Acupuncture for Depression During Pregnancy
A Randomized Controlled Trial

Rachel Manber, PhD, Rosa N. Schnyer, DAOM, LAc, Deirdre Lyell, MD, Andrea S. Chambers, PhD,
Aaron B. Caughey, MD, PhD, Maurice Druzin, MD, Erin Carlyle, MS, Christine Celio, MS,
Jenna L. Gress, BA, Mary I. Huang, MS, Tasha Kalista, MA, Robin Martin-Okada, BS,
and John J. B. Allen, PhD

OBJECTIVE: To estimate the efficacy of acupuncture for depression during pregnancy in a randomized controlled trial.

METHODS: A total of 150 pregnant women who met *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) criteria for major depressive disorder were randomized to receive either acupuncture specific for depression or one of two active controls: control acupuncture or massage. Treatments lasted 8 weeks (12 sessions). Junior acupuncturists, who were not told about treatment assignment, needled participants at points prescribed by senior acupuncturists. All treatments were standardized. The primary outcome was the Hamilton Rating Scale for Depression, administered by masked raters at baseline and after 4 and 8 weeks of treatment. Continuous data were analyzed using mixed effects models and by intent to treat.

RESULTS: Fifty-two women were randomized to acupuncture specific for depression, 49 to control acupuncture, and 49 to massage. Women who received acupuncture specific for depression experienced a greater rate of decrease in symptom severity ($P<.05$) compared with the combined controls (Cohen's $d=0.39$, 95% confidence interval [CI] 0.01–0.77) or control acupuncture alone ($P<.05$; Cohen's $d=0.46$, 95% CI 0.01–0.92). They also had significantly greater response rate (63.0%) than the combined controls (44.3%; $P<.05$; number needed to treat, 5.3; 95% CI 2.8–75.0) and control acupuncture alone (37.5%; $P<.05$: number needed to treat, 3.9; 95% CI 2.2–19.8). Symptom reduction and response rates did not differ significantly between controls (control acupuncture, 37.5%; massage, 50.0%).

CONCLUSION: The short acupuncture protocol demonstrated symptom reduction and a response rate comparable to those observed in standard depression treatments of similar length and could be a viable treatment option for depression during pregnancy.

CLINICAL TRIAL REGISTRATION: Clinicaltrials.gov, www.clinicaltrials.gov, NCT00186654.

(Obstet Gynecol 2010;115:511–20)

LEVEL OF EVIDENCE: I

Major depressive disorder during pregnancy can have deleterious effects on mothers, infants, and families regardless of the timing of its onset.[1] The point prevalence of a major depressive disorder diagnosis during pregnancy ranges from 3–5%, and up to 14% of pregnant women are estimated to have probable major depressive disorder.[2] These rates are comparable to those seen among similarly aged nonpregnant women[3] and among women during the postpartum period,[4–6] yet there are far fewer treatment studies of depression during pregnancy than during the postpartum period.[7,8]

Decisions about treatment of depression in pregnant women are clinically based, with no definitive controlled studies to guide the provider.[8,9] Although the use of antidepressants during pregnancy doubled between 1999 and 2003,[10] pharmacologic treatments of

depression during pregnancy increasingly raise concerns about safety for the developing fetus,[11] and pregnant women are often reluctant to take antidepressant medications.[12] Only one form of psychotherapy (ie, interpersonal psychotherapy) has been specifically tested during pregnancy and found to be effective for pregnant women,[13] producing 52% reduction in depression severity, but the availability of interpersonal psychotherapy is limited. In general, depression during pregnancy is underdetected and undertreated,[14] and few pregnant women who are referred to a mental health treatment attend at least one visit.[15]

We previously conducted a pilot study of acupuncture for treatment of depressed pregnant women and found response rates comparable to those observed in conventional treatment studies for depression in nonpregnant samples.[16] When properly implemented, acupuncture has relatively mild and transient, if any, side effects[17–19] and therefore holds the promise as a safe alternative to antidepressant medications for treatment of depression during pregnancy. The objective of the present study was to estimate the efficacy of acupuncture for treatment of depression during pregnancy in an evaluator-blinded, randomized trial.

PARTICIPANTS AND METHODS

In this randomized controlled trial, participants were randomized to acupuncture specifically designed to address depression or to one of two control treatments: acupuncture that was not specific for depression and prenatal massage. Massage was conceptualized as a control treatment because, although it improves mood immediately after a session, there is insufficient evidence to support its efficacy as a treatment for depression.[20] Outcome was assessed by blind raters. We hypothesized that receiving acupuncture specific for depression would lead to better clinical outcome than the combined control conditions of acupuncture not specific for depression, and acupuncture not specific for depression and prenatal massage, and that the two control conditions would not differ in clinical outcome from each other.

The Institutional Review Board of Stanford University approved the protocol, and written informed consent was obtained from all participants at the time of enrollment. Data were collected at Stanford University.

Depressed pregnant women with viable pregnancies were recruited between 2003 and 2008 through advertising in parent and baby publications and from local clinics. To be included, participants had to be between 12 and 30 weeks of gestation, 18 years or older, meet criteria for major depressive disorder according to the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision) (*DSM-IV-TR*),[21] determined by the Structured Clinical Interview for the *DSM-IV*,[22] and score at least 14 on the 17-item Hamilton Rating Scale for Depression.[23] Participants were excluded for the following: 1) other current primary Axis I psychiatric disorders, except social phobia; 2) seasonal affective disorder or psychotic features; 3) abnormal thyroid panel or drug screen results; 4) serious uncontrolled medical conditions or conditions that may be a medical basis of depression; 5) cluster B personality disorders (determined by the Structured Clinical Interview for *DSM-IV* interview for Axis II disorders[24]); 6) current psychotherapy, herbs, or psychotropic medications; 7) electroconvulsive therapy or vagal nerve stimulation in the past year; 8) current active suicidal potential necessitating immediate treatment; 9) absence of prenatal care; and 10) conditions necessitating bed rest.

Qualified participants were randomized to acupuncture specific for depression, acupuncture not specific for depression, or prenatal massage. Blocked randomization was achieved by electronically generating a list of random permutations of three elements (groups) before opening the enrollment period. The randomization sequence was concealed until the interventions were assigned. The randomization table was generated by the primary author (R.M.). The study coordinator enrolled and allocated participants to treatment groups. All other study personnel, including the primary author, were not told about group assignment. Participants who received acupuncture were not told which of the two types of acupuncture they were receiving. The consent stated that "Participants in one of these two groups will receive acupuncture that focuses on depression symptoms and the other treatment will not." To blind the treating acupuncturists, the assessment and treatment planning were separated from the needling (acupuncture treatment) as described below. Massage therapists and participants who received massage were not blinded to treatment assignment.

Treatments were provided two times per week for the first 4 weeks and weekly for 4 more weeks. Each treatment lasted approximately 25 minutes. Treatment providers were instructed to minimize verbal communication and refrain from providing any counseling, dietary or other advice, or playing background music during the session.

Stainless steel needles (0.18 mm or 0.20 mm) were inserted to standard depth[25] and retained for 20 minutes; 0.25-mm needles were allowed for larger

patients. Neutral to moderate needle stimulation was applied until "DeQi" sensation (a dull aching sensation) was obtained.

Acupuncture specific for depression was tailored individually to address each participant's depression-related patterns of disharmony according to the principles of traditional Chinese medicine and following a published standardized treatment manual.[26] Acupuncture not specific for depression was also standardized and needles were inserted in real acupuncture points that did not address depression-relevant patterns of disharmony according to traditional Chinese medicine. The manual for standardized acupuncture not specific for depression is available on request from the second author (R.N.S.). In both treatments, points needled varied by person and by treatment week, and points that are either forbidden or advised for use with caution during pregnancy[26] were excluded. Seven to 12 points were needled in each session and were distributed across the same general areas of the body for both treatments.

To blind the treating acupuncturists, needling of the patient was separated from the determination of which acupuncture points should be needled (point prescription). Senior acupuncturists (the assessing acupuncturists), with at least 5 years of experience, assessed the participants monthly and provided a prescription of points to be needled at each session during the following month. The senior acupuncturists were not told to which treatment the participant was assigned and designed both acupuncture not specific for depression and acupuncture specific for depression treatment prescriptions for each participant. Junior acupuncturists (treating acupuncturists), with less than 2 years of experience, provided the prescribed treatments and did not evaluate the participant's symptoms and signs (pulse and tongue) and did not suggest, prescribe, or provide herbal remedies or massage. Acupuncturists were nationally board certified (National Certification Commission for Acupuncture and Oriental Medicine) and licensed in the state of California.

Swedish massage was provided in a standardized fashion and included effleurage and pétrissage strokes. Approximately 5 minutes was spent on each of the following: back, face, head, neck and shoulder, and feet while participants were lying on their side. Massage therapists were California state board certified and trained in the treatment protocol by a senior massage therapist. The assessing acupuncturists assessed and designed specific and control acupuncture treatments for participants receiving prenatal massage. Although this assessment was not necessary for treatment, it equated the amount of contact with study personnel in all treatment groups. Moreover, to avoid differential nonverbal and verbal input from the assessing acupuncturists, they were blind to treatment assignment.

The primary measure of outcome was the 17-item Hamilton Rating Scale for Depression, administered at baseline and after 4 and 8 weeks of treatment by raters blind to treatment group. Interpretation of Hamilton Rating Scale for Depression scores is as follows: less than 7, nondepressed; 8–13, mild depression; 14–18, moderate depression; 19–22, severe depression; more than 23, very severe depression.[27] The intraclass correlation for the total Hamilton Rating Scale for Depression score among raters in our laboratory is 0.96. Secondary outcomes were treatment response and depression remission rates. The major depression section of the Structured Clinical Interview for *DSM-IV* was administered immediately after each Hamilton Rating Scale for Depression interview to determine whether *DSM-IV* criteria for major depressive disorder were still met. As is common in depression research, response was defined as 1) at least 50% reduction in the Hamilton Rating Scale for Depression score from baseline, 2) Hamilton Rating Scale for Depression more than 7 and less than 14, and 3) failure to meet full criteria for the *DSM-IV*. Major depressive disorder remission was defined by the absence of the core symptoms of depression (depressed mood and anhedonia) and Hamilton Rating Scale for Depression score of 7 or less. Participants' expectations of benefits and providers' beliefs that the treatment they provide will help the patient were measured after the first treatment session, before expectations are affected by response to treatment. Higher scores indicated greater expectation of benefit. Participant and provider expectations provided a measure for the success of blinding.

The primary analysis was conducted on the intent-to-treat sample (all 150 randomized participants). Mixed model regression analyses were used to test for differential effects of treatment on the main outcome measure (Hamilton Rating Scale for Depression). Two planned independent contrasts were included in the model 1) between those receiving acupuncture specific for depression and the two control groups combined and 2) between the two control groups (acupuncture not specific for depression and prenatal massage). Treatment assignment, time (week 4 and week 8), and treatment×time interaction were included as fixed effects. Time was log-transformed, according to Keene,[28] to lessen the effects of steep local descents or ascents, outliers, and heteroscedasticity.[29] Mixed effects models provide a contemporary approach to missing

data, allowing for true intent-to-treat analysis, by using estimated individual time trend lines based on available data for each individual, augmented by information from data for all other individuals in the sample.[30]

Chi square analyses were performed to compare groups regarding response and remission and to compare groups regarding the incidence of dropout rates, adverse events, and side effects. These analyses included the same independent contrasts, using the last observation carried forward, including only cases that provided data at least once after randomization. Exploratory analyses compared acupuncture specific for depression to each of the two controls with respect to Hamilton Rating Scale for Depression scores, response, and remission, using mixed effects models and χ^2 tests, as was done for the primary analyses. All statistical analyses were conducted with SPSS version 16 (SPSS Inc., Chicago, IL).

To detect a moderate effect size (Cohen's $d=0.5$) with $\alpha=0.05$ and a 1:2 allocation for acupuncture specific for depression versus the combined control groups and 90% power, we needed to recruit 156 participants. No interim analysis was conducted.

RESULTS

A total of 183 participants were enrolled, 150 were randomized, and 141 began treatment. Figure 1 provides Consolidated Standards of Reporting Trials information. Demographic characteristics were similar except for the racial composition of groups (Table 1), with a higher proportion of blacks in the group receiving acupuncture not specific for depression than the other two groups. Depression severity and history were similar in all groups (Table 2).

Participants in the group receiving acupuncture specific for depression experienced a significantly greater reduction in Hamilton Rating Scale for Depression scores than the participants in the combined control interventions ($P<.05$; Cohen's d effect size for change in Hamilton Rating Scale for Depression=0.39; 95% confidence interval [CI] 0.01–0.77) and there were no differences between the two control conditions ($P=.43$; Cohen's $d=0.13$; 95% CI −0.32 to 0.58). Figure 2 depicts the change in observed Hamilton Rating Scale for Depression scores with treatment by group among treatment completers. Exploratory mixed model analyses revealed a greater reduction in Hamilton Rating Scale for Depression scores in those receiving acupuncture specific for depression than in those receiving acupuncture not specific for depression ($P<.05$; Cohen's $d=0.46$, 95% CI 0.01–0.92) but no difference from those receiving prenatal massage ($P=.13$; Cohen's $d=0.33$; 95% CI −0.10 to 0.76).

Response rates were significantly higher for the group receiving acupuncture specific for depression (29 of 46, 63.0%) than for the combined control groups (39 of 88, 44.3%; $P<.04$). The control interventions did not differ from each other, 15 of 40 (37.5%) for the group receiving acupuncture not specific for depression and 24 of 48 (50%) for the group receiving prenatal massage; $P=.24$). The number needed to treat effect size was 5.3 (95% CI 2.8–75.0) for the group receiving acupuncture specific for depression compared with the combined control groups and 8.0 for the group receiving acupuncture not specific for depression versus acupuncture not specific for depression and prenatal massage. Exploratory analysis revealed that the group receiving acupuncture specific for depression had a greater response rate than the group receiving acupuncture not specific for depression ($P<.05$; number needed to treat 3.9; 95% CI 2.2–19.8) but was not different from the group receiving acupuncture not specific for depression and prenatal massage ($P=.20$; number needed to treat 7.7).

Remission rates were not significantly different between the group receiving acupuncture specific for depression (16 of 46, 34.8%) and the combined control groups (26 of 88, 29.5%; number needed to treat 19.1); the remission rates for the groups receiving acupuncture not specific for depression and prenatal massage did not differ (11 of 40, 27.5%; and 15 of 48, 31.2%, respectively; number needed to treat 26.7). Acupuncture specific for depression remission rates did not differ from either the group receiving acupuncture not specific for depression ($P=.47$; number needed to treat 13.7) or prenatal massage ($P=.72$; number needed to treat 28.3).

There were no significant group differences in participants' or acupuncturists' expectations between those receiving acupuncture specific for depression and the combined control conditions ($P>.36$). Participants' expectations did not differ between the two acupuncture groups. The expectations of the treating acupuncturists (but not the patients) were significantly lower for the group receiving acupuncture not specific for depression than the group receiving acupuncture specific for depression ($P<.01$). This suggests that, whereas we succeeded in blinding the participants, the treating acupuncturists were not adequately blinded. To assess whether the difference in provider expectations could account for the observed differential efficacy, the mixed effects analyses were repeated after adding provider expectations as a covariate. This did not change the outcome.
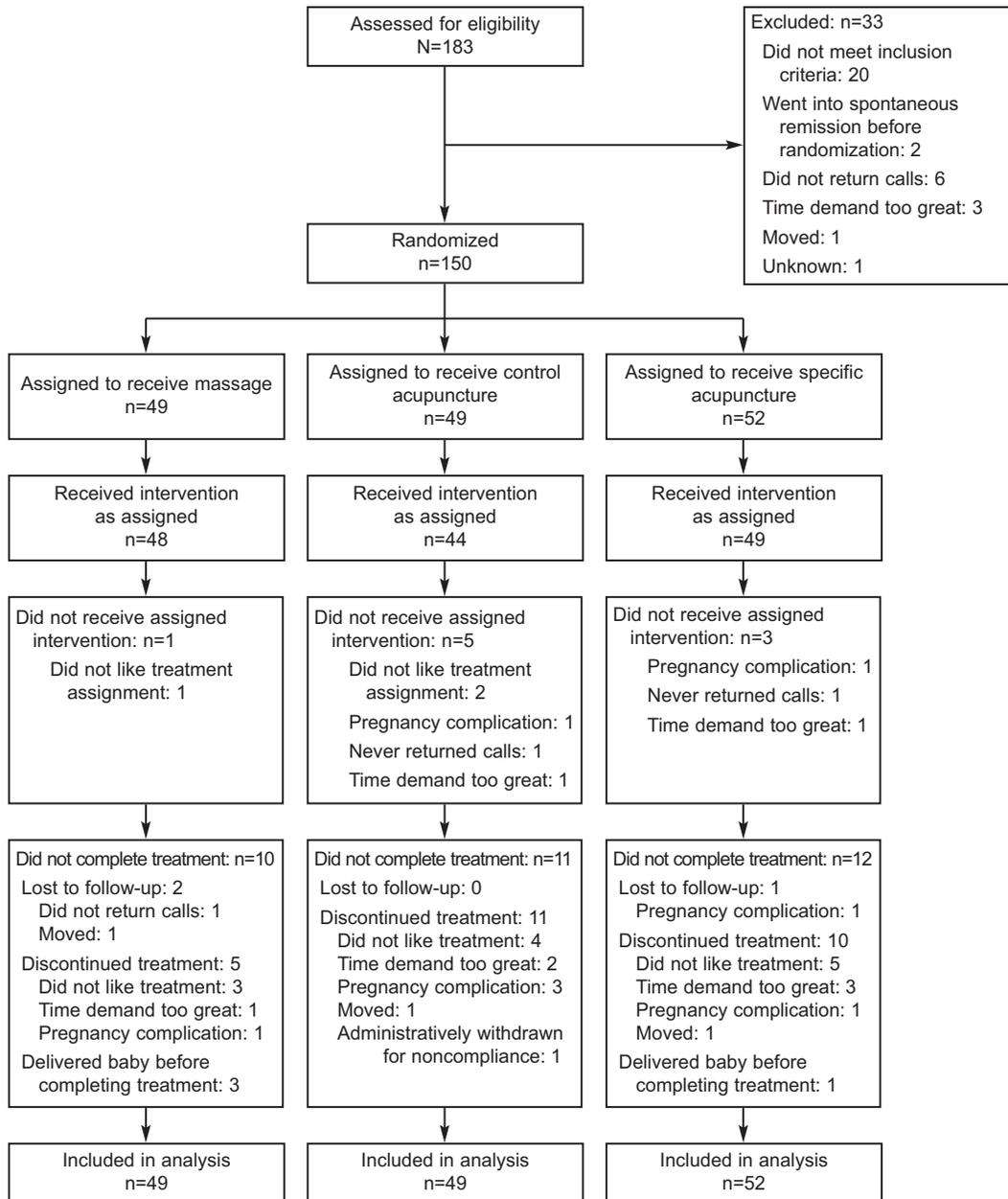
Fig. 1. Participants' flow through the study.

Manber. Acupuncture for Depression in Pregnancy. Obstet Gynecol 2010.

Discontinuation of treatment occurred in 33 of 141 participants who started treatment (23%), of whom 10 of 33 (30%) were for pregnancy-related reasons (early delivery or pregnancy complications). Non–pregnancy-related reasons for discontinuation were as follows: not liking study treatment/starting nonstudy treatment (n=12); burden of time commitment (n=6); move (n=3); and other reasons (n=2). No patient was withdrawn from treatment for suicidality. The proportion of participants who dropped out for each of these reasons did not differ by group (P>.52).

Ten unexpected/adverse events occurred, including the following: 1) premature delivery of twins with one neonatal demise and the surviving twin receiving prolonged neonatal intensive care (acupuncture specific for depression); 2) pregnancy loss (acupuncture not specific for depression); 3) congenital defects among two neonates (one acupuncture specific for depression and prenatal massage); 4) hospitalization for esophageal spasms (prenatal massage); 5) hospitalization with dehydration and low amniotic fluid (acupuncture not specific for depression); 6) hospitalization for isolated atrial

Table 1. Demographics of Analyzable Sample

Variable	Acupuncture Specific for Depression (n=52)	Acupuncture Not Specific for Depression (n=49)	Prenatal Massage (n=49)
Age (y)	32.4 (4.0)	33.4 (5.0)	32.8 (5.6)
Gestation week at intake	19.8 (6.2)	21.29 (5.4)	21.06 (5.6)
No. of previous pregnancies/births	2.1 (1.5)	2.2 (1.4)	2.5 (1.6)
Hispanic ethnicity	23.1	8.3	22.4
Racial distribution			
Native American/Alaska Native	0	2.1	0
Black or African American	0	12.5	4.2
Asian	7.8	14.6	4.2
White	68.6	62.5	64.6
Other	23.5	8.3	27.1
Highest education level			
High school	1.9	6.2	2.0
Some college	19.2	16.7	26.5
College	38.5	45.8	42.9
Graduate school	40.4	29.2	28.6
Work status			
Work	65.4	61.2	57.1
Student	1.9	0%	6.1
Unemployed/homemaker	32.7	38.8	36.7
Household income bracket			
Less than $20,000	5.8	4.4	14.3
$20,001–$59,999	28.8	23.8	32.5
More than $60,000	65.3	71.7	63.2

Data are mean (SD) or %.

Participants indicated their ethnicity and race using the classification system of the National Institutes of Health. χ^2 analyses revealed a significant difference in the racial composition of the treatment groups ($P<.05$), with a higher representation of African Americans in the group receiving acupuncture not specific for depression. No other significant differences were detected.

fibrillation (prenatal massage); 7) hospitalization because of premature contractions (prenatal massage); and 8) preeclampsia (two in acupuncture specific for depression). The study investigators and the Data Safety and Monitoring Board classified all events as unrelated to treatment. The rates of adverse events were not significantly different for the three treatment groups ($P=.69$).

Participants recorded side effects weekly. Treatment providers recorded side effects they observed or those mentioned by the participants during a session. Acupuncture-related side effects included transient discomfort at the point of needle insertion (seven in the group receiving acupuncture not specific for depression and 14 in the group receiving acupuncture

Table 2. Clinical Information of Analyzable Sample

Variable	Acupuncture Specific for Depression (n=52)	Acupuncture Not Specific for Depression (n=49)	Prenatal Massage (n=49)
Depression severity at intake			
Hamilton Rating Scale for depression (17-item total)	21.5 (3.8)	20.3 (3.6)	20.4 (3.6)
Beck Depression Inventory	30.5 (7.2)	30.9 (7.9)	29.4 (7.6)
Length of index episode (mo)	6.3 (9.0)	4.6 (2.3)	5.24 (3.5)
Patients with onset of depression			
Before pregnancy	32.7	41.7	44.9
During pregnancy	67.3	58.3	55.1
No. of past depressive episodes	3.2 (2.6)	2.8 (1.8)	3.1 (4.4)
Age of onset of first depressive episode	20.0 (8.4)	20.2 (9.0)	20.9 (9.1)
Patients with history of chronic depression	15.4	31.2	28.6

Data are mean (SD) or %.

Chi-square and analysis of variance analyses revealed no group differences on any of the clinical variables (all $P>.1$).
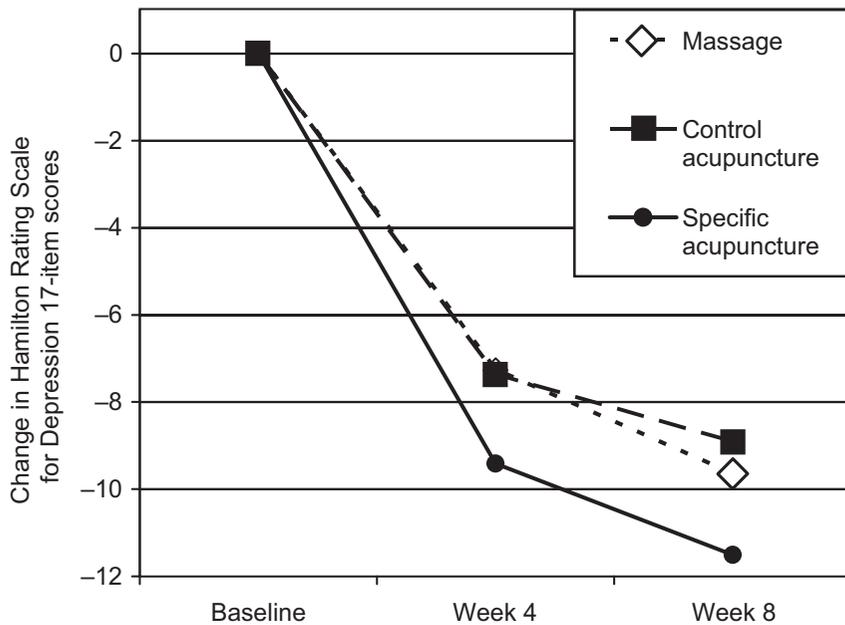
Fig. 2. Change in depression severity with treatment.

Manber. Acupuncture for Depression in Pregnancy. Obstet Gynecol 2010.

specific for depression) and bleeding at the needling site (one in a the group receiving cupuncture specific for depression). Massage-related side effects included transient discomfort (five participants). None of these side effects led to discontinuation from the study. Table 3 summarizes the number of participants reporting side effects that were not treatment specific. Side effects of any type were reported by 43 participants (four in the group receiving prenatal massage, 19 in the group receiving acupuncture not specific for depression, and 20 in the group receiving acupuncture specific for depression). Significantly fewer participants reported any side effects in the group receiving prenatal massage than in the two acupuncture groups ($P<.01$).

DISCUSSION

Acupuncture specific for depression was associated with a significantly greater decrease in depression symptom severity and a higher rate of response compared with the combined controls and relative to the control acupuncture (acupuncture not specific for depression). The relative efficacy of acupuncture specific for depression was greater when compared with the control acupuncture (acupuncture not specific for depression) than with the combined control groups (larger effect size). Prenatal massage produced intermediate levels of reduction in symptom severity and response rates that were not significantly different from acupuncture not specific for depression.

The benefits observed with 8 weeks of acupuncture specific for depression are clinically meaningful when considered within the broad context of depression treatment studies. One psychotherapy study of depression during pregnancy reported a 52% reduction in Hamilton Rating Scale for Depression scores and 19% remission after 16 weeks of interpersonal psychotherapy[13]; the present study found a 53% re-

Table 3. Side Effects Not Directly Associated With Treatment

Event	Acupuncture Specific for Depression (n=52)	Acupuncture Not Specific for Depression (n=49)	Prenatal Massage (n=49)
Tiredness after treatment	10	9	4
Irritability or agitation after treatment	2	2	0
Sleep disturbance after treatment	1	2	0
Headache after treatment	3	1	0
Nausea after treatment	2	0	0
Aggravation of depression	1	1	0
Total no. of participants reporting any side effects	13/49	4/44	4/48

Data are the number of patients reporting.

duction in Hamilton Rating Scale for Depression scores and 29% remission rates after half the length of time (8 weeks) of acupuncture specific for depression. Within the broader context of depression research in mixed gender outpatient samples, treatment usually lasts 12 to 16 weeks.[31] One study that provided only 8 weeks of treatment[32] found that the reductions in Hamilton Rating Scale for Depression scores with antidepressant medications (from 20.3 to 14.8) and cognitive therapy (from 20.6 to 15.7) were comparable to the 21.5 to 11.5 average endpoint scores with acupuncture. Moreover, the observed average 10-point reduction with acupuncture specific for depression, which represents an average drop of two Hamilton Rating Scale for Depression–based severity categories (from the severe group to the mild group), is particularly noteworthy and clinically meaningful, as some naturalistic studies have suggested that depression severity tends to worsen with increased gestational age.[2]

Consistent with the results of the present study, a meta-analysis of acupuncture for depression concluded that acupuncture is an effective treatment for depression.[30] One study in this meta-analysis by Allen et al[33] used a similar acupuncture control group and a similar acupuncture specific for depression treatment but found a very low response rate for acupuncture specific for depression (27%) that was not different than control acupuncture (32%). The difference in findings might stem from the fact that the sample of Allen et al was mixed gender and older, and had a greater number of previous depressive episodes. It is also possible that depression during pregnancy is more amenable to change with treatment in general, but this possibility has never been tested. Somatic treatments, such as acupuncture and massage, might be particularly relevant to pregnant women, as they alleviate some of the physical discomfort of pregnancy that overlaps with depression. Although this might explain the higher rate of response in the present study, it does not explain why the studies differed in detecting differential response to acupuncture specific for depression, relative to the controls.

Several sample characteristics limit the generalizability of the results, including the high education and socioeconomic status, predominance of whites (67%), and exclusion of comorbid mental and medical disorders. Therefore, results might not generalize to specific minority groups that were underrepresented in our sample. The results can also not be generalized to pregnant women with bipolar depression or to those with suicide plans or psychotic features. An-other limitation is the restricted ecologic validity of acupuncture specific for depression and prenatal massage treatments. The acupuncture provided in this study was delivered by acupuncturists who did not assess the patient, and was adjusted only once per month. In contrast, in naturalistic settings assessment, prescription and insertion are performed by the same acupuncturist, who reevaluates and adjusts treatment at each session. The massage therapy provided in this study was shorter than standard practice. Moreover, the natural environments were tightly controlled, proscribing conversation, music, advice, and herbs, which are common in standard practice of these treatments. The restricted ecologic validity might have reduced the efficacy of all treatments delivered in the study relative to naturalistic settings, but the enhanced quality control and lack of comorbidity likely enhanced outcomes, making it difficult to discern the net effect on the generalizability of the results.

Methodologic strengths include 1) the use of two active control treatments; 2) low dropout rate; 3) statistical evaluation of the possibility that providers' expectations could have accounted for the difference between acupuncture specific for depression and acupuncture not specific for depression; and, importantly, 4) the standardization of individualized acupuncture, thus facilitating replication in research and implementation in clinical practice. Although outcome was assessed by blinded raters, we cannot fully rule out the possibility that outcome was affected by nonspecific therapeutic elements such as unblinding of the treatment providers. Very few antidepressant trials measure the success of blinding of participants or clinicians, as was performed in the present study. Another methodologic strength is the control for nonspecific shared therapeutic elements, including beliefs in the efficacy of the treatment, attention, respite from daily stress, being in a relaxing environment, receiving treatment, and spending time with and being touched by a treatment provider.

The field of acupuncture research continues to grapple with finding the best control condition. Both insertive and noninsertive procedures influence expectation, sensation, and contextualization, and both have effects in brain areas controlling sensation, cognition, and affect.[34–38] The noninsertive shams are associated with less biological activity[39,40] but are more prone to unblinding of the practitioners, who are trained to sense the physiologic sensation produced by needle insertion. This was the main reason we opted to use insertive control at actual acupuncture points. Unfortunately, despite our ef-

forts, we were not able to fully blind the providers. The possibility that a noninsertive control might have yielded different results and the determination of optimal dose and frequency of acupuncture will need to be tested in future designs. Overall, the acupuncture protocol we tested yielded a response rate comparable to the rates observed in standard treatments for depression and was associated with relatively few and mild side effects, suggesting that this standardized acupuncture protocol could be a viable treatment option for depression during pregnancy.

REFERENCES

1. Bonari L, Pinto N, Ahn E, Einarson A, Steiner M, Koren G. Perinatal risks of untreated depression during pregnancy. Can J Psychiatry 2004;49:726–35.

2. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol 2005;106: 1071–83.

3. Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evid Rep Technol Assess (Summ) 2005;119:1–8.

4. Eberhard-Gran M, Tambs K, Opjordsmoen S, Skrondal A, Eskild A. Depression during pregnancy and after delivery: a repeated measurement study. J Psychosom Obstet Gynaecol 2004;25:15–21.

5. Heron J, O'Connor TG, Evans J, Golding J, Glover V. The course of anxiety and depression through pregnancy and the postpartum in a community sample. J Affect Disord 2004;80: 65–73.

6. Johanson R, Chapman G, Murray D, Johnson I, Cox J. The North Staffordshire Maternity Hospital prospective study of pregnancy-associated depression. J Psychosom Obstet Gynaecol 2000;21:93–7.

7. Manber R, Blasey C, Allen JJ. Depression symptoms during pregnancy. Arch Womens Ment Health 2008;11:43–8.

8. Bledsoe S, Grote N. Treating depression during pregnancy and the postpartum: a preliminary meta-analysis. Res Soc Work Pract 2006;16:109–20.

9. Nonacs R, Cohen LS. Depression during pregnancy: diagnosis and treatment options. J Clin Psychiatry 2002;63(Suppl 7):24–30.

10. Cooper WO, Willy ME, Pont SJ, Ray WA. Increasing use of antidepressants in pregnancy. Am J Obstet Gynecol 2007;196: 544.e1–5.

11. Pearlstein T. Perinatal depression: treatment options and dilemmas. J Psychiatry Neurosci 2008;33:302–18.

12. O'Mahen HA, Flynn HA. Preferences and perceived barriers to treatment for depression during the perinatal period. J Womens Health (Larchmt) 2008;17:1301–9.

13. Spinelli MG, Endicott J. Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. Am J Psychiatry 2003;160: 555–62.

14. Kelly R, Zatzick D, Anders T. The detection and treatment of psychiatric disorders and substance use among pregnant women cared for in obstetrics. Am J Psychiatry 2001;158: 213–9.

15. Smith MV, Shao L, Howell H, Wang H, Poschman K, Yonkers KA. Success of mental health referral among pregnant and postpartum women with psychiatric distress. Gen Hosp Psychiatry 2009;31:155–62.

16. Manber R, Schnyer RN, Allen JJ, Rush AJ, Blasey CM. Acupuncture: a promising treatment for depression during pregnancy. J Affect Disord 2004;83:89–95.

17. Wang H, Qi H, Wang BS, Cui YY, Zhu L, Rong ZX, et al. Is acupuncture beneficial in depression: a meta-analysis of 8 randomized controlled trials? J Affect Disord 2008;111: 125–34.

18. Norheim A. Adverse effects of acupuncture: a study of the literature for the years 1981–1994. J Altern Complement Med 1996;2:291–7.

19. Yamashita H, Tsukayama H, Hori N, Kimura T, Tanno Y. Incidence of adverse reactions associated with acupuncture. J Altern Complement Med 2000;6:345–50.

20. Coelho HF, Boddy K, Ernst E. Massage therapy for the treatment of depression: a systematic review. Int J Clin Pract 2008;62:325–33.

21. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: APA; 2000.

22. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV axis I disorders, patient edition (SCID-I/P, version 2.0). New York (NY): Biometrics Research Department, New York State Psychiatric Institute; 1995.

23. Hamilton M. Development of a rating scale for primary depressive illness. Br J Soc Psychol 1967;6:278–96.

24. First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS. Structured clinical interview for DSM-IV axis II disorders (SCID-II). Washington, DC: American Psychiatric Press; 1997.

25. Shanghai College of Traditional Medicine. Acupuncture: a comprehensive text. Chicago (IL): Eastland Press; 1981.

26. Schnyer RN, Allen JJB, Hitt SK, Manber R. Acupuncture in the treatment of depression: A manual for research and practice. Edinburgh: Churchill Livingstone; 2001.

27. Kearns NP, Cruickshank CA, McGuigan KJ, Riley SA, Shaw SP, Snaith RP. A comparison of depression rating scales. Br J Psychiatry 1982;141:45–9.

28. Keene ON. The log transformation is special. Stat Med 1995; 14:811–9.

29. Gibbon J, Church RM. Time left: linear versus logarithmic subjective time. J Exp Psychol Anim Behav Process 1981;7: 87–107.

30. Gibbons RD, Hedeker D, Elkin I, Waternaux C, Kraemer HC, Greenhouse JB, et al. Some conceptual and statistical issues in analysis of longitudinal psychiatric data. Application to the NIMH treatment of Depression Collaborative Research Program dataset. Arch Gen Psychiatry 1993;50:739–50.

31. Gloaguen V, Cottraux J, Cucherat M, Blackburn IM. A meta-analysis of the effects of cognitive therapy in depressed patients. J Affect Disord 1998;49:59–72.

32. Blackburn IM, Moore RG. Controlled acute and follow-up trial of cognitive therapy and pharmacotherapy in out-patients with recurrent depression. Br J Psychiatry 1997; 171:328–34.

33. Allen JJ, Schnyer RN, Chambers AS, Hitt SK, Moreno FA, Manber R. Acupuncture for depression: a randomized controlled trial. J Clin Psychiatry 2006;67:1665–73.

34. Wu MT, Hsieh JC, Xiong J, Yang CF, Pan HB, Chen YC, et al. Central nervous pathway for acupuncture stimulation: localization of processing with functional MR imaging of the

brain–preliminary experience. Radiology 1999;212: 133–41.

35. Wu MT, Sheen JM, Chuang KH, Yang P, Chin SL, Tsai CY, et al. Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. Neuroimage 2002;16:1028–37.

36. Kong J, Gollub RL, Rosman IS, Webb JM, Vangel MG, Kirsch I, et al. Brain activity associated with expectancy-enhanced placebo analgesia as measured by functional magnetic resonance imaging. J Neurosci 2006;26:381–8.

37. Napadow V, Webb JM, Pearson N, Hammerschlag R. Neurobiological correlates of acupuncture: November 17–18, 2005. J Altern Complement Med 2006;12:931–5.

38. Pariente J, White P, Frackowiak RS, Lewith G. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. Neuroimage 2005;25:1161–7.

39. Birch S. A review and analysis of placebo treatments, placebo effects, and placebo controls in trials of medical procedures when sham is not inert. J Altern Complement Med 2006;12: 303–10.

40. Langevin HM, Hammerschlag R, Lao L, Napadow V, Schnyer RN, Sherman KJ. Controversies in acupuncture research: selection of controls and outcome measures in acupuncture clinical trials. J Altern Complement Med 2006; 12:943–53.