Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Supplemental Methods

The study protocol followed the CONSORT, STRICTA and IMPRINT recommendations[1-6]and was designed by the multidisciplinary steering committee of the National Clinical Trial Base and approved prior to initiation by the State Administration of Traditional Chinese Medicine of the People's Republic of China – the appointed scientific advisory board. The Collaborative Center for Statistics and Science at Yale University served as the data coordination committee. The international Data and Safety Monitoring Board consisted of American and Chinese scientists monitored the data quality and safety of clinical trial every three months.

Patients

Inclusion criteria

All participants fulfilled the diagnostic criteria of polycystic ovary syndrome[7,8]: Oligomenorrhea (defined as an intermenstrual interval >35 days and <8 menstrual bleedings in the past year) or amenorrhea (defined as an intermenstrual interval >90 days), together with biochemical/clinical hyperandrogenism (hirsutism determined by modified Ferriman–Gallwey Score ≥ 5[9,10]) and/or polycystic ovaries (≥ 12 antral follicles 2-9 mm or ovarian volume ≥ 10 cm^3).

Exclusion criteria

The exclusion criteria mainly included: (1) Exclusion of other endocrine disorders resembling PCOS, including hyperprolactinemia, uncorrected thyroid disease, Type I or Type II diabetes, and Cushing's syndrome. (2) Use of hormonal or other medication including Chinese herbal prescriptions in the past 3 months. (3) Pregnancy within the past 6 weeks. (4) Within 6 weeks postabortion or postpartum. (5) Breastfeeding within the last 6 months. (6) Not willing to give written consent to the study. More detained information referred to protocol as Supplement appendix 1.

Biochemical Analyses

Total testosterone, estradiol, progesterone, follicle stimulating hormone, luteinizing hormone and insulin was analyzed with electro-chemiluminescence immune assay (ECLIA) (Roche Diagnostic, Basel,

Switzerland), sex hormone-binding globulin with immunolite (Siemens Diagnostic, Munich, Germany), free testosterone with radioimmunoassay (DIA source, Louvain-la-Neuve , Belgium), and glucose with HK (Maker, Chengdu, China).The sensitivity range, intra-assay coefficient of variability (CV) and inter-assay CV for total testosterone were 0.025-15.0 ng/ml, 4.7 and 8.4; estradiol were 5.0-4300 pg/ml, 4.3 and 9.9; progesterone 0.03-60 ng/ml, 2.4 and 5.4; follicle stimulating hormone were 0.1-200 mIU/ml 1.8 and 5.3; and luteinizing hormone were 0.1-200 mIU/ml 1.8 and 5.2; insulin were 0.20-1000 µIU/ml, 1.9 and 2.6; sex hormone-binding globulin were 0.2-180 nmol/L, 6.9 and 123; free testosterone were 0.25-65 pg/ml, 5.7 and 6.72; and glucose 0.02-40 nmol/L, 3.7 and 4.2.

Study Interventions

The two acupuncture protocols follow STRICTA recommendations[1]and the rationale and description has been described.[7] The acupuncturists were postgraduates in Traditional Chinese Medicine and were specifically trained in the acupuncture protocols and medical English[8] prior to the study start. Regular training and site visits were performed during the entire study to confirm that acupuncturists followed the fixed protocols. Acupuncturists were not blinded to the treatment whereas patient got the information that two acupuncture protocols were tested and that we don't know which is the most effective.

Needle placement and acupuncture points used are illustrated in Fig. S1 and full name, location, tissue and innervation is given in Table S1. At each acupuncture treatment, the result of pregnancy test was recorded, the time of the day when the patient received acupuncture, acupuncturist name and stimulation intensity (mA) was recorded. Also, any other events that may affect the treatment (positive or negative) or adverse events were recorded.

Active Acupuncture

Needles and insertion. In the active acupuncture protocol (Fig. S1 and Table S1), needles (single use) were made of stainless steel and sized 0.25 x 30 mm, 0.30 x 40, and 0.35 x 50mm (Hwoto, Suzhou Medical Appliance Fact. 215005 Suzhou, China). The needle insertion was gentle. The skin was tightened by pressing around the area of needle insertion and then gently inserted. When placed, needles were inserted to a depth of 15-35mm into skeletal muscle or fibrous tissue. The depth of needle insertion could vary

between patients depending on body mass index (BMI) and the depth was deep enough to reach muscle/fibrous tissue.

Stimulation. When needle was inserted, they were simulated by manual rotation ~180 degrees back and forth to evoke tingling sensation, so called de qi, reflecting activation of sensory afferents (Fig. S1 and Table S1). As soon as de qi was reached, the needle should not hurt or cause any pain or discomfort. Needles in abdominal and leg muscles was connected to an electrical stimulator (AS Super 4 Digital, schwa-medico GmbH, Ehringshausen, Germany) and stimulated with low–frequency, 2Hz with a 0.5 ms pulse length. The intensity was adjusted to produce local muscle contractions without pain or discomfort. The patient was instructed that the intensity of stimulation should be as high as possible without pain or discomfort. After 10 minutes, needles without electricity were stimulated manually and the intensity of the electrical stimulation was adjusted. This was repeated after 20 minutes and again after 30 minutes when stimulator was turned off and needles removed.

Control Acupuncture

Needle insertion. In the control acupuncture protocol (Fig. S1 and Table S1), needles (single use) were made of stainless steel and sized 0.20 x 20 mm (Hwoto, Suzhou Medical Appliance Fact. 215005 Suzhou, China). The needle insertion was gentle, superficial and oblique <5mm.

Stimulation. No stimulation. Electrodes were attached to the needles and the stimulator was turned on at an intensity of zero (no active current) in order to mimic electrical stimulation in the active acupuncture group. Patients were told that the stimulation was subliminal and would most likely not cause any sensation.
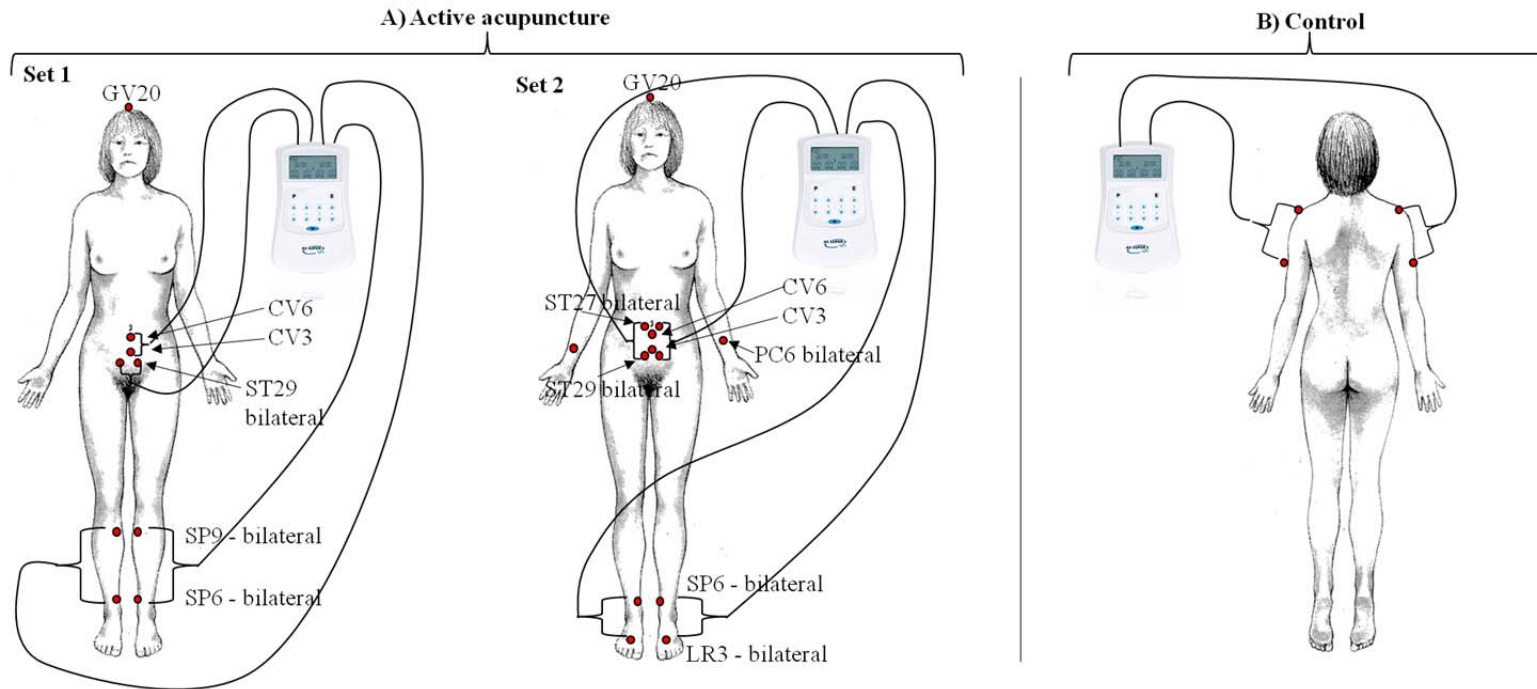
Clomiphene or Placebo

The study drug, clomiphene was manufactured by Fertilan, Codal Sytnor Ltd, Limassol, Cyprus and the placebo drug by Baoquanling Pharmaceutic, Harbin, China. Over encapsulated clomiphene citrate pills and matching placebo pills were packaged by data coordination committee and Baoquanling Pharmaceutic. The study drug and the placebo was tested at Analytical Research Laboratories, Oklahoma City, OK, US and found to be 101.2% clomiphene and 100% not detectible clomiphene placebo (ARL#:176807-01. May 25 and 29, 2012).

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eFigure. Acupuncture Point Localization in the Active Acupuncture and Control Acupuncture Groups

A) Active acupuncture

Set 1
GV20
CV6
CV3
ST29 bilateral
SP9 - bilateral
SP6 - bilateral

Set 2
GV20
ST27 bilateral
CV6
CV3
PC6 bilateral
ST29 bilateral
SP6 - bilateral
LR3 - bilateral

B) Control

Set 1 and 2 was alternated every other treatment to reduce sorness. In Set 1, large intestine (LI) 4 between the thumb and index finger was inserted as well. All needles (in total 11 in Set 1 and 13 in Set 2) were inserted to a depth of 15 to 35 mm into skeletal muscle and stimulated manually by rotation when inserted. Acupuncture points in abdominal and leg muscle were connected to an electrical stimulator and stimulated with low-frequency (2Hz). Points in hands and head were stimulated manually every 10 minutes during 30 minutes of treatment. Electrical stimulation was as high as possible without pain or discomfort. CV, conception vessel; GV, governor vessel; LR, liver; PC, percardium; SP, spleen; ST, stomach.

Thin needles were inserted superficially, < 5 mm, in non-acupuncture points at acromion and lateral on humerus. Needles were not stimulated by manual rotation when inserted. Electrical stimulator was attached to the needles but no stimulation was delivered.

eTable 1. Distribution of Number of Patients by Site and Treatment Arm

Sites	Hospital Name	Active Acupuncture + Clomiphene	Control Acupuncture + Clomiphene	Active Acupuncture + Placebo	Control Acupuncture + Placebo	Randomization Number
1.	Department of Obstetrics and Gynecology, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang Province	12	12	12	12	48
	Department of Obstetrics and Gynecology, Second Affiliated Hospital, , Heilongjiang University of Chinese Medicine, Harbin, Harbin, Heilongjiang Province					
2.	Centre for Reproductive Medicine, Yuhuangding Hospital, Yantai, Shandong Province	12	12	12	12	48
3.	Centre for Reproductive Medicine, Daqing Oilfield General Hospital, Daqing, Heilongjiang Province	12	12	12	12	48
4.	Department of Obstetrics and Gynecology, Daqing Longnan Hospital, Daqing, Heilongjiang Province	12	12	12	12	48
5.	Department of Obstetrics and Gynecology, First Affiliated Hospital, Liaoning University of Chinese Medicine, Shenyang, Liaoning Province	12	12	12	12	48
6.	Department of Gynecology, First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin	12	12	12	12	48
7.	Department of Infertility, Tanggu District Maternal and Children's Hospital, Tianjin	12	12	12	12	48
8.	Department of Gynecology, Wenzhou City Hospital of Chinese Medicine, Wenzhou, Zhengjiang Province Wenzhou Zhongshan Hospital, Wenzhou, Zhengjiang Province	12	12	12	12	48
9.	Centre for Reproductive Medicine, Zhejiang Province Hospital of Integrative Medicine, Hangzhou, Zhejiang Province Department of Gynecology, Hangzhou City Hospital of Chinese Medicine, Hangzhou, Zhejiang Province	12	12	12	12	48
10.	Department of Obstetrics and Gynecology, Shanxi Province Hospital of Chinese Medicine, Taiyuan, Shanxi Province	12	12	12	12	48
11.	Henan Province Hospital of Chinese Medicine, Zhengzhou, Henan Province	12	12	12	12	48

eTable 1. Distribution of Number of Patients by Site and Treatment Arm (continued)

Sites	Hospital Name	Active Acupuncture + Clomiphene	Control Acupuncture + Clomiphene	Active Acupuncture + Placebo	Control Acupuncture + Placebo	Randomization Number
12.	Outpatient Department, Xuzhou Maternal and Children's Hospital, Xuzhou, Jiangsu Province Xuzhou City Hospital of Chinese Medicine, Xuzhou, Jiangsu Province	12	12	12	12	48
13.	Centre for Reproductive Medicine, Huaian Maternal and Children's Hospital, Huaian, Jiangsu Province	12	12	12	12	48
14.	Department of Gynecology, Suzhou City Hospital of Chinese Medicine, Suzhou, Jiangsu Province	12	12	12	12	48
15.	Institute of Integrated Traditional and Western Medicine, Tongji Hospital, Medical College, Huazhong University of Science and Technology, Wuhan, Hubei province Department of Obstetrics and Gynecology, Hubei Province Hospital of Chinese Medicine, Wuhan, Hubei province	12	12	12	12	48
16.	Centre for Reproductive Medicine, Dalian Maternal and Children's Centre, Dalian, Liaoning Province	12	12	12	12	48
17.	Department of Gynecology, Second Hospital, Jiangxi University of Chinese Medicine, Nanchang, Jiangxi Province	12	12	12	12	48
18.	Department of Obstetrics and Gynecology, First Affiliated Hospital, Hunan University of Chinese Medicine, Changsha, Hunan Province	12	12	12	12	48
19.	Department of Chinese Medicine, First Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong Province	12	12	12	12	48
20.	Department of Traditional Technology, Guangdong Province Hospital of Chinese Medicine, Guangzhou, Guangdong Province Department of Infertility, Liwan District Hospital of Chinese Medicine, Guangzhou, Guangdong Province	12	12	12	12	48
21.	Department of Obstetrics and Gynecology, Affiliated Hospital, Anhui University of Chinese Medicine, Hefei, Anhui Province	10	10	10	10	40
	TOTAL	250	250	250	250	1000

eTable 2. Acupuncture Points, Stimulation, Localization, Tissue in Which Needles Are Inserted, and Innervation Area in Active Acupuncture, Which Consists of Two Protocols That Are Alternated Every Other Treatment, and Control Acupuncture[7]

Point	Stimulation	Localization	Tissue	Muscle Innervation
Active acupuncture 1				
Zhongji; CV3	EA	4 cun caudal to the umbilicus	Fibrous tissue, linea alba	L1
Qihai; CV6		1.5 cun caudal to the umbilicus	Fibrous tissue, linea alba	Th11
Guilai; ST29	EA	1 cun cranial to the pubic bone and 2 cun lateral to the midline	M rectus abdominis	Th6-12
Sanyinjiao; SP6	EA	3 cun proximal to the medial malleolus	Mm. flexor digitorum longus, tibialis posterior	L4-5, S1-2
Yinlingquan; SP9		Below medial tibiachondyle	M. gastrocnemius	S1-2
Hegu; LI4	Manual 4 times	On the highest point at m. interosseous dorsalis	Mm. interosseous dorsalis I, lumbricalis II, adductor pollicis	C8, Th1
Baihui; GV20	Manual 4 times	On the top of the head	Aponeurosis epicranii	C2-3, N. trigeminus
Active acupuncture 2		**Localization**	**Tissue**	**Muscle Innervation**
Zhongji; CV3	Manual 4 times	1 cun cranial to the pubic bone in the midline	Fibrous tissue, linea alba	L1
Qihai; CV6	Manual 4 times	1.5 cun caudal to the umbilicus	Fibrous tissue, linea alba	Th11
Guilai; ST29	EA	1 cun cranial to the pubic bone and 2 cun lateral to the midline	M rectus abdominis	Th6-12
Tianshu; ST25		2 cun lateral to the midline at the level of the umbilicus	M rectus abdominis	Th6-12
Sanyinjiao;SP6	EA	3 cun proximal to the medial malleolus	Mm. flexor digitorum longus, tibialis posterior	L4-5, S1-2
Taichong; LR3		Between metatarsale I and II, just distal to the caput	M. Interosseous dorsalis I	S2-3
Neiguan; PC6	Manual 4 times	2 cun proximal to processus styloideus radii, between the tendons of palmaris longus and flexor carpi radialis	M. flexor digitorum superficialis	C8, Th1
Baihui; GV20	Manual 4 times	On the top of the head	Aponeurosis epicranii	C2-3, N. trigeminus
Control acupuncture		**Localization**	**Tissue**	**Skin innervation**
No known point	No stimulation	On top of acromion	Skin	C3-4, n. supraclavicularis
No known point	No stimulation	On humerus lateral side, behind LI14	Skin	C5-6, n. cutaneous brachiilateralis

Abbreviations: EA, electroacupuncture; C, cranial; Th, thoracic; CV, conception vessel; ST, stomach; SP, spleen; LI, large intestine; GV, governor vessel; LR, liver; PC, pericardium.[7]Kuang H, Li Y, Wu X, et al. Acupuncture and clomiphene citrate for live birth in polycystic ovary syndrome: study design of a randomized controlled trial. Evid Based Complement Alternat Med 2013; 2013: 527303.

eTable 3. Secondary Reproductive and Metabolic Outcome Changes From Baseline to Last Visit Measures

	Active Acupuncture + Clomiphene (n=233) [a]	Control Acupuncture + Clomiphene (n=235) [a]	Active Acupuncture + Placebo (n= 222) [a]	Control Acupuncture + Placebo (n=228) [a]	P Value [b]
Biometric features					
BMI, Mean (95%CI)	-0.0 (-0.1 to 0.1)	-0.1 (-0.2 to 0.0)	-0.2 (-0.3 to -0.0)	-0.2 (-0.3 to -0.0)	0.18
Weight, Mean (95%CI), kg	-0.1 (-0.4 to 0.1)	-0.3 (-0.6 to 0.1)	-0.6 (-0.9 to -0.2)	-0.4 (-0.7 to -0.1) [227]	0.26
Waist-hip-ratio, Mean (95%CI)	-0.0 (-0.0 to 0.0)	-0.0 (-0.0 to 0.0)	-0.0 (-0.0 to 0.0)	-0.0 (-0.0 to 0.0)	0.71
Modified Ferriman-Gallwey score[c], Mean (95%CI)	-0.3 (-0.4 to -0.2)	-0.4 (-0.5 to -0.3)	-0.3 (-0.4 to -0.2)	-0.1 (-0.3 to -0.0)	0.19
Acne score[d], Mean (95%CI)	-0.1 (-0.1 to 0.0)	-0.2 (-0.2 to -0.1) [230]	-0.1 (-0.2 to -0.0) [216]	-0.2 (-0.3 to -0.1) [219]	0.35
Reproductive index					
FSH, Mean (95%CI), mIU/mL	-2.6 (-3.0 to -2.1) [221]	-2.5 (-2.9 to -2.0) [215]	-1.3 (-1.7 to -0.9) [209]	-1.2 (-1.6 to -0.8) [214]	<0.001
LH, Mean (95%CI), mIU/mL	-2.3 (-3.9 to -0.8) [221]	-2.8 (-4.1 to -1.5) [215]	0.3 (-1.1 to 1.7) [208]	-0.3 (-1.5 to 0.9) [213]	<0.001
Progesterone, Mean (95%CI), ng/mL	13.5 (11.2 to 15.7) [219]	12.9 (10.4 to 15.4) [215]	6.8 (4.8 to 8.7) [208]	6.1 (4.3 to 7.8) [214]	<0.001
Total testosterone, Mean (95%CI), ng/dL	17.9 (12.9 to 23.0) [221]	20.8 (15.2 to 26.4) [215]	3.7 (1.0 to 6.3) [210]	4.9 (1.9 to 7.9) [214]	<0.001
Estradiol, Mean (95%CI), pg/mL	435.9 (336.3 to 535.5) [221]	410.4 (317.0 to 503.8) [214]	141.1 (81.1 to 201.0) [210]	180.5 (116.2 to 244.7) [214]	<0.001
SHBG, Mean (95%CI), µg/mL	2.97 (2.35 to 3.59) [222]	2.45 (1.74 to 3.14) [211]	0.29 (-0.24 to 0.81) [206]	0.89 (0.31 to 13.47) [213]	<0.001
Metabolic index					
Glucose, Mean (95%CI), mg/dL	0.8 (-2.7 to 4.2) [219]	1.7 (-1.2 to 4.6) [214]	-2.2 (-5.4 to 1.0) [212]	-2.3 (-5.6 to 1.0) [217]	0.41
Insulin, Mean (95%CI), µIU/mL	0.9 (-1.4 to 3.1) [220]	2.8 (0.8 to 4.8) [215]	1.4 (-1.2 to 3.9) [208]	-0.4 (-1.8 to 1.0) [212]	0.18
Triglycerides, Mean (95%CI), mg/dL	-5.1 (-14.5 to 4.2) [218]	1.8 (-9.0 to 12.6) [215]	-14.3 (-25.0 to -3.6) [210]	-1.1 (-11.0 to 8.9) [216]	0.47
Total cholesterol, Mean (95%CI), mg/dL	-3.5 (-11.0 to 3.9) [217]	-9.6 (-15.9 to -3.3) [214]	-7.1 (-13.9 to -0.3) [209]	-2.0 (-8.7 to 4.7) [216]	0.43
HDL-C, Mean (95%CI), mg/dL	2.5 (0.1 to 4.9) [219]	0.4 (-1.7 to 2.4) [214]	1.0 (-1.0 to 2.9) [211]	1.8 (-0.2 to 3.8) [217]	0.54
LDL-C, Mean (95%CI), mg/dL	-7.1 (-12.6 to -1.6) [217]	-10.8 (-15.2 to -6.4) [214]	-4.4 (-9.6 to 0.7) [206]	-3.3 (-8.3 to 1.7) [214]	0.11

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FSH, follicle-stimulating hormone; LH, luteinizing hormone; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SHBG, sex hormone-binding globulin; CI, confidence interval.

SI conversion factors: To convert LH and FSH to IU/L, multiply by 1.0; progesterone to nmol/L, multiply by 3.18; estradiol to pmol/L, multiply by 3.671; total testosterone to nmol/L, multiply by 0.0347; sex hormone–binding globulin to nmol/L, multiply by 8.896; glucose to mmol/L, multiply by 0.0555; insulin to pmol/L, multiply by 6.945; triglycerides to mmol/L, multiply by 0.0113; and total cholesterol, HDL-C, and LDL-C to mmol/L, multiply by 0.0259.

[a] Variables expressed as mean (95%CI) with sample sizes that differ from the complete sample in the intervention group, the numbers of patients are indicated in brackets.
[b] Kruskal-Wallis test was used to compare the difference in change from baseline to last visit among the four treatment groups.
[c] Scores on the modified Ferriman-Gallwey scale for hirsutism range from 0 to 44, with higher scores indicating a greater degree of hirsutism.
[d] Scores on the acne scale range from 0 to 5, with higher scores indicating a greater degree of acne.

eTable 4. Secondary Quality-of-Life Outcomes Score Changes From Baseline to Last Visit Measures

Characteristic	Active Acupuncture + Clomiphene (n=233) [a]	Control Acupuncture + Clomiphene (n=235) [a]	Active Acupuncture + Placebo (n=222) [a]	Control Acupuncture + Placebo (n= 228) [a]	*P* Value [b]
PCOSQ [c], Mean (95%CI)	0.0 (-0.1 to 0.2)	-0.0 (-0.1 to 0.1)	-0.0 (-0.1 to 0.1)	0.0 (-0.1 to 0.1)	0.57
SF-36 [d], Mean (95%CI)	-1.5 (-3.0 to -0.0)	-2.7 (-4.1 to -1.3)	-2.3 (-3.6 to -0.9)	-1.3 (-2.7 to 0.1)	0.63
ChiQO [e], Mean (95%CI)	-2.2 (-4.1 to -0.2)	-2.9 (-5.0 to -0.8)	-2.9 (-4.7 to -1.0)	-1.8 (-4.2 to 0.6)	0.54
SAS [f], Mean (95%CI)	0.3 (-0.7 to 1.3)	0.7 (-0.2 to 1.7)	1.9 (0.9 to 2.9)	0.0 (-0.9 to 1.0)	0.16
SDS [g], Mean (95%CI)	1.6 (0.3 to 2.9)	0.7 (-0.4 to 1.9)	1.1 (-0.2 to 2.3)	0.7 (-0.4 to 1.8)	0.23

Abbreviations: PCOSQ, The Polycystic Ovary Syndrome Health-Related Quality of Life Questionnaire; SF-36, 36-Item Short Form Health Survey; ChiQOL, Chinese Quality of Life Instrument; SAS, Zung Self-Rating Anxiety Scale; SDS, Zung Self-Rating Depression Scale; CI, confidence interval.

[a] For variables expressed as mean (95% CI).

[b] Kruskal-Wallis test was used to compare the scores changes among the four treatment groups.

[c] Scores on the PCOSQ, a questionnaire for measuring health-related quality of life in women with the polycystic ovary syndrome[9-11], range from 1 to 7, with higher scores indicating better function.

[d] Scores on the SF-36, a generic health-related quality of life measure, range from 0 to 100, with higher scores indicating better function.[12] The minimal clinically important difference magnitude was 1.58 points for improvement and -7.91 points for deterioration of SF-36 questionnaire.[16]

[e] Scores range from 50 to 250, with higher scores indicating better function[13].

[f] Scores range from 25 to 100, with higher scores indicating more severe Anxiety[14].

[g] Scores range from 25 to 100, with higher scores indicating more severe depression[15].

eTable 5. Exploratory Outcomes With Regard to Fecundity [a]

Outcome	Active Acupuncture + Clomiphene (n=235)	Control Acupuncture + Clomiphene (n=236)	Active Acupuncture + Placebo (n=223)	Control Acupuncture + Placebo (n=232)	Absolute Difference [e] (95% CI)						P Value for Interaction [l]
					Effect of Active Acupuncture			Effect of Clomiphene			
					Clomiphene [f]	Placebo [g]	Overall [h]	Active Acupuncture [i]	Control Acupuncture [j]	Overall [k]	
Primary outcomes											
Singleton live birth among all live births	63/69 (91.3)	61/66 (92.4)	31/31 (100.0)	37/39 (94.9)	-1.1 (-10.3 to 8.1)	5.1 (-1.8 to 12.1)	0.7 (-6.0 to 7.3)	-8.7 (-15.3 to -2.0)	-2.4 (-11.9 to 7.0)	-5.3 (-11.3 to 0.8)	0.36
Twin live birth among all live births	6/69 (8.7)	5/66 (7.6)	0/31	2/39 (5.1)	1.1 (-8.1 to 10.3)	-5.1 (-12.1 to 1.8)	-0.7 (-7.3 to 6.0)	8.7 (2.0 to 15.3)	2.4 (-7.0 to 11.9)	5.3 (-0.8 to 11.3)	0.36
Infant [b]											
Weight, Mean (95%CI), g	3304 (3165 to 3443) [75]	3324 (3196 to 3451) [70]	3335 (3173 to 3497) [31]	3129 (2845 to 3414) [40]	-19.2 (-206.9 to 168.5)	205.8 (-142.6 to 554.1)	60.4 (-108.1 to 228.9)	-30.5 (-268.6 to 207.5)	194.4 (-74.4 to 463.2)	94.6 (-84.4 to 273.7)	0.19
Sex ratio at birth, (boys: girls)	37/38 (0.97)	31/39 (0.79)	13/18 (0.72)	21/19 (1.11)	5.0 (-11.2 to 21.3)	-10.6 (-33.8 to 12.7)	-0.1 (-13.4 to 13.2)	7.4 (-13.3 to 28.1)	-8.2 (-27.6 to 11.1)	-1.0 (-15.2 to 13.2)	0.25
Pregnancy											
Duration of pregnancy [b], Mean (95%CI), wk	39.1 (38.7 to 39.5) [69]	39.3 (38.9 to 39.6) [65]	39.7 (39.2 to 40.2) [31]	38.4 (37.5 to 39.3) [38]	-0.2 (-0.7 to 0.4)	1.3 (0.2 to 2.4)	0.3 (-0.2 to 0.9)	-0.6 (-1.2 to 0.0)	0.8 (-0.0 to 1.7)	0.2 (-0.4 to 0.7)	0.007
Singleton pregnancy among all pregnancies	67/74 (90.5)	64/70 (91.4)	33/33 (100.0)	39/41 (95.1)	-0.9 (-10.2 to 8.5)	4.9 (-1.7 to 11.5)	0.7 (-6.1 to 7.4)	-9.5 (-16.1 to -2.8)	-3.7 (-13.0 to 5.6)	-6.3 (-12.3 to -0.4)	0.36
Time to conception [c], Mean (95%CI), d	63.8 (57.0 to 70.7) [108]	60.6 (53.9 to 67.4) [106]	62.4 (52.4 to 72.5) [51]	72.5 (62.3 to 82.8) [55]	3.2 (-6.4 to 12.8)	-10.1 (-24.3 to 4.1)	-1.3 (-9.3 to 6.6)	1.4 (-10.7 to 13.5)	-11.9 (-23.7 to -0.1)	-5.4 (-13.8 to 3.0)	0.12

eTable 5. Exploratory Outcomes With Regard to Fecundity [a] (continued)

Outcome	Active Acupuncture + Clomiphene (n=235)	Control Acupuncture + Clomiphene (n=236)	Active Acupuncture + Placebo (n=223)	Control Acupuncture + Placebo (n=232)	Absolute Difference [e] (95% CI)						P Value for Interaction [l]
					Effect of Active Acupuncture			Effect of Clomiphene			
					Clomiphene [f]	Placebo [g]	Overall [h]	Active Acupuncture [i]	Control Acupuncture [j]	Overall [k]	
Pregnancy loss among women who conceived											
Loss in first trimester	36/108 (33.3)	33/106 (31.1)	18/51 (35.3)	14/55 (25.5)	2.2 (-10.3 to 14.7)	9.8 (-7.6 to 27.3)	4.8 (-5.4 to 14.9)	-2.0 (-17.8 to 13.9)	5.7 (-8.8 to 20.2)	2.1 (-8.7 to 12.8)	0.48
Loss in second or third trimester	2/108 (1.9)	4/106 (3.8)	1/51 (2.0)	2/55 (3.6)	-1.9 (-6.4 to 2.5)	-1.7 (-7.9 to 4.6)	-1.8 (-5.5 to 1.8)	-0.1 (-4.7 to 4.5)	0.1 (-6.0 to 6.3)	-0.0 (-3.9 to 3.8)	>0.99
Biochemical Pregnancy [d]	28/108 (25.9)	27/106 (25.5)	12/51 (23.5)	13/55 (23.6)	0.5 (-11.3 to 12.2)	-0.1 (-16.3 to 16.1)	0.3 (-9.2 to 9.8)	2.4 (-11.9 to 16.7)	1.8 (-12.1 to 15.8)	2.1 (-7.9 to 12.1)	0.99
Ectopic pregnancy	1/108 (0.9)	2/106 (1.9)	1/51 (2.0)	0/55	-1.0 (-4.1 to 2.2)	2.0 (-1.8 to 5.8)	0.0 (-2.4 to 2.5)	-1.0 (-5.2 to 3.2)	1.9 (-0.7 to 4.5)	0.5 (-2.0 to 2.9)	0.38
Fecundity among women who ovulated											
Conception	108/221 (48.9)	106/218 (48.6)	51/156 (32.7)	55/162 (34.0)	0.2 (-9.1 to 9.6)	-1.3 (-11.6 to 9.1)	-0.2 (-7.2 to 6.8)	16.2 (6.3 to 26.1)	14.7 (4.8 to 24.5)	15.4 (8.4 to 22.4)	0.80
Singleton pregnancy	67/221 (30.3)	64/218 (29.4)	33/156 (21.2)	39/162 (24.1)	1.0 (-7.6 to 9.5)	-2.9 (-12.1 to 6.3)	-0.6 (-6.9 to 5.7)	9.2 (0.3 to 18.0)	5.3 (-3.7 to 14.2)	7.2 (0.9 to 13.5)	0.53
Singleton live birth	63/221 (28.5)	61/218 (28.0)	31/156 (19.9)	37/162 (22.8)	0.5 (-7.9 to 8.9)	-3.0 (-12.0 to 6.0)	-0.9 (-7.1 to 5.3)	8.6 (-0.0 to 17.3)	5.1 (-3.6 to 13.9)	6.9 (0.7 to 13.0)	0.54
Twin pregnancy	7/221 (3.2)	6/218 (2.8)	0/156	2/162 (1.2)	0.4 (-2.8 to 3.6)	-1.2 (-2.9 to 0.5)	-0.2 (-2.2 to 1.7)	3.2 (0.9 to 5.5)	1.5 (-1.2 to 4.3)	2.3 (0.5 to 4.1)	0.30
Twin live birth	6/221 (2.7)	5/218 (2.3)	0/156	2/162 (1.2)	0.4 (-2.5 to 3.3)	-1.2 (-2.9 to 0.5)	-0.3 (-2.1 to 1.6)	2.7 (0.6 to 4.9)	1.1 (-1.6 to 3.7)	1.9 (0.2 to 3.6)	0.30

eTable 5. Exploratory Outcomes With Regard to Fecundity [a] (continued)

Outcome	Active Acupuncture + Clomiphene (n=235)	Control Acupuncture + Clomiphene (n=236)	Active Acupuncture + Placebo (n=223)	Control Acupuncture + Placebo (n=232)	Absolute Difference [e] (95% CI)						P Value for Interaction [l]
					Effect of Active Acupuncture			Effect of Clomiphene			
					Clomiphene [f]	Placebo [g]	Overall [h]	Active Acupuncture [i]	Control Acupuncture [j]	Overall [k]	
Fecundity among ovulated cycles											
Conception	108/511 (21.1)	106/519 (20.4)	51/275 (18.5)	55/294 (18.7)	0.7 (-4.2 to 5.7)	-0.2 (-6.6 to 6.2)	0.4 (-3.5 to 4.3)	2.6 (-3.2 to 8.4)	1.7 (-3.9 to 7.4)	2.1 (-1.9 to 6.2)	0.79
Singleton pregnancy	67/511 (13.1)	64/519 (12.3)	33/275 (12.0)	39/294 (13.3)	0.8 (-3.3 to 4.9)	-1.3 (-6.7 to 4.2)	0.1 (-3.2 to 3.3)	1.1 (-3.7 to 5.9)	-0.9 (-5.7 to 3.9)	0.1 (-3.3 to 3.5)	0.55
Singleton live birth	63/511 (12.3)	61/519 (11.8)	31/275 (11.3)	37/294 (12.6)	0.6 (-3.4 to 4.6)	-1.3 (-6.6 to 4.0)	-0.1 (-3.3 to 3.1)	1.1 (-3.6 to 5.8)	-0.8 (-5.5 to 3.9)	0.1 (-3.2 to 3.4)	0.55
Twin pregnancy	7/511 (1.4)	6/519 (1.2)	0/275	2/294 (0.7)	0.2 (-1.2 to 1.6)	-0.7 (-1.6 to 0.3)	-0.1 (-1.0 to 0.9)	1.4 (0.4 to 2.4)	0.5 (-0.8 to 1.8)	0.9 (0.1 to 1.7)	0.30
Twin live birth	6/511 (1.2)	5/519 (1.0)	0/275	2/294 (0.7)	0.2 (-1.0 to 1.5)	-0.7 (-1.6 to 0.3)	-0.1 (-1.0 to 0.8)	1.2 (0.2 to 2.1)	0.3 (-1.0 to 1.5)	0.7 (-0.1 to 1.5)	0.30

[a] Live birth was defined as the delivery of a live-born infant (≥ 20 weeks' gestation). Ovulation was defined as a serum progesterone level according to the standard of local site lab (minimum value of luteal phase). Conception was defined as any positive serum level of human chorionic gonadotropin. Pregnancy was defined as an intrauterine pregnancy with foetal heart motion, as determined by ultrasonography. There were no triple or higher-order pregnancies except twin pregnancies in this trial. Ovulation was defined as a serum progesterone level according to the standard of the local site laboratory (minimum value of luteal phase).

[b] Infant data and duration of pregnancy data were not available in 2 live births (one in Group Control Acupuncture plus Clomiphene, one in Group Control Acupuncture plus Placebo).

[c] Time to conception was the time between the first day that the patient took the study drug and the first day that a positive pregnancy test was recorded.

[d] Biochemical pregnancy was defined as positive urine or serum human chorionic gonadotropin test only without baby and gestational sac visible on ultrasound.

[e] Differences are expressed as percentage points (95% confidence interval) for six comparisons outcomes by factorial design, except birth weight, duration of pregnancy, and time to conception for which the absolute differences between mean values were shown.

[f] Active Acupuncture plus Clomiphene vs. Control Acupuncture plus Clomiphene

[g] Active Acupuncture plus Placebo vs. Control Acupuncture plus Placebo

[h] Acupuncture main effect: (Active Acupuncture plus Clomiphene) + (Active Acupuncture plus Placebo) vs. (Control Acupuncture plus Clomiphene) + (Control Acupuncture plus Placebo)

[i] Active Acupuncture plus Clomiphene vs. Active Acupuncture plus Placebo

[j] Control Acupuncture plus Clomiphene vs. Control Acupuncture plus Placebo

[k] Clomiphene main effect: (Active Acupuncture plus Clomiphene) plus (Control Acupuncture plus Clomiphene) vs. (Active Acupuncture plus Placebo) + (Control Acupuncture plus Placebo)

[l] P values of the interaction between active acupuncture and clomiphene treatments