR, Sterne JAC. Essential Medical Statistics. Second ed. Oxford: Blackwell Publishing Ltd; 2003.

69. Laake P, Olsen BR, Benestad HB. Forskning i medisin og biofag. Oslo: Gyldendal Akademiske; 2008.

70. Vickers A, Goyal N, Harland R, Rees R. Do Certain Countries Produce Only Positive Results? A Systematic Review of Controlled Trials. Controlled Clinical Trials1998;19(2):159-66.

Appendix I

Table 1. *Search Results from their inception date until January 2009 with Time and Time Range*

Database	Time Range	Terms	Hits	SR	RCT
Cochrane Library	**No specific**	**MESH-description: Depression/acupuncture/ electroacupuncture Keywords: depress*ti,ag,kw/dysthymi*ti,ab,kw/ Acupuncture*ti,ab,kw/ electroacupuncture*ti,ab,kw**	**131**	**3**	**28**
Cochrane Reviews			**3**	**3**	
DARE			**4**	**4**	
Controlled Trials			**123**		**28**

MedLine	**1966-2009**	**MESH terms: depressive disorder/depressive disorder, major/dysthymic disorder Acupuncture therapy/acupuncture, ear/electroacupuncture/moxibustion Keywords: depress$/dysthymi$/acupuncture$/ electroacupuncture$/moxibustion$**	**66**	**4**	**14**
Embase	**1980-2009**	**Search terms the same as in Medline**	**644**	**2**	**16**
AMED	**1985-2009**	**MESH terms: Depression/acupuncture. Keywords the same as in Medline**	**135**	**1**	**6**
PubMed	**No specific**	**MESH terms: depression/acupuncture Keywords: depression/dysthymia/acupuncture/ acupuncture therapy**	**104**	**1**	**14**
PsycINFO	**1950-2009**	**MESH terms: endogenous/depression/depression/ major depression/acupuncture Keywords the same as in Embase**	**119**	**1**	**5**

Table 2: *Primary outcome measures of RCTs, data used in the Meta Analysis*

Study ID	Treatment group	Control group	Outcome measure	Treatment Mean/SD	Control Mean/ SD
Acupuncture versus medication (El-acupuncture)					
Duan DM 2008	23	23	Reduc. in severity of depr/HAMD	14.86 2.37	15.21 2.03
Fu WB 2003	32	30	Same as above	7.6 7.3	8.7 6.9
Li SJ 2007	32	24	Same as above	13.22 6.32	14.29 6.39
Lou H 1985	27	20	Same as above	12.8 10.5	14.2 8.3
Luo H 1988	133	108	Same as above	8.3 8.7	10.4 11.4
Luo H 1998	8	11	Same as above	11.6 2.54	9.9 2.3
Yan M 2004	19	11	Same as above	12.84 5.41	14.21 3.87
Zhang GJ 2007	22	20	Same as above	7.2 3.2	9.8 4.1
Zhang H 2003	210	250	Same as above	14.3 3.1	15.3 3.2
Zhao J 2006	30	30	Same as above	17.7 4.57	18.96 4.61
Acupuncture versus medication (classical)					
Fan L 2005	28	24	Reduc. In severity of depr/ HAMD	16.52 7.13	15.48 6.01
Fu WB 2003	32	30	Same as above	7.6 7.3	8.7 6.9
Fu WB 2008	176	176	Same as above	13.78 5.63	14.9 6.75
Han C 2002	30	31	Same as above	11.73 6.13	9.98 6.0
Yang X 1994	20	21	Same as above	15.5 6.74	12.8 9.27
Zhou SH 2007	30	28	Same as above	8.9 4.06	6.36 3.23

Acupuncture versus waiting list (classical)				
Allen JJB 1998	12	11	Reduc. In severity of depr/HAMD	-11.7 7.3 -6.10 10.9
Allen JJB 2006	42	44	Same as above	
Acupuncture versus placebo (classical)				
Allen JJB 1998	12	11	Improvement of depr/HAMD	-11.7 7.3 -2.9 7.9
Allen JJB 2006	42	44	Same as above	-8.1 5.1 -10.1 8.2
Eich H 2000	28	28	Same as above	11.6 6.3 14.5 7.5
Lou H 2003	31	32	Same as above	-12.23 5.26 -8.96 7.17
Manber R 2004	16	19	Same as above	-11.4 7.1 -8.4 6.9
Quah-Smith 2005	14	12	Same as above	-16.1 7.86 -6.8 4.49
Acupuncture versus placebo (classical)				
Allen JJB 1998	12	11	Reduc.In severity of Depr/HAMD	-11.7 7.3 -6.1 10.9
Fan L 2005	28	25	Same as above	16.52 7.13 20.37 6.29
Fu WB 2008	176	88	Same as above	13.78 5.63 18.56 6.63
Lou H 1985	27	20	Same as above	12.8 7.3 14.2 8.3

Table 3: *Analysis of Intervention details according to the STRICTA-Checklist for 17 included RCTs, whether or not each item was reported.*

	Acupuncture Rationale		
Study	**Acupuncture Style**	**Reasoning for Treatment**	**Treatment Variation**
Luo 85	Yes	Yes	Yes
Lou 88	Yes	Yes	Yes
Lou 98	Yes	Yes	Yes
Lou 03	Yes	Yes	Yes
Yang 94	Yes	Yes	Yes
Allen 98	Yes	Yes	Yes
Röschke 00	Yes	Yes	Yes
Han 02	Yes	Yes	Yes
Eich 00	Yes	Yes	Yes
Manber 04	Yes	Yes	Yes
Li 94	Yes	Yes	Yes
Q-Smith 05	Yes	Yes	Yes
Allen 06	Yes	Yes	Yes
Fu 03	Yes	Yes	Yes
Zhang 03	Yes	Yes	Yes
Zhao 06	Yes	Yes	Yes
Zhang 07	Yes	Yes	Yes

	Needling Details						
Study	**Number**	**Name**	**Depth**	**Responses**	**Stimulation**	**Retention**	**Type**
Luo 85	Yes	Yes	Yes	Yes	Yes	Yes	No
Lou 88	Yes	Yes	Yes	Yes	Yes	Yes	No
Lou 98	Yes	Yes	Yes	Yes	Yes	Yes	No
Lou 03	Yes	Yes	Yes	Yes	Yes	Yes	No
Yang 94	Yes	Yes	No	Yes	Yes	No	No
Allen 98	Yes	Yes	Yes	Yes	Yes	Yes	No
Röschke 00	Yes	Yes	Yes	No	No	Yes	Yes
Han 02	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Eich 00	Yes	Yes	No	No	No	No	Yes
Manber 04	Yes	Yes	Yes	Yes	Yes	Yes	No
Li 94	Yes	Yes	No	No	Yes	Yes	No
Q-Smith 05	Yes	Yes	No	No	Yes	Yes	Yes
Allen 06	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Fu 03	Yes	Yes	No	Yes	No	Yes	No
Zhang 03	Yes	Yes	Yes	Yes	Yes	Yes	No
Zhao 06	Yes	Yes	No	No	Yes	Yes	Yes
Zhang 07	Yes	Yes	No	No	Yes	Yes	No

Treatment Regimen

Study	Number of Sessions	Frequency/Duration of Sessions
Luo 85	Yes	Yes/Yes
Lou 88	Yes	Yes/Yes
Lou 98	Yes	Yes/Yes
Lou 03	Yes	Yes/Yes
Yang 94	Yes	Yes/No
Allen 98	Yes	Yes/Yes
Röschke 00	Yes	Yes/Yes
Han 02	Yes	Yes/Yes
Eich 00	Yes	Yes/No
Manber 04	Yes	Yes/Yes
Li 94	Yes	Yes/Yes
Q-Smith 05	Yes	Yes/Yes
Allen 06	Yes	Yes/Yes
Fu 03	Yes	Yes/Yes
Zhang 03	Yes	Yes/Yes
Zhao 06	Yes	Yes/Yes
Zhang 07	Yes	Yes/Yes

Other Components of Treatment

Study	Other Interventions to Acup Group	Instruction to practitioner/Info to patients	
Luo 85	No other intervention given	No	No
Lou 88	No other intervention given	No	No
Lou 98	Yes	No	No
Lou 03	Yes	No	No
Yang 94	No other intervention given	No	No
Allen 98	No other intervention given	Yes	Yes
Röschke 00	Yes	No	No
Han 02	No other intervention given	No	No
Eich 00	No other intervention given	No	No
Manber 04	No other intervention given	Yes	Yes
Li 94	No other intervention given	No	No
Q-Smith 05	No other intervention given	Yes	Yes
Allen 06	No other intervention given	Yes	Yes
Fu 03	No other intervention given	No	No
Zhang 03	Yes	No	No
Zhao 06	No other intervention given	No	No
Zhang 07	Yes	No	No

Practitioner Background			
Study	**Qualification**	**Years of Practice**	**Relevant Experience**
Luo 85	No	No	No
Lou 88	No	No	No
Lou 98	No	No	No
Lou 03	No	No	No
Yang 94	No	No	No
Allen 98	Yes	Yes	No
Röschke 00	Yes	No	No
Han 02	No	No	No
Eich 00	Yes	No	No
Manber 04	No	No	No
Li 94	No	No	No
Q-Smith 05	Yes	Yes	No
Allen 06	Yes	Yes	No
Fu 03	Yes	Yes	Yes
Zhang 03	No	No	No
Zhao 06	No	No	No
Zhang 07	No	No	No

Control or Comparator Interventions			
Study	**Rational**	**Source to justify Choice**	**Precise description of Control**
Luo 85	No	No	Yes
Lou 88	No	No	Yes
Lou 98	No	No	Yes
Lou 03	No	No	Yes
Yang 94	No	No	Yes
Allen 98	Yes	Yes	No
Röschke 00	No	No	Yes
Han 02	No	No	Yes
Eich 00	No	No	Yes
Manber 04	Yes	Yes	No
Li 94	No	No	Yes
Q-Smith 05	Yes	Yes	Yes
Allen 06	Yes	Yes	No
Fu 03	No	No	No
Zhang 03	No	No	No
Zhao 06	No	No	No
Zhang 07	No	No	Yes

Appendix II

Table 4: *Methodological quality of New Included RCTs*

Eight studies extracted

1 Study Fu Wen Bin 2008

Acupuncture for treatment of depressive neurosis: a multi center randomized controlled study

Methods	With a multi-center randomized controlled study, 440 cases were randomly divided into an acupuncture group, a prozac group, a non-acupoint needling group. It took simple random method to implement a multi-center randomization with the ratio of 2:2:1 by using PEMS3.1 software and used opaque sealed envelope. In the acupuncture group, Hegu (L I 4) and Taichong (LR 3) were selected, and the Prozac group was treated with administration of 20 mg/ d and the non-acupoint needling group was treated with needling the points deviating from the acupoints. The therapeutic effect was evaluated by HAMD score reduction rate, and Asberg's anti-depressant side-effect rating scale (SERS) and severe adverse reaction were used for safety evaluation. **Statistic method:** used double- double entry method to enter data from the trial, used SPSS 11.0 software or PEMS3.1 made by West China University of Medical Sciences to analyze the data. Firstly used covariance analysis to find there were center effects, then used PEMS3.1 for meta analysis; Secondly, used u test for HAMD score before and after treatment in three groups; Thirdly, adopted Cochrane's and Mantel-Haenszel statistics of SPSS 13. 0 software to analyze curative effects of three groups; At last, used ANOVA and Rank sum test to analyze the side effects of three groups.
Participants	440 patients were selected from Acupuncture and Moxibustion clinic or Psychological clinic in four different hospitals from October 2004 to December 2006, who were randomly divided into three groups as following: **The acupuncture group**: 176 patients ,67 males and 109 females, average age was(41.87±12.29) **The prozac group:** 176 patients, 54 males and 122 females, average age was (39.88±11.04) **The non-acupoint needling group:** 88 patients, 28 males and 60 females, average age was (43.51±11.43) years. They were diagnosed according to clear western medicine criteria and traditional Chinese medicine syndrome differentiation criteria. Western medicine diagnosed criteria is CCMD-2-R, which is Chinese classification of mental disorders with the diagnostic criteria made in 1994. TCM syndrome differentiation criteria referred to TCM disease and syndrome diagnosing and treating criteria issued by State bureau of TCM admin in 1995. And the article also reported inclusive and exclusive criteria.
Interventions	(1)**The acupuncture group** was treated with two steps that are fist step of body acupuncture (BC) and second step of auricular acupuncture (AC). BC: Hegu (LI 4), Taichong (LR3), Baihui (DU20) and Yintang (EX-HN3)

	were selected and 0. 35 mm × 25 mm needles were used, firstly, needling LI4 and LR3 with 15 mm depth, slowly and perpendicularly, then twirling and lifting and thrusting the needle equably until the responses were elicited (obtain Qi), secondly, quick needling DU20 at approximately 30°angle with 15mm depth, thirdly, horizontal needling EX-HN3 by lifting-kneading inserting with 15mm depth, both DU20 and EX-HN3 with twirling and lifting and thrusting the needle equably until the responses were elicited (obtain Qi). After that, the needles were retained with *"qi-inducing method"*, which asked patients to breathe deeply with nose until the needles were pulled out for 30 minutes. **AA**: after BA, ear points needle embedding in Xin (heart) and Gan (liver) point of one ear, used pushpin-shaped intradermal imbedding needles, fixed by straps, for three days, two ears alternatively. Treatment above lasted for twelve weeks, twice every week. (2)**The Prozac group** were treated with administration of 20 mg/ d: took after breakfast in the morning , lasting for twelve weeks (3)**The non-acupoint** needling group was treated with needling sham acupoints including body and ear. Body sham acupoints are 0.5cm near LI 4 radial side, 0.5cm near LR3 medial side, 0.5cm near DU20 left side, 0.5cm near EX-HN3 left side, which were applied like the acupuncture group. Ear sham acupoints were selected on the back of Xin (heart) and Gan (liver) point of the same ear like the acupuncture group. The rest were the same with the acupuncture group.
Outcomes	(1) Outcome measures: the total score of the 24 items HAMD, Asberg's anti-depressant side-effect rating scale (SERS) and severe adverse reaction were recorded (2) Observational time: before and after the treatment The therapeutic effect was evaluated by HAMD score reduction rate, and Asberg's anti-depressant side-effect rating scale (SERS) and severe adverse reaction were used for safety evaluation, and the data were analyzed with ITT. 64 cases dropped out or were excluded at the end of treatment. The total effective rate was 86. 4 % in the acupuncture group, which was better than 59.1 % in the non-acupoint needling group and 72.7% in the prozac group; HAMD score in the acupuncture group was similar to that in the Prozac group, which was better than that in the non-acupoint needling group; the SERS scores in the acupuncture group and the non-acupoint needling group were significantly lower than that in the Prozac group, with no severe side-effects found for acupuncture.
Notes	About the masking: the author reported that patients would not make difference between the acupuncture group and the non-acupoint needling group and the evaluator would have nothing to do with the treatment. This trial is a National Administration of Traditional Chinese Medicine-funded project.
Allocation concealment	Serially numbered , opaque, sealed envelopes

2 Study Duan Dong Mei 2008

Assessment of effectiveness of electroacupuncture and Fluoxetine for treatment of depression with physical symptoms

Methods	Seventy five cases were randomly divided into a western medicine group (group A), an eIectroacupunctue group (group B) and an eIectroacupuncture plus medicine group (group C), by using random number table, 25 cases in each group. The group A were treated by oral Fluoxetine, 20 mg each day; the group B by electroacupuncture with Baihui(GV20)and Yintang (EX-HN3)selected as main points; the group C by oral administration of Fluoxetine plus electroacupunctue. HAMD depression scale was used for assessment of clinical therapeutic effect and TESS adverse reaction scale was used for adverse reactions. **Statistic method:** used SPSS 12.0 software, enumeration data of curative effect were statistically analyzed by Chi-square test, measurement data such as the score of HAMD and the score of side effects used x±s, and t test.
Participants	Seventy five cases diagnosed in the inpatient or outpatient department of Nerve Medicine and Clinical Psychology at Chinese PLA general hospital and were divided randomly into three groups. The three groups are a western medicine group (group A), an eIectroacupunctue group (group B) and an eIectroacupuncture plus medicine group (group C), each group with 25 cases. Patients were diagnosed according to the western medicine diagnosed criteria, CCMD-3, which is Chinese classification of mental disorders with the diagnostic criteria made in 2001 and selected following inclusive and exclusive criteria. **Group A:** 4 males and 21 females, average age was (49.72±5.47) years **Group B:** 6males and 19 females, average age was (50.12±4.32) years **Group C:** 5 males and 12 females, average age was (48.93±4.34) years
Interventions	**Group A** were treated with oral Fluoxetine (Prozac): 20 mg each day, lasting for six weeks. **Group B** were treated with electroacupuncture with Baihui (GV20) and Yintang (EX-HN3)selected as main points; **Electroacupuncture method:** G-6805-1 electric apparatus was applied on the points of Baihui and Yintang for 30 minutes , continuous wave was selected, frequency was 120-250 times/ minute, the strength depended on individual's tolerance, the needles retained for one hour, once a day , continuously for 6 days, one day interval between treatment courses, six courses in total. Meanwhile there are five sub-groups of coordinated acupoints with the main points according to TCM syndrome differentiation and treatment as following: Liver-Qi stagnation pattern coordinated with combined with Hegu, Taichong, and so on. Fire transmission due to stagnation of qi pattern coordinated with Xingjian and Xiaxi melancholily beingnerve - racking pattern coordinated with Anmian, Shenmen, and Neiguan Heart and sp leen deficiency pattern coordinated with Sanyinjiao and Zusanli Effulgent yin deficiency fire pattern coordinated with Taixi and Zhaohai **Group C** was treated with oral administration of Fluoxetine plus electroacupuncture which was applied like Group B.
Outcomes	HAMD depression scale was used for assessment of clinical therapeutic effect and TESS adverse reaction scale was used for adverse reactions. The clinical effective rate was 78.3 in the group A; 82.6 in the group B and 91.7 in the group C, with significant differences between group C and A, group C and B ($P< 0.05$). Groups B and C had significant therapeutic effects in improvement of physical symptoms, and the adverse reaction of Fluoxetine in

	the group C was less than that in the group A. There were five dropped cases including three cases caused by serious side effects, which were not analyzed as for curative effects and general scores of HAMD assessing. The five dropped cases were two cases from group A caused by Fluoxetine, one case from group B becoming serious because of mother's death, one case dropped because of business trip and one case from group C caused by Fluoxetine. The three serious side effects cases were analyzed by using TESS adverse reaction scale. There was no analysis with ITT.
Notes	This trial is a Beijing Municipal Natural Science Foundation key project. There were needling details about performing on main points, Baihui (GV20) and Yintang (EX-HN3) but not on coordinated acupoints
Allocation concealment	Not mentioned

3 Study Li Shijun 2007

Clinical Observation on Treatment of Melancholia by Acupuncture Following Principle of Relieving Depression and Regulating Mentality

Methods	Randomized controlled trial according to the order of hospitalization. Patients were divided randomly into two groups. The observed group was treated with needling and electroacupuncture (EA) and the control group orally took Fluoxetine or Paroxetine. The curative effect, Hamilton Depression Scale scores (HAMD), effect initiating time and sustaining time were observed and compared. **Statistic method:** used SPSS11.5 software statistically to analyze including Chi-square test, t test and Rank sum test.
Participants	Thirty seven patients with depression, who were treated in the Depression out patient clinic of Acupuncture Department of First affiliated Hospital, Tianjin University of Traditional Chinese Medicine and were selected between March 2001 and September 2002 with the agreement of the patients or their guardian. Patients were divided randomly into two groups, the experimental group and the control group. Patients were diagnosed according to the western medicine diagnosed criteria CCMD-3, which is Chinese classification of mental disorders with the diagnostic criteria made in 2001.And patients were selected according to the diagnostic criteria of depression of CCMD-3. Meanwhile, Hamilton rating scale for depression (HAMD) (24 items), Beck depression inventory (BDI) were used together to evaluate depression. Mild depression: HAMD score>20, BDI score is 5-13; Moderate depression: HAMD score>26, BDI score is 14-20; Severe depression: HAMD score>35, BDI score is>21; **The experimental group:** 32 patients with 15 males ,17 females, age from 22 to 67, average age was (49.19±13.46), treatment course is from 1month to 4 years, average treatment course was (13.25±12.76) months. There were three different degrees of depression in this group including 5 mild cases, 18moderate cases and 9 severe cases. **The control group:** 24 patients with 10 males ,14 females, age from 22 to 65, average age was (47.00±13.08) months, treatment course is from 2 weeks to 2 years, average treatment course was (9.50±7.96) months. The

	different degrees of depression in this group including 3 mild cases, 16moderate cases and 5 severe cases. There were not clear inclusive and exclusive criteria reported in this article.
Interventions	**The patients in acupuncture group** were treated with needling and electroacupuncture (EA) following principle of relieving depression and regulating mentality, once each day , one treatment course two weeks ,six weeks in total Selected points: thirteen selected points are Fengchi, Anmian, Sishencong, Yintang, Baihui, Shenmen, Jianshi, Hegu, Taichong, Sanyinjiao, Qiuxu, Shuaigu, Zusanli. Coordinated points were also selected according to different depressive symptoms as following: Palpitation chest distention, and short breath plus Neiguan and Shanzhong; insomnia plus era points (Xin and Shenmen); gastrointestinal symptoms such as anepithymia plus Zhongwan;defecation obstruction plus Tianshu. Procedure: the size of needles are 0.25 mm×60～75 mm, twirling were mainly used, Shenmen should be needled gently and shallowly, Zhongwan needled with reducing method in reinforcing or reducing method by manipulating the needle in cooperation with the patients' respiration, **Yintang and Baihui** with EA depended on the patients' tolerance, when needling patients should close eyes, breathe smoothly and relax, the needles were retained for 30 min, once each day, two weeks a treatment course, depending on the degree of severity and prognosis, treatment time to a maximum of 6 weeks, and then evaluated the curative effect. **The patients in control group** took oral Fluoxetine or Paroxetine, 20 mg each day, every morning, six weeks in total.
Outcomes	The total effective rate was 87.5 % and 79.1 % in the observed group and the control group respectively, showing insignificant difference between them ($P > 0.05$), but comparison of the initiating time and sustaining time between the two groups did show significant different ($P < 0.01$). There were five dropped patients, who were not analyzed and not ITT analysis.
Notes	None
Allocation concealment	None

4 Study Zhou Shenghong 2007

Acupuncture in the treatment of female climacteric depression in 60 cases

Methods	All of patients were randomly divided into acupuncture group and control group by drawing lots, 30 cases in each. They knew and agreed the treating methods. HAMD reducing rate was regarded as the criteria to assess the therapeutic effect (HAMD reducing rate= (post-treatment scores-pre-treatment scores)/pre-treatment scores×100%). Recovery: HAMD reducing rate≥75%; remarkable improvement: HAMD reducing rate ≥50%; improvement: HAMD reducing rate≥25%; ineffective: HAMD reducing rate < 25%. Recovery and remarkable improvement were obviously effective; recovery and remarkable improvement added improvement were effective, the rates of obviously effective and effective at different time were calculated. Side effects appeared in the patients were observed. **Statistic method:** used SPSS10.0 software statistically to analyze including

	Chi-square test for curative effect analysis in two groups, paired t test for scale core changing comparison before and after treatment and just counted the number when side effect appeared.
Participants	Totally 60 patients of female climacteric depression were enrolled from Psychiatrical Clinic of the Second Hospital attached to Shandong University of Traditional Chinese Medicine between September 2005 and June 2006. All of them accorded with diagnostic criteria of depressive episode of the Chinese Classification and Diagnostic Criteria of Mental Disorders Third-Edition (CCMD-3). Meanwhile HAMD-21items version (pre-17 items' score >17) and modified Kupperman index assessment (the index >1.5) were used. Patients' age is from 41-58, the average age was (50±3) years, treatment course is from 5 months to 8 years, and the average treatment course is was (25±11) months. 40 cases were natural climacteric, 1 case was artificial climacteric; 19 patients had catamenia (17 cases with disorder catamenia. 2 cases with normal catamenia). Patients were divided randomly into two groups as following: Acupuncture group with 30 patients and Control group with 30 patients There were not clear inclusive and exclusive criteria reported in this article.
Interventions	**Acupuncture group:** prescription: Ganshu(BL 18), Shenshu(BL 23), Xinshu(BL 15), Zusanli(ST36), Sanyinjiao(SP 6)of bilateral, Shenting (DU 24), Benshen(GB 13), Shencong(Extra). Moderate reinforcing and reducing techniques was used to treat patients once a day, rest 1 day after treating 6 days, and 6 continuous weeks as one course. The patients were accessed with Hamilton Rating Scale for Depression (HAMD) at pre-treatment and the end of weeks 2, 4, 6 during the course of treatment, respectively (21 items, graded by 5 classes, 0: none, 1: mild degree, 2: moderate degree, 3: severe degree, 4: very severe degree). **Control group** was administrated with 20 mg Fluoxetine Hydrochloride Capsules (Eli Lilly and Company), once daily and 6 continuous weeks as a course. The controls were evaluated at pre-treatment and the end of weeks 2, 4, 6 during the course of treatment, respectively.
Outcomes	Comparison of HAMD scores between pre-and post-treatment of two groups: HAMD scores of the control group at the end of weeks 2, 4, 6 after treatment was (18.79±3.64), (11.52±5.31), (6.36±3.23) points, which were lower than the scores of pre-treatment [(24.17±5.26) points, P<0.05-0.01].HAMD scores of the acupuncture group at the end of weeks 4, 6 after treatment were(16.51±4.47), (8.90±4.06)point, which were lower than that of Pre-treatment [(25.83±5.72)points, P<0.01]. (2)After being treated for 6 weeks, the obviously effective rate of the acupuncture group was 26.7%(8/30)and 42.8%(12/28), which was higher than that of week 2 after treatment 3.3%(1/30),7.1% (2/28),P<0.05, 0.01]. After being treated for 6 weeks, the effective rate of acupuncture group and control group were 86.7%(26/30) and 92.9% (26/28)respectively, which was higher than that of week 4 after treatment 33.3%(10/30). 64.2% (18/28),P< 0.01]. There was no side effect in acupuncture group during the course of treatment, and there were 5 patients in control group appeared light side effect such as nausea, dizzy etc. But no other high-grade side effect was found. There were significant differences between two groups in the side effect pre-and post-treatment (P<0.05). There were two dropped patients in control group because of no continuing

	treatment who were not analyzed. There was no ITT analysis.
Notes	It was founded by Shandong Province Sanitation office founded project
Allocation concealment	Not mentioned

5 Study Hou Qing 2005

Tiaoshen shugan acupuncture versus routine acupuncture for intervention of depression and anxiety

Method	Seventy two patients, according to the order of hospitalization, were randomly divided into 2 groups: acupuncture group with 40 cases and control group with 32 cases. At the moment of diagnosis and one month after treatment, the patients filled out the self rating depressive scale (20 terms ,4 grades, 1-4points for little symptom to most of time with the symptom, but 2,5,6,11,12,14,16,17,18, and 20 terms was anti assessment question with 4-1 points. The range of test time was the latest one week. The adding of the 20 terms score to gain the total mark, over 41 was positive), and the Zung self rating anxiety scale (20terms ,4grade, 1-4 points for little time with the symptom to most of time with the symptom, but 5,9,13,17 and 19 terms was anti assessment question with4-1 points. The range of test time was the latest one week. The adding of the 20 terms score to gain the total mark, after the total mark multiplies with 1.25; the integer number was gained to obtain the standard mark which over 50 points for positive.) to assess the depressive and anxiety condition and severity degree objectively. The depressive severity index = total mark /80; The anxiety severity index= standard mark/80。 **Statistic method:** used SPSS10.0 software statistically to analyze including one-way ANOVA and α=0.05
Participants	Seventy two patients with depression, who were treated in the Department of Acupuncture and out patient clinic, First affiliated Hospital, Tianjin University of Traditional Chinese Medicine were selected between March 2001 and September 2002 with the agreement of the patients or their guardian. There were inclusive and exclusive criteria reported clearly in this article but not diagnostic criteria (some content of diagnostic criteria were in inclusive criteria). 72 patients were 22 males and 50 females, the average age was (40±18), including 12 cases with involutional depression, 20 with anxiety disorder and 40 with depression. Cases with involutional depression and anxiety disorder accorded with the diagnostic criteria of Practical Medicine and cases with depression accorded with the diagnostic criteria of Chinese protocol about classification of mental illness and diagnostic criteria (the revised 2nd edition)
Interventions	(1) **The patients in acupuncture group** were treated with tiao shen shu gan and dated the points: Neikuan (PC6), Philtrum, Paihui (Du20), Yint'ang (Extra), Sanyinjiao（SP6） and Taichong(LR3). Neikuan: The twirling combined with lifting and thrusting the needle reinforcing reducing method was conducted. Needled bilateral Neikuan to the depth of 5-10cm with an angle of 90° for one minute. Philtrum: At the first three days of patients' treatment, Then acupuncture on Renzhong was followed using oblique direction to column of nose into 5 cm using bid-peck needling and reduction in acupuncture method until the eyeball became moist or weeping, then replaced by Baihui and Yintang after three

	days. Paihui: horizontally needled towards the back at the depth of 5 cm and twirling reinforcing method was done with lower amplitude and high frequency for one minute. Yint'ang: The twirling reinforcing method was done with lower amplitude and high frequency for one minute by skin-kneading and oblique inserting to 5 cm. Sanyinjiao: The twirling and lifting and thrusting the needle reinforcing method were conducted. Needled to the depth of 5-12cm with an angle of 90° for one minute. Taichong: The twirling and lifting and thrusting the needle reinforcing method were conducted. Needled to the depth of 5cm with an angle of 90° for one minute. (2) **The patients in control group** were performed routine acupuncture and the points were gained: Ch'ime (Front – Mu point of the liver, Liv14), Yangligch'van (He-Sea point, GB34), Shenmen(Shu-stream and Yuan Source Point, H7) and Chienshih (jing-River Point,P5). According to differentiation of symptoms and signs, reinforcing or reducing or uniform reinforcing reducing method were conducted.
Outcome	Totally 72 patients were involved in the result analysis without dropping. (1) The comparison of the depressive total mark between the patients in the two groups before and after treatment: It significantly decreased after treatment compared with before treatment in acupuncture group and after treatment in control group [33.40±7.71, 52.70±6.80, 39.58±8.50 (t=7.91, 7.61, P<10.05)]. (2) The comparison of the depressive severity index before and after treatment in the patients in the two groups : It significantly decreased after treatment compared with before treatment in acupuncture group and after treatment in control group[0.40±0.07,0.66±0.09,0.48±0.10(t=7.3,7.14 P<0.05)] (3) comparison of the anxiety standard mark before and after treatment in the patients in the two group: It significantly decreased after treatment compared with before treatment in acupuncture group and after treatment in control group [27.96±8.35,0.59±0.07,0.45±0.05(t=7.26,7.09 ,P<0.05)]. It didn't report ITT analysis.
Notes	None
Allocation Concealment	Not mentioned

6 Study Fan Li 2005

Effect of acupuncture at routine acupoint and non-acupoint on depressive neurosisi evaluated with Hamilton depression scale

Methods	Randomized controlled trial by using simple random method. Used PEMS3.1 statistic software made by West China University of Medical Sciences to prepare serially numbered, opaque, sealed envelopes according to sample size calculation They were assessed with the 24-item HAMD at 3 months after treatment, and the therapeutic effect was evaluated with the rate of decreasing score. **Statistic method:** used SPSS10.0 software statistically to analyze by epidemiology research office of Guangdong Hospital of TCM including enumeration data with Chi-square test and Rank sum test, measurement data

	with ANOVA. Blind-method evaluation implemented by the third party.
Participants	Eighty one patients with depressive neurosis, who were treated at outpatient department in Guangdong Provincial Hospital of Traditional Chinese Medicine between May 2004 and February 2005, were randomly divided into routine acupoint acupuncture group (n=28), Prozac group (n=24) and non-acupoint acupuncture group (n=25). There were inclusive and exclusive criteria reported clearly in the article but not diagnostic criteria (some content of diagnostic criteria were in inclusive criteria). 81 patients were 43 males and 38 females, the average age was 32.6.
Interventions	**Routine acupoint acupuncture group (n=28):** selected acupoints: Siguan(Taichong on both sides and Hegu),Baihui, Yintang. Used 0.35× 25mm needles. Firstly needled Siguan perpendicularly and slowly to the depth of 0.5 cun by twirling and lifting and thrusting the needle equably until the responses were elicited (obtain Qi), secondly, quick needling DU20 at approximately 30°angle with 0.5 cun depth, thirdly, horizontal needling EX-HN3 by lifting-kneading inserting with 0.5 cun depth, both DU20 and EX-HN3 with twirling and lifting and thrusting the needle equably until the responses were elicited (obtain Qi). After that, the needles were retained with "qi-inducing method", which asked patients to breathe deeply with nose until the needles were pulled out for 30 minutes. After acupuncture above, **ear points with cowherb seeds** buried in Xin (heart) and Gan (liver) point of one ear, for three days, two ears alternatively. Treatment above twice every week. **The Prozac group (n=28)** were treated with administration of 20 mg/d. **The non-acupoint needling group (n=25)** was treated with needling sham acupoints including body and ear. Body sham acupoints are 0.5cm near LI 4 radial side, 0.5cm near LR3 medial side, 0.5cm near DU20 left side, 0.5cm near EX-HN3 left side, which were applied like the acupuncture group. Ear sham acupoints were selected on the back of Xin (heart) and Gan (liver) point of the same ear like the acupuncture group. The rest were the same with the acupuncture group. All three groups were combined with an available psychotherapy and some patients were allowed to use Estazolam to treat insomnia tentatively at the beginning of the trial. Treatment course: 3 months.
Outcome	They were assessed with the 24-item HAMD at 3 months after treatment, and the therapeutic effect was evaluated with the rate of decreasing score. Finally 77 cases were involved in the analysis of results. (1) The scores of HAMD after treatment in the routine acupoint acupuncture group, Prozac group and non-acupoint acupuncture group were obviously lower than those before treatment[(26.01±3.99,16.52±7.13); (25.14±5.78,15.48±6.01); (25.65±3.42, 20.37±6.29), P<0.05]. (2)The HAMD score in the routine acupoint acupuncture group was insignificantly different from the Prozac group (t=0.57,P>0.05),but significantly different from that in the non-acupoint acupuncture group(t=2.14,P<0.05).(3)The therapeutic effect in the routine acupoint acupuncture group was similar to that in the Prozac group(Z=-2.09,P=0.03).(4) Gastrointestinal abnormality occurred in 4 cases of the Prozac group, no adverse event was observed in the acupuncture groups Gastrointestinal abnormality occurred in 4 cases of the Prozac group and

	dropped, which was not analyzed. There was no ITT reported.
Notes	None
Allocation Concealment	Serially numbered, opaque, sealed envelopes

7 Study Huang Yong 2004

Clinical observation of scalp electricoacupuncture for treatment of 30 cases with depression

Methods	Randomized controlled trial. Sixty patients with depression were selected for the trial in which scalp electricoacupuncture was used for treatment of 30 cases. Hamilton Rating Scale for Depression (HRSD) and Beck scale were used for assessing the curative effects from both doctors' and patients' sides. Sixty cases were randomly divided into a western medicine group taking oral Fluoxetine Hydrochlorlde and a scalp eIectroacupuncture group accepting scalp eIectroacupuncture, 30 cases in each group. **Statistic method:** used SPSS software statistically to analyze data including Chi-square test.
Participants	Sixty patients with depression from four different hospitals, who are outpatients and inpatients, included 16 males and 44 females and were selected from October 2001 to December 2002. The average age were 19～57 years and (36.37±4.29) years; the average treatment course were one to 14 months and (45. 22 ±9. 58) days. There was no clear diagnostic, inclusive, and exclusive criteria reported in this article. It reported that patients selected according to the western medicine diagnosed criteria, CCMD-3.
Interventions	**Scalp eIectroacupuncture group** accepted scale eIectroacupuncture, one day off every six days. Acupoints were on middle line of vertex(MS5), middle line of forehead (MS1)and bilateral lateral line 1 of forehead (MS2), G6805 electric apparatus was applied after patients' responses were elicited (obtain Qi) for 30 minutes, continuous wave was selected, followed by wave 50 Hz and intensity 4 V, once a day for six days per week **Western medicine group** took oral Fluoxetine Hydrochlorlde, 20-40 mg/day. All the patients had been treated for six weeks.
Outcome	All patients were evaluated before and after treatment by using HRSD (24 items version) and Beck (67 items version) scale. There were one case with gastrointestinal discomfort, which occurred 4 weeks after treatment and one case with insomnia, which occurred 5 weeks after treatment in control group. There were three patients complaining with the pain caused by acupuncture in treatment group. There is no significant difference between two groups in HRSD scale and Beck scale ($P > 0.05$). There is a significant difference in both groups before and after treatment according to Beck scale. There were no dropped cases and ITT reported in this article.
Notes	This trial is a National Natural Science Foundation of China project. There was no random method reported in this article.

Allocation Concealment	Not mentioned

8 Study Yan Ming 2004

Comparison of electroacupuncture and amitriptyline in treating depression

Methods	Randomized controlled trial by the way of simple random sampling. Thirty patients with depression were divided randomly into electroacupuncture group (n=19) and amitriptyline group (n=11), and the treatment course was six weeks in both group. All the patients were evaluated with the Hamilton rating scale for depression (HAMD) and clinical global impression scale (CGIS) before and after treatment, respectively, and once a week during the treatment. **Statistic method:** used SPSS 10.0 software statistically to analyze data including Chi-square test and t test.
Participants	Thirty patients with depression including 13 males and 17 females, who were treated at both out patient and in patient clinic in Nanning Hospital in Tianjin from May 1998 to December 2003. electroacupuncture group (n=19): 10 males and 9 females, the average age was (38±5); amitriptyline group (n=11): 3 males and 8 females, the average age was (36±8); There were only inclusive criteria reported in this article and not diagnostic and exclusive criteria.
Interventions	**Electroacupuncture group** (n=19): Oblique needling Baihui (DU20) and Yintang (EX-HN3) to 1 cun depth then used G605 electric apparatus at the level of seeing local muscle tic and making patients feel comfortable. Frequency was 80-90 times/min, 1h/time, 1time/d, 30 times a treatment course. **Amitriptyline group** (n=11): 250 mg/d in the first week, and then average dose was 130mg/d with modification according to patients' condition and side effects, six weeks a treatment course. One treatment course in both groups.
Outcomes	All the patients were evaluated with the Hamilton rating scale for depression (HAMD) and clinical global impression scale (CGIS) before and after treatment, respectively, and once a week during the treatment. There was no significant difference tin curative effect between the two groups (X^2=14.9, P>0.05). The scores of HAMD were significantly different before and after treatment in both groups (t=8.48, 4.97, P<0.01), while there was no significant difference between the two groups (t=0.31, P>0.05). There was no significant difference in the score of CGIS, except efficacy index, before and after treatment between the two groups (t=0.864, P>0.05). It reported that there were no dropped cases and not ITT.
Notes	None
Allocation concealment	Not mentioned

Table 5: *Outcome Data from Chinese Trials extracted by Jianping Liu*

20-05-2009

Study Fu WB 2008 **HAMD scores**

Group	No. cases	Before treatment	After treatment
Acup	176	27.40±4.75	13.78±5.63
Prozac (fluoxetine)	176	26.11±4.75	14.90±6.75
Non-acupoint needling	88	26.33±4.25	18.56±6.63

Study Duan DM 2008 **HAMD scores**

Group	No. cases	Before treatment	After treatment
fluoxetine (A)	23	27.91±2.43	15.21±2.03
Electronic acup (B)	23	27.57±3.46	14.86±2.37
EA + fluoxetine (C)	24	28.12±2.56	10.20±3.31

TESS score of group A and C (no data on group B)

Group	No. cases	2 weeks after treatment	4 weeks after treatment	6 weeks after treatment
Group A	25	12.34±5.32	11.20±3.28	9.86±2.25
Group C	25	8.26±1.68	5.65±1.26	4.22±0.56

Study Li SJ 2007 **HAMD total scores**

Group	No. cases	Before treatment	After treatment
Acup	32	30.31±6.03	13.22±6.32
Fluoxetine or Paroxetine	24	28.83±5.72	14.29±6.39

Study Zhou SH 2007 **HAMD scores**

Groups	n	Before treatment	After treatment (weeks)		
			2	4	6
Acup	30	25.83±5.72	22.75±3.68	16.51±4.47	8.90±4.06
fluoxetine	28	24.17±5.26	18.79±3.64	11.52±5.31	6.36±3.23

Study Hou Q 2005 **Self rating depressive scale scores**

Groups	n	Total scores of self-rating depressive scale		Depression severity index	
		Before treatment	After treatment	Before treatment	After treatment
Acup	40	52.70±6.80	33.40±7.71	0.66±0.09	0.40±0.07
Routine acup	32	52.13±7.47	39.58±8.50	0.65±0.09	0.48±0.10

The scale was composed of 20 items, and the total score over 41 was diagnosed as depression with higher score, severer of the depression. Depression severity index = total scores divided by 80. No reference was given regarding this scale and method.

Study Fan L 2005 **HAMD scores**

Group	No. cases	Before treatment	After treatment
Acup	28	26.01±3.99	16.52±7.13
Prozac (fluoxetine)	24	25.14±5.78	15.48±6.01
Non-acupoint needling	25	25.65±3.42	20.37±6.29

Study Yan M 2004 **HAMD scores**

Group	No. cases	Before treatment	After treatment
Electronic acup	19	29.74±12.15	12.84±5.41
amitriptyline	11	22.27±8.31	14.21±3.87

Study Huang Y 2004

Tab 1 reduction rate of total scores of Hamilton Rating Scale for depression (HRSD)

Group	n	marked effective	effective	ineffective
		n (%)	n (%)	n (%)
Scalp elec-acup	30	17 (56.67)	11 (36.67)	2 (6.66)
fluoxetine	30	19 (63.33)	8 (26.67)	3 (10.00)

Marked effective: defined as reduction rate over or equal to 50%; effective as over or equal to 25%, and ineffective defined as less than 25%.
reduction rate = (pre-treatment scores –posttreatment scores)/ pre-treatment scores *100%

Tab 2 Beck score before and after treatment

group	n	severe	moderate	mild	no or very mild
Scalp e-acupt					
Pre-treatment	30	8	12	10	0
Post-treatment	30	1	3	8	18
fluoxetine					
Pre-treatment	30	9	12	9	0
Post-treatment	30	0	4	6	20