

# The effectiveness of acupuncture for depression

## – a systematic review of randomised controlled trials

Yoshito Mukaino, Jongbae Park, Adrian White, Edzard Ernst

Yoshito Mukaino  
professor  
Faculty of Sports and  
Health Science  
Fukuoka University  
Japan.

Jongbae Park  
acupuncturist  
researcher  
Division for Research  
and Education in  
Complementary and  
Integrative Medical  
Therapies  
Harvard Medical  
School, Boston, USA

Adrian White  
acupuncturist  
researcher  
Peninsula Medical  
School  
Plymouth, UK

Edzard Ernst  
professor  
Peninsula Medical  
School  
Exeter, UK

Correspondence:  
Yoshito Mukaino

mukaino@fukuoka-u.ac.jp

### Abstract

**Objective** To summarise the existing evidence on acupuncture as a therapy for depression.

**Methods** RCTs were included, in which either manual acupuncture or electroacupuncture was compared with any control procedure in subjects with depression. Data were extracted independently by two authors. The methodological quality was assessed. Pre and post means and SDs for depression specific measures were extracted, when available, for meta-analysis.

**Results** Seven randomised comparative trials involving 509 patients were included. The evidence is inconsistent on whether manual acupuncture is superior to sham, and suggests that acupuncture was not superior to waiting list. Evidence suggests that the effect of electroacupuncture may not be significantly different from antidepressant medication, weighted mean difference -0.43(95% CI -5.61 to 4.76). There is inconclusive evidence on whether acupuncture has an additive effect when given as an adjunct to antidepressant drugs.

**Conclusion** The evidence from controlled trials is insufficient to conclude whether acupuncture is an effective treatment for depression, but justifies further trials of electroacupuncture.

### Keywords

*Depression, acupuncture, electroacupuncture, systematic review.*

### Introduction

The most common conventional treatments for depression, ie psychotherapy and antidepressant medication, are well-researched and known to be efficacious. However, their effectiveness in practice is reduced by high rates of dropout, lack of effect in some individuals, and relapse.<sup>1-4</sup> Many patients terminate treatment with antidepressant medications prematurely because of intolerable adverse effects.<sup>2</sup> Psychotherapy appears to produce equivalent outcomes to those obtained with antidepressant medication, but not to be uniformly accepted,<sup>2</sup> and the rate of withdrawal from treatment is similar to that with antidepressants.<sup>5</sup> Faced with these limitations of conventional treatments, patients suffering from depression often seek alternative treatment.<sup>6</sup> A recent survey revealed the popularity of complementary and alternative medicine (CAM) such as acupuncture for psychiatric and emotional disorders.<sup>7</sup> In China, Japan and Korea; acupuncture has long

been used for emotional, psychological and spiritual disorders including anxiety, stress, insomnia and depression. There seems to be an increasing demand for acupuncture in this field among western countries as well. According to a recent survey of acupuncture in the UK, acupuncturists are dealing with emotional, psychological and spiritual disorders in 9% of their patients, which is higher than acute and chronic back pain at 6%.<sup>8</sup> The results of three overviews of CAM for treating depression indicate that acupuncture is a promising modality.<sup>9-11</sup> Recently the efficacy of acupuncture for depression has attracted the attention of conventional researchers and three new studies on this subject are underway.<sup>12-14</sup> Despite the importance of the subject matter, there has been no comprehensive review of studies using acupuncture for depression.

We therefore undertook a review with the aim of summarising the existing evidence for or against the hypothesis that acupuncture is an efficacious therapy for depression.

## **Methods**

### ***Data Sources***

Computerised literature searches for controlled trials of acupuncture for depression were conducted on the following databases: Medline (1969-May 2003), The Cochrane Library (Issue 2, 2003), Embase, PsycINFO and the Centralised Information Service for Complementary Medicine (1988-May 2003) which includes the British Library Alternative Medicine database AMED as well as some complementary medicine publications that are not included in the standard databases. Additionally, personal files of all reviewers were searched. In addition, an attempt was made to access relevant Eastern literature: a major Japanese database was accessed through the *Igaku Chuo Zashi* (Japan Centra Revuo Medicina) (1981-May 2003); a Korean researcher hand-searched the two leading Korean acupuncture journals (the *Journal of Korean Acupuncture Society*, and *Kyung-Hee University Oriental Medicine Journal*) for relevant studies; and Chinese literature was accessed through a website of Chinese Medical Psychiatry (<http://chinesemedicalpsychiatry.com>) in addition to the above-described databases. The search terms ('acupuncture', 'electroacupuncture' or 'laser acupuncture') and ('depression' or 'depressive state' or 'mental disorders' or 'dysthymia') were used. Copies of all original reports were obtained whenever possible, and reference lists of these papers were searched for further relevant trials. Whenever necessary, the authors were contacted to obtain further information.

### ***Study Selection***

All articles which reported randomised comparative trials in which subjects with clinically diagnosed depression were allocated to receive either acupuncture or any control procedure were included. Any article which included needle acupuncture, electroacupuncture or laser acupuncture was acceptable. Moxibustion and acupressure were excluded. No language restrictions were applied and when a trial was reported in more than one language, the English article was chosen. Studies that only included subjects with generalised anxiety disorder were excluded. Studies for inclusion were decided upon by two authors independently.

### ***Data Extraction***

Data were extracted independently by the first two authors, using a specially prepared form. All differences were settled by discussion between the first two authors. For each study, trial design, randomisation, blinding and handling of dropouts were recorded, in addition to inclusion and exclusion criteria, details of treatment and control procedures, main outcome measure and study result. Pre and post means and SD's for measures specific for depression were extracted, when available, for a meta-analysis.

### ***Quality Assessment***

The degree to which bias was excluded in each of the studies was assessed using a modified Jadad score.<sup>15</sup> Points were awarded as follows: described as randomised, 1 point; additional point for appropriate method, 1 point; inappropriate randomisation method, deduct 1 point; subjects blinded to intervention (ie the control procedure was indistinguishable from acupuncture), 1 point; evaluator blinded to therapy, 1 point; therapist blinded to the study hypothesis and the specific acupuncture method, 1 point; and description of withdrawals and drop-out, 1 point. Our method differs from the usual Jadad score in not scoring simply 'double-blinding', and is more appropriate for research into a manual procedure such as acupuncture. The maximum number of points available was six. Subject blinding was assumed where the control intervention was indistinguishable from acupuncture, even if the word 'blinding' was not specified in the report. Observer blinding was only allowed if specified in the text.

### ***Data Synthesis***

Where more than one trial existed for any comparison, and participants appeared clinically homogeneous, data for Hamilton Rating Scale for Depression (HRSD) scores were combined in a meta-analysis using Cochrane RevMan 4.1 Software. This was set to calculate the mean difference between treatment and control arms for all studies, using the (conservative) random effects model. Where there were insufficient studies using the same outcome measure, or where studies were clinically too heterogeneous to combine, a narrative review was performed.

## Results

We found a total of 27 potentially relevant articles, of which six were finally included in the review (see Table 1).<sup>16-22</sup> The reasons for excluding reports were as follows: comparative trial that was not randomised,<sup>23</sup> not purely clinical depression,<sup>24-26</sup> reports of uncontrolled studies,<sup>27-33</sup> not using acupuncture as defined,<sup>34</sup> duplicate publication of an included study,<sup>35,16</sup> foreign language versions of included studies also reported in English.<sup>36-37</sup> One article,<sup>38</sup> was a second report of an included study,<sup>17</sup> but provided some additional data which were included; another article,<sup>39</sup> was excluded as it was a review of other included trials.<sup>16,17</sup> Three additional reports were excluded because they reported either outcomes other than depression,<sup>40-41</sup> in included studies,<sup>19,22</sup> or extended follow up of one study.<sup>42,19</sup> One RCT included patients who had either depression or generalised anxiety disorder;<sup>22</sup> we obtained additional data from the author and excluded patients with anxiety. None of the articles located through Korean acupuncture journals or the Japanese database met our inclusion criteria.

The six studies included in this review involved 10 group comparisons and enrolled 509 patients, of whom 253 received acupuncture. All patients were recruited from hospital care (in- and/or out-patients) except one study which recruited through a newspaper advertisement.<sup>19</sup> For diagnosing depression, three Western studies<sup>16,19,21</sup> used DSM-III or DSM-IV,<sup>43</sup> and one used the WHO diagnostic criteria.<sup>22,44</sup> The four oriental studies<sup>16-18,38</sup> used the diagnostic criteria of the Chinese Psychiatric Association.<sup>45</sup> All studies targeted subjects with major depression except one which included patients suffering from minor depression.<sup>22</sup>

### Methodological quality

No study achieved the maximum quality score. In particular, the randomisation procedure was not reported in adequate detail in any of them. Three of the six studies used evaluator- and subject-blinding.<sup>19,21,22</sup> In one of these,<sup>19</sup> the study design involved the therapist being blinded to the treatment plan: patients received either 'specific' acupuncture, individually tailored to the patient's depression, or 'non-specific' acupuncture designed to treat a pattern of disharmony, such as neck pain, that was not related to the individual's depression. Only two studies

described the number and reason for withdrawal of subjects.<sup>19,22</sup>

### Synthesis

There were four main types of comparison: (1) acupuncture vs sham control (three studies); (2) acupuncture vs waiting list (one study); (3) electroacupuncture vs antidepressant medication (four studies); and (4) electroacupuncture or manual acupuncture as an adjunct to antidepressant medication vs antidepressant medication (two studies).

(1) In comparison with sham acupuncture, one study,<sup>19</sup> using a revised version of the HRSD,<sup>47</sup> showed that specific acupuncture therapy was superior to non specific acupuncture ( $P < 0.01$ ). However, neither genuine nor sham acupuncture was better than waiting list (see below), so we regard the study as uninterpretable. A second study showed no effect of acupuncture,<sup>21</sup> but this result should be treated cautiously because all subjects were given antidepressants as well. The third study found a significantly greater responder rate in the real acupuncture group.<sup>22</sup> All these studies scored at least 3/6 points on our quality scale.

(2) One study comparing acupuncture and waiting list found no significant difference.<sup>19</sup>

(3) Four studies comparing electroacupuncture and antidepressant medication, and using the HRSD in a total of 358 patients, were entered into a meta-analysis.<sup>16-18,38,47</sup> The weighted mean difference was  $-0.43$  (95% confidence interval  $-5.61$  to  $4.76$ ), which was not significant. The quality of these studies was low, at two points or less out of six.

(4) Adjunctive manual acupuncture in addition to antidepressant treatment improved the course of depression more than antidepressant alone ( $P < 0.05$ ) in two of three primary outcome measures,<sup>21</sup> ie Clinical Global Impression (CGI)<sup>48</sup> and Global Assessment Scale (GAS)<sup>49</sup>, but not the third, Beck Rafaelsen Melancholia Scale (BRMS).<sup>50</sup> In a second study,<sup>38</sup> electroacupuncture in addition to medications did not increase the effect of antidepressant treatment. However, the dosage of antidepressant in the electroacupuncture group was smaller than in the antidepressant-only group, making interpretation difficult. Both studies were of moderate quality.

Follow-up comparison is only available from one study: fifty-five of those who responded well

Table 1 Study characteristics and results of RCTs of acupuncture for depression.

First author, Year	N total (N acup)	Intervention (Sessions/weeks)	Design	Control (N)	Primary outcomes, follow up	Dropouts (acup)	Main results vs control	Validity score (max 6)
Luo, 1985	47 (27)	EA, 80-90 Hz (30/5)	Open	Amitriptyline (20)	HRSD, none	Not stated	NS, not stated	1
Luo, 1990	241 (133)	EA, 80-100Hz* (42/6)	Open	Amitriptyline (108)	HRSD, 2-4 years	Not stated	NS, t-test	1
Yang, 1994	41 (20)	EA+MA, 80-100Hz (36/6)	Open	Amitriptyline (21)	HRSD, none	Not stated	NS, not stated	1
Allen, 1998	38 (12)	MA (12/8)	SB, EB, TB	1. Non specific MA (11) 2. Waiting list (11)	DepHRSD, 6 months	5	1. P<0.01 2. NS, ANOVA	5
Luo, 1998	29 (18)	1. EA 2Hz (N=8) 2. EA 2Hz with amitriptyline (N=10) (36/6)	EB	3. Amitriptyline (11)	HRSD, none	Not stated	NS, t test	2
Röschke, 2000	70 (22)	MA with mianserin (12/4)	SB, EB	1. Mianserin alone (24) 2. Non-point needling with mianserin (24)	GAS, BRMS, CGI, none	Not stated	1. P<0.05 2. NS, ANOVA	3
Eich, 2000	43 (21)	MA (10/2)	SB, EB	Non-point needling (22)	CGI, none	12 (4)	P<0.02, Mann-Whitney	4

Abbreviations: N=number; acup=acupuncture; EA=electroacupuncture MA=manual acupuncture; NS=not significant.

Design: SB=subject blind; EB=evaluator blind; TB=therapist blind.

Outcomes: HRSD=Hamilton Rating Scale for Depression; DepHRSD=modified version of the Hamilton Rating Scale for Depression; CGI=Clinical Global Impression Scale; GAS=Global Assessment Scale;

BRMS=Beck Rafielsens Melancholia Scale.

were followed up for two to four years, during which period the relapse rate was 67% of the electroacupuncture group and 50% of the antidepressant group (difference not significant).<sup>17</sup>

#### *Adverse effects and withdrawal from treatment*

The patients' estimate of 'efficacy index' (benefit score divided by side effect score) was reported as significantly ( $P < 0.01$ ) in favour of acupuncture in one study.<sup>16</sup>

Adverse events were carefully monitored in one study.<sup>17</sup> In the antidepressant group, 23% had abnormal electrocardiographs, compared with none of the electroacupuncture group; and 55% had raised serum glutamic pyruvic transaminase concentrations compared with none of the electroacupuncture group. Regarding the dropout rates with acupuncture and antidepressant medications in four studies that compared them,<sup>16-18,38</sup> the data are not reported in sufficient detail to be able to compare groups.

#### *Discussion*

This systematic review of seven RCTs of acupuncture for depression found evidence in four types of comparison: inconsistent evidence on whether manual acupuncture is superior to sham, and difficulty in interpreting the results of these studies; evidence from one small study that acupuncture was not superior to waiting list; evidence from four poor quality studies suggesting that the effect of electroacupuncture may not be significantly different from antidepressant medications; and inconclusive evidence from two studies on whether acupuncture is an effective adjunct to antidepressant medications. The majority of studies enrolled patients with severe depression, and excluding the single study in patients with mild depression makes no meaningful difference to the findings.<sup>22</sup>

Any conclusions from this work must be limited by the small number and diversity of the available studies, and the small sample size and poor quality of several of them. The eastern literature may not be well represented in the results of our searches because our resources were limited; however, including such literature might have introduced some bias, since Chinese research into acupuncture is known to be generally positive.<sup>51</sup>

Subject blinding is problematic in studies of acupuncture. Evaluator blinding represents an important attempt to reduce measurement bias and was used in four of the seven studies. Subject blinding was achieved in three studies (all manual acupuncture) by inserting the needles in inappropriate sites in the control group. In addition, one of these studies is remarkable for achieving therapist blinding,<sup>19</sup> which is extremely rare in trials of acupuncture.<sup>52</sup> Although the therapists were supposed to be blinded to the fact that the trial was about depression, it is theoretically possible that they may have become unblinded during the course of the study if they identified that all the patients had depression. This high quality study was inconclusive, possibly because of its small sample size, and a larger study is being conducted by the same research group,<sup>12</sup> which should produce definitive data on the effectiveness of manual acupuncture for depression.

In conclusion, the evidence from RCTs is insufficient to conclude whether or not acupuncture treatment is an effective treatment for depression. Until further research is available, it is not possible to recommend acupuncture for routine use in depressed patients on the basis of trial evidence. As some trials generated promising results, large-scale RCTs are warranted. Certainly further research on the effects of acupuncture on depression is justified by the current findings, particularly in view of the fact that acupuncture is established as safe in the hands of properly trained therapists.<sup>53</sup>

#### *Note*

This work was conducted when Prof Mukaino was a visiting researcher at the department of Complementary Medicine, Peninsula Medical School.

#### *Reference list*

1. Schnyer RN, Allen JJ. *Acupuncture in the treatment of depression: a manual for practice and research*. New York: Churchill Livingstone, 2001.
2. Elkin J, Shea MT, Watkins JT, Imber SD, Sotsky SM, Collins JF et al. National Institute of Mental Health Treatment of Depression Collaborative Research Program. General effectiveness of treatments. *Arch Gen Psychiatry* 1989;46(11):971-82.
3. Burrows GD. Long-term clinical management of depressive disorders. *J Clin Psychiatry* 1992;53 Suppl:32-5.

4. Montgomery SA, Kasper S. Side effects, dropouts from treatment and cost consequences. *Int Clin Psychopharmacol* 1998;13 Suppl 2:S1-S5.
5. Keller MB, McCullough JP, Klein DN, Arnow B, Dunner DL, Gelenberg AJ, et al. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. *N Engl J Med* 2000;342(20):1462-70.
6. Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States. *N Engl J Med* 1993;328(4):246-52.
7. Eisenberg DM, Davis R, Eitner SL, Appel S, Wilkey S, Van Rompay M, et al. Trends in alternative medicine use in the United States, 1990-1997. *JAMA* 1998;280(18):1569-75.
8. Wadlow G, Peringer E. Retrospective survey of patients of practitioners of traditional Chinese acupuncture in the UK. *Complement Ther Med* 1996;4(1):1-7.
9. Ernst E, Rand JJ, Stevinson C. Complementary therapies for depression: an overview. *Arch Gen Psychiatry* 1998;55(11):1026-32.
10. Jorm AF, Christensen H, Griffiths KM, Rodgers B. Effectiveness of complementary and self-help treatments for depression. *Med J Aust* 2002;176 Suppl:S84-S96.
11. Manber R, Allen JJ, Morris MM. Alternative treatments for depression: empirical support and relevance to women. *J Clin Psychiatry* 2002;63(7):628-40.
12. University of Arizona. Acupuncture in the Treatment of Depression. <http://www.clinicaltrials.gov>. Accessed 23 December 2004.
13. University of Texas southwestern Medical Centre. Acupuncture for treatment of patients with bipolar disorder. <http://www.newswise.com>. Accessed 23 December 2004.
14. The Whole Clinic and TCM Health Care. Acupuncture to treat depression. <http://www.flyinghomeopath.com/wholeclinic/acursrch.htm>. Accessed 23 December 2004.
15. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomised clinical trials: is blinding necessary? *Controlled Clin Trials* 1996;17(1):1-12.
16. Luo H, Jia Y, Zhan SY. Electro-acupuncture vs. amitriptyline in the treatment of depressive states. *J Tradit Chin Med* 1985;5(1):3-8.
17. Luo H, Jia Y, Wu X, Dai W. Electro-acupuncture in the treatment of depressive psychosis. *Int J Clin Acupunct* 1990;1(1):7-13.
18. Yang X, Liu X, Luo H, Jia Y. Clinical observation on needling extrachannel points in treating mental depression. *J Tradit Chin Med* 1994;14(1):14-8.
19. Allen JJB, Schnyer RN, Hitt SK. The efficacy of acupuncture in the treatment of major depression in women. *Psychological Science* 1998;9:397-401.
20. Luo H, Meng F, Jia Y, Zhao X. Electro-acupuncture in the treatment of depressive psychosis. *Psychiatry Clin Neurosci* 1998;52 suppl:S338-S340.
21. Roschke J, Wolf C, Muller MJ, Wagner P, Mann K, Grozinger M, et al. The benefit from whole body acupuncture in major depression. *J Affect Disord* 2000;57(1-3):73-81.
22. 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]. *Fortschr Neurol Psychiatr* 2000;68(3):137-44.
23. Han C, Li XW, Luo HC. [Comparative study of electroacupuncture and maprotiline in treating depression]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2002;22(7):512-4, 521.
24. Romoli M, Giommi A. Ear acupuncture in psychosomatic medicine: the importance of the Sanjiao (triple heater) area. *Acupunct Electrother Res* 1993;18(3-4):185-94.
25. Bennett C. Treatment effects of acupuncture on anxiety and depression in working women. *Diss Abst Int* 1998;58(11-B):5886.
26. Nakamura M, Nawata T, Matsuoka K. The acupuncture treatment of masked depression. *Zen Nippon Shinkyo Gakkai Zashi* 1983;33(2):177-84.
27. Poliakov SE. [Acupuncture in the treatment of patients with endogenous depression]. *Zh Nevropatol Psikhiatr Im S S Korsakova* 1987;87(4):604-8.
28. Chen A. An introduction to sequential electric acupuncture (SEA) in the treatment of stress related physical and mental disorders. *Acupunct Electrother Res* 1992;17(4):273-83.
29. Xu L. Twenty-seven cases of spleen-qi deficiency syndrome treated by heat-producing needling at zusanli. *J Tradit Chin Med* 2000;20(1):40-1.
30. Liu G, Jia Y, Zhan L, Luo H. Electroacupuncture treatment of presenile and senile depressive state. *J Tradit Chin Med* 1992;12(2):91-4.
31. Cocchi R, Fusari A, Lorini G, Rocca L. [Acupuncture, "vital" drugs and psychopharmacological agents in the treatment of psychiatric patients with deep depressive disorders, with considerations on the probable neurophysiological mechanisms of the synergism of action]. *Minerva Med* 1977;68(33):2309-14.
32. Cocchi R, Fusari A, Favuto F, Lorini G. [Acupuncture, "vital" drugs and psychotropic agents in psychiatric patients. 50 cases]. *Minerva Med* 1978;69(44):3003-9.
33. Frydrychowski A, Landowski J, Watrobski Z, Ostrowska B. [Use of acupuncture in the treatment of depressive syndromes]. *Psychiatr Pol* 1984;18(3):247-50.
34. Morozov GV, Antropov I, Asanova LM, Shkanov SM. [The treatment of neurotic depression by using extremely high-frequency electromagnetic radiation]. *Zh Nevropatol Psikhiatr Im S S Korsakova* 1996;96(6):28-31.
35. Han JS. Electroacupuncture: an alternative to antidepressants for treating affective diseases? *Int J Neurosci* 1986;29(1-2):79-92.
36. Luo HC, Shen YC, Jia YK. [Clinical study of electroacupuncture on 133 patients with depression in comparison with tricyclic amitriptyline]. *Zhong Xi Yi Jie He Za Zhi* 1988;8(2):77-80, 68.
37. Roschke J, Wolf C, Kogel P, Wagner P, Bech S. [Adjuvant whole body acupuncture in depression. A placebo-controlled study with standardized mianserin therapy]. *Nervenarzt* 1998;69(11):961-7.
38. Luo H, Meng F, Jia Y, Zhao X. Clinical research on the therapeutic effect of the electro-acupuncture treatment in patients with depression. *Psychiatry Clin Neurosci* 1998;52 Suppl:S338-S340.
39. Luo H, Jia Y, Feng X, Zhao X, Tang LC. Advances in clinical research on common mental disorders with computer controlled electro-acupuncture treatment. *Adv Exp Med Biol* 1995;363:109-22.
40. Agelink MW, Sanner D, Eich H, Pach J, Bertling R, Lemmer W, et al. [Does acupuncture influence the cardiac autonomic nervous system in patients with minor depression or anxiety disorders?]. *Fortschr Neurol Psychiatr* 2003;71(3):141-9.

41. Chambers AS, Allen JJ. Vagal tone as an indicator of treatment response in major depression. *Psychophysiology* 2002;39(6):861-4.
42. Gallagher SM, Allen JJ, Hitt SK, Schnyer RN, Manber R. Six-month depression relapse rates among women treated with acupuncture. *Complement Ther Med* 2001;9(4): 216-8.
43. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Washington DC: American Psychiatric Association; 1994.
44. World Health Organisation. ICD-10 Classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: WHO; 1992.
45. Anon. Clinical diagnosis criteria for depressive disorders [Chinese]. *Chin J Neurol Psychiatry* 1985;18:317.
46. Gelenberg AJ, Wojcik JD, Falk WE, Baldessarini RJ, Zeisel SH, Schoenfeld D, et al. Tyrosine for depression: a double-blind trial. *J Affect Disord* 1990;19(2):125-32.
47. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56-62.
48. National Institutes of Mental Health. CGI: Clinical Global Impressions. In Guy W, Borato R, eds. *Manual for the ECDE Assessment Battery*, Chevy Chase, MD: NIMH; 1970.
49. Luborsky L. Clinicians' judgments of mental health: specimen case descriptions and forms for the health-sickness rating scale. *Bull Menninger Clin* 1975;39(5):448-80.
50. Beck P, Rafaelsen OJ. The melancholia state: development, consistency, validity and utility. In Sartorius N, Ban PA, eds. *Assessment of Depression*, Berlin: Springer Verlag; 1986.
51. Vickers A, Goyal N, Harland R, Rees R. Do certain countries produce only positive results? A systematic review of controlled trials. *Control Clin Trials* 1998;19:159-66.
52. White AR, Filshie J, Cummings M. Clinical trials of acupuncture: consensus recommendations for optimal treatment, sham controls and blinding. *Complement Ther Med* 2001;9(4):237-45.
53. White A, Hayhoe S, Hart A, Ernst E. Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. *Acupunct Med* 2001;19(2):84-92.