Front. Med. 2024, 18(1): 46–67
https://doi.org/10.1007/s11684-023-1051-5

REVIEW

Effects and mechanisms of acupuncture on women related health

Huichao Qin[1,2], Jiaxing Feng[2], Xiaoke Wu (✉)[2]

[1]Department of Reproductive Medicine, Heilongjiang Provincial Hospital, Harbin Institute of Technology, Harbin 150036, China; [2]Department of Obstetrics and Gynecology, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin 150040, China

Abstract **Globally, public health interventions have resulted in a 30-year increase in women's life expectancy. However, women's health has not increased when socioeconomic status is ignored. Women's health has become a major public health concern, for those women from developing countries are still struggling with infectious and labor-related diseases, and their counterparts in developed countries are suffering from physical and psychological disorders. In recent years, complementary and alternative medicine has attracted wide attentions with regards to maintaining women's health. Acupuncture, a crucial component of traditional Chinese medicine, has been used to treat many obstetric and gynecological diseases for thousands of years due to its analgesic and anti-inflammatory effects and its effects on stimulating the sympathetic/parasympathetic nervous system. To fully understand the mechanism through which acupuncture exerts its effects in these diseases would significantly extend the list of available interventions and would allow for more reasonable advice to be given to general practitioners. Therefore, by searching PubMed and CNKI regarding the use of acupuncture in treating obstetric and gynecological diseases, we aimed to summarize the proven evidence of using acupuncture in maintaining women's health by considering both its effectiveness and the underlying mechanisms behind its effects.**

Keywords acupuncture; women health; clinical efficacy; mechanism

Introduction

Since 1900, public health interventions have resulted in a 30-year increase in women's life expectancy. Although women are living longer, they tend to have poorer health outcomes and are predisposed to chronic disease-related disability compared with men [1]. Generally, women's lifespan can be divided into seven stages, including the fetal period, neonatal period, childhood, adolescence, sexual maturity period, perimenopause, and post-menopause. Of these, the reproductive period lasts about 30 years, and this is the time during which they suffer the greatest diversity of both physical and psychological diseases [2], for example, infertility has become the most common disease among reproductive-age women seeking medical care. When women get pregnant, nausea and vomiting can affect up to 80% of pregnant women [3], resulting in termination of a wanted pregnancy in some severe cases. Meanwhile, some perinatal complications can be life-threatening [4]. When women enter the menopausal transition, due to the loss of steroid hormones they often experience symptoms including hot flashes, resulting in a greater burden of disease and more frequent gynecologic visits [5]. Although many diseases can be ameliorated by surgical or pharmaceutical interventions, such treatments cannot solve these diseases if we pay more attention to the overall state of the patients. Therefore, multiple approaches can be utilized, including physical treatments and complementary and alternative medicine, which has been shown to be effective for many conditions such as chronic pain [6,7]. Acupuncture, which is an important part of traditional Chinese medicine (TCM), has been applied in clinical practice for over 2000 years [8,9]. Written between 476 and 221 BC, the theory related to acupuncture is still used in clinical practice today and accounts for diseases linked to women's health, including threatened miscarriage, irregular menstruation, and nausea and vomiting of pregnancy (NVP) [7]. Although the use of acupuncture to treat disease has a long history, it only attracted attention and became widespread when it was reported on New York Times as a front-page story in July 1971 [10], and

Received October 6, 2023; accepted November 30, 2023
Correspondence: XiaoKe Wu, xiaokewu2002@vip.sina.com

now clinics in over 100 countries are using it for treating and preventing diseases [11]. Based on the theory of meridians and TCM, this technique utilizes fine needles to stimulate specific points on the body surface referred to as acupoints to invoke sensations of soreness, numbness, fullness, or heaviness, which is termed "De Qi" [12,13]. Apart from the traditional form of manual acupuncture, multiple variants of acupuncture have been developed and applied nowadays, including electroacupuncture (EA), laser acupuncture (LA), and transcutaneous electronic acupoint stimulation (TEAS). Proven evidence indicates that acupuncture is effective for many disorders, especially for functional diseases like chronic low back pain [14]. Acupuncture has also been extensively applied to treat obstetric and gynecological diseases to maintain women's health. In the present work we have conducted a literature review of acupuncture's application in obstetrics and gynecology and discuss its effectiveness and mechanisms of action.

Search strategy and selection criteria

The strategy was developed to search literature in PubMed and tailored in CNKI when necessary. We only included randomized controlled trials (RCTs) and meta-analysis that analyzed the evidence relevant to the acupuncture treating obstetric and gynecological diseases. The literature, published from January 1985 to September 2023, were retrieved from the database. The term was used including "primary dysmenorrhea," "endometriosis," "natural vaginal delivery and cesarean delivery," "polycystic ovary syndrome," "*in-vitro* fertilization/ embryo transfer," "nausea and vomiting of pregnancy," "perinatal complications," "menopausal transition," "acupuncture," "electroacupuncture," "laser acupuncture," "transcutaneous electronic acupoint stimulation," "acupoint injection," "acupressure," and "auriculotherapy."

Pain-related conditions affected women's health

Overview

Pain, a condition that can be non-cyclic or cyclic, not only adversely influences women's well-being, but is also a major public health issue. For women, a few physiological conditions and many diseases contribute to or reinforce the pain, including primary dysmenorrhea (PD), endometriosis, and natural vaginal delivery and cesarean delivery [15,16]. It is estimated that up to 95% of menstruating women are affected by PD, and about one fourth of reproductive-age women suffer from severe cases [17]. PD is considered a physical condition that arises due to the excessive release of prostaglandin within the uterus. Thus, non-steroidal anti-inflammatory drugs are recommended as the first-line treatment, yet their use is sometimes limited due to the increased risk of developing ulcers [18]. Acupuncture, as a non-pharmacological treatment, could be effective in pain relief linked to many diseases, including PD, while pain related to the endometriosis can only be improved a small amount until the pathogenic causes are eliminated. Contraceptive drugs is frequently prescribed to alleviate the symptoms including pain, however, the long-term usage increases the risk of venous thrombosis [19] and abnormal menstruation [20]. Labor pain presents a great psychological and physiological challenge for pregnant women, which is regarded as the most severe pain a woman can experience, and therefore painless labor has become an essential part of medical care [21,22] supported by labor analgesia and non-pharmacological treatment, including acupuncture. During the past decades, labor analgesia has been widely accepted by the general population around the world [23], although it raises some concerns including prolonged labor, high costs, and maternal side effects such as intrapartum fever, dural puncture, and postpartum headache [24]. Given the analgesic properties of acupuncture, it might be a promising approach for supporting analgesia during labor.

Clinical efficacy

It has been shown that both manual acupuncture and EA can, to some extent, alleviate the abdominal pain resulting from PD [25]. A study compared the efficacy for treating PD with multiple acupoints with the single one, namely Shiqizhui (EX-B8). The findings indicated that pain was significantly relieved in the acupuncture groups compared with the no-treatment group [26]. Moreover, scores for measuring the severity of pain were lower during both menstruation and follow-up in those who received acupuncture at multiple acupoint prior menstruation. Even if receiving vitamin K3 injection at the Sanyinjiao (SP6) rather than acupuncture, it yielded analgesic effects [27], indicating a crucial role of acupoint in pain relief of acupuncture.

For pain related to endometriosis, a study conducted by Li and colleagues showed that compared with sham acupuncture the visual analog scale (VAS) score in the acupuncture group was significantly lower (–3.87 vs. −0.98), despite the difference was no longer significant at the end of 24 weeks [28]. Similarly, acupuncture significantly improved all areas of the Endometriosis Health Profile in women with endometriosis based on standard care [29]. Nevertheless, limited evidence is available to support the acupuncture application to treating endometriosis, further studies are needed.

For pain associated with vaginal and cesarean delivery, it has been reported that women receiving EA had

significant lower numbers of analgesic pump compressions and pain scores as well as reduced fentanyl consumption at 48 h after surgery [30]. Another trial showed that acupuncture reduced the average intensity of pain and increased the rate of mobilization and removal of the Foley catheter on the first day after operation compared with placebo acupuncture [31]. Recently, Wu *et al.* investigated the analgesic effect of combined spinal-epidural anesthesia (CSEA) with acupoint injection (AI) on labor pain. The findings indicated that CSEA plus AI significantly reduced VAS scores and the dosage of medication and shortened the duration of labor compared to CSEA alone [32]. Based on the available literature, the most commonly used acupoints included Hegu (LI4), SP6, and Zusanli (ST36) [33]. Table 1 lists the RCTs mentioned above.

Mechanism

Excessive prostaglandin release is responsible for the pain related to PD [34], whereas the blood supply, infection, and chronic inflammatory damage are responsible for the pain linked with endometriosis [35]. Acupuncture exerts both anti-inflammatory and analgesic effects by restraining cyclooxygenase synthesis in the local site within the uterus [36]. A study reported that low-intensity EA could invoke the $PROKR2^{ADV}$ neurons, which subsequently activate the vagal-adrenal axis to inhibit systemic inflammation. Meanwhile, EA with a 0.5-mA current stimulating on ST36 could reduce TNF and IL-6 levels by 50% compared to the control [37]. It has also been demonstrated that the acupoints are surrounding clusters of mast cells [38], and acupuncture can activate TRPV channels on the membrane of mast cells to release bioactive substances that subsequently activate neural receptors to generate the analgesic effects [39]. On the other hand, acupuncture can also disturb the match between the ascending excitatory route and the descending pain control system thus producing analgesic effects [40]. In addition, acupuncture can directly regulate the release of both opioid and non-opioid neurotransmitters, including gamma-aminobutyric acid (GABA), norepinephrine, and 5-hydroxytryptamine (5-HT), they are delivered to a specific spot to reduce pain [41]. EA can also downregulate the biosynthesis of inflammatory cytokines by inhibiting the activation of p38 mitogen-activated protein kinases (MAPK) [42] and accelerate the removal of pain-inducing substances by enhancing uterine artery blood flow [43,44].

Labor pain is caused by the uterine contractions and stretching and dilatation of the cervix, vagina, which are initially linked to the posterior nerve root ganglia at the T10 to L1 levels [45] and then shifted to the S2 to S4 level of the spinal cord as the labor progression [46]. One of the mechanisms through which acupuncture alleviates labor pain may be that it can effectively inhibit the release of endogenous pain-associated substances and inflammatory mediators such as bradykinin, acetylcholine, serotonin, histamine, potassium ions, prostaglandins, leukotrienes, substance P, and lactic acid and thereby effectively relieve the pain by upregulating the pain threshold [12]. Moreover, it has been shown that both pregnancy and labor lead to changes in the helper T cell 1 (Th1)/helper T cell 2 (Th2) balance [47]. A study has shown that spinal epidural anesthesia (CSEA) coupled with AI can successfully alleviate labor pain by rectifying the Th1/Th2 imbalance [32]. Therefore, the capacity of acupuncture to regulate the immune system is another possible mechanism. In addition, by reducing smooth muscle spasms and local ischemia and hypoxia and inhibiting the oxidative stress response of the uterus, acupuncture has unique benefits in improvement of labor pain [48].

The analgesic effect of acupuncture benefits women who are suffering from pain-related conditions, and thus acupuncture might be another option or a useful supplement to standard treatments including painkillers.

Polycystic ovary syndrome (PCOS)

Overview

Globally, PCOS has become the most common endocrinal and metabolic disease, affecting about 10% of reproductive-age women. The typical clinical manifestations are oligo-amenorrhea, hirsutism, overweight or obesity, alongside with or without glucose and lipid metabolic disorder, anxiety and depression [49]. However, the main impetus for women with PCOS to seek medical care is the infertility which make them struggling from physical and mental disorders [50,51]. The treatments of PCOS include lifestyle change, medications, surgery, and complementary and alternative medicine [52]. Numerous evidence has suggested that acupuncture benefits women with PCOS including hyperandrogenism, ovulation disorder, glucose and lipid metabolism dysfunctions, and anxiety and depression.

Clinical efficacy

Hyperandrogenism and anovulation

Low frequency electroacupuncture (LF-EA) has been shown to be effective in treating anovulation and hyperandrogenism in infertile women with PCOS. After treatment, the level of circulating testosterone decreased by 25%, androsterone glucuronide by 30%, and androstane-3α and 17β-diol-3-glucuronide by 28% in the EA group compared with physical exercise. In addition, menstrual frequency increased to 0.69 from 0.28/month at

Table 1 The RCTs of acupuncture for pain-related conditions affecting women's health.

Ref. ID	Disease entities	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
25	PD	RCT	74	12 treatments over the course of three menstrual cycles	Group A: LF-MA Group B: HF-MA Group C: LF-EA Group D: HF-EA	Acupuncture can reduce the intensity and duration of pain, with no difference between the four groups, and the effect can be sustained for one year after entering the trial	Small sample size; the acupoint protocol was not provided
26	PD	RCT	600	Three menstrual cycles	Group A: before menstruation at Shiqizhui (EX-B8) Group B: when pain occurred, treated at EX-B8 Group C: before menstruation at Sanyinjiao (SP6), Diji (SP8), Ciliao (BL32), and EX-B8 Group D: when pain occurred, treated at SP6, SP8, BL32, and EX-B8 Group E: no treatment	Treating before menstruation is better than immediately treating when pain occurs; a single point is better than multiple points when treating as soon as pain occurs; and EX-B8 is a convenient point	Adverse events were not mentioned
27	PD	RCT	80	One session	Group A: saline injection at SP6 and the right buttock Group B: vitamin K deep muscle injection in the right buttock and saline injection at a non-acupoint near but not including SP6 Group C: vitamin K injection at SP6 and saline injection in the right buttock	Acupoint injection of vitamin K3 quickly relieves menstrual pain	Small sample size; no mention of adverse events
28	Endometriosis	RCT	106	A 30-min session once per day, 3 times a week, for 12 weeks giving a total of 39 sessions	Acupuncture: Guanyuan (CV4), bilateral SP6, Taichong (LR3), Zhaohai (KI6), and Qichong (ST30) Sham acupuncture: performed at non-acupoints	Acupuncture can relieve dysmenorrhea, shorten the pain time, and improve well-being and quality of life in women with endometriosis, although its efficacy recedes after the termination of therapy	No mention of adverse events; acupuncturists not blinded to treatment
29	Endometriosis	RCT	31	Twice a week with intervals of at least 48 h for 16 sessions over 8 weeks	Acupuncture + usual care group: SP6, SP8, Xuehai (SP10), Guilai (ST29), Zusanli (ST36), Zhongji (CV3), CV4, and LR3 Usual care group	Acupuncture is an acceptable and well tolerated therapy that may relieve pelvic discomfort and enhance quality of life	Small sample size

(*Continued*)

Ref. ID	Disease entities	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
30	Cesarean delivery	RCT	174	Four sessions at 6, 12, 24, and 48 h after surgery	PCIA + sham EA group: PCIA combined with sham acupoints (20 mm away from ST36 and SP6) PCIA + 2 Hz EA group: PCIA combined with acupuncture at ST36 and SP6 at a frequency of 2-Hz continuous wave PCIA + 20/100 Hz EA group: PCIA combined with acupuncture at ST36 and SP6 at the frequency of 20/100 Hz continuous wave	EA can be a safe and effective routine complementary therapy for patient-controlled intravenous analgesia for pain management after cesarean delivery	Limited patient demographic variability; the presence of confounding factors such as mood and sleep
31	Cesarean delivery	RCT	180	One session within 20 min of the cesarean delivery	Acupuncture group: auricular acupoints — namely MA-SC (kidney), MA-TF1, MA-IC1 (lung), MA-AT1 (subcortex) — and body acupoints, including LI4, ST36, SP6, BL25, BL26, and BL27 Placebo acupuncture group: the skin areas around acupoints were treated with a SVESA neural pen Standard care group: received the standard postoperative analgesia	Acupuncture is effective and safe in relieving pain and accelerating the mobilization of patients after cesarean delivery and can be a supplemental or routine therapy for pain control in patients after cesarean delivery	The inability to blind the practitioners; non-randomized groups; a single-center design
32	Vaginal delivery	RCT	360	One session	CSEA + AI group: acupoint injection at ST36 and SP6 combined with CSEA CSEA-only group AI group: acupoint injection at ST36 and SP6 Control group: no intervention	The CSEA + AI group had significantly lower VAS scores, adverse events, and dose of ropivacaine/sufentanil and had shorter labor duration	Not completely double blinded

Note: RCT, randomized clinical trial; LF-MA, low-frequency manual acupuncture; LF-MA, high-frequency manual acupuncture; EA, electroacupuncture; LF-EA, low-frequency EA; HF-EA, high-frequency EA; PCIA, patient controlled intravenous analgesia; CSEA, combined spinal-epidural anesthesia; AI, acupoint injection; VAS, visual analog scale.

baseline in the EA group [53]. Another RCT demonstrated that the ovulation rate was higher and the serum levels of estrone, estrone sulfate, E_2, dehydroepiandrosterone, dehydroepiandrosterone sulfate, androstenedione, testosterone, free testosterone, dihydrotestosterone, androsterone glucuronic acid, androstane-3α, 17β-diol-3-glucuronic acid, androstane-3α, 17β-diol-17-glucuronic acid in the acupuncture group were lower than those in the control group ($P < 0.05$) after 10–13 weeks intervention [54]. Moreover, Wu and his colleagues found that the acupuncture, together with clomiphene, significantly improved the live birth to 29.4% [55], as it had been reported that live birth was just 19.1% and 22.5% in women with PCOS treated with clomiphene alone [56,57]. However, the ovulation rate seemed to little change in women receiving active acupuncture. The discrepancy may attribute to sham acupuncture design which are frequently designed as superficial insertion at non-acupoint and non-penetration at acupoint. As the superficial insertion has been demonstrated to produce certain effects invoked by active acupuncture, this would largely narrow the difference between active and sham acupuncture in acupuncture trial, resulting in "negative" results.

Glucose and lipid metabolism

Also, acupuncture has been demonstrated to be effective in improving glucose and lipid metabolism in women with PCOS. In a recent systematic review that compared metformin alone and acupuncture combined with metformin in the treatment of PCOS patients, the pregnancy rate (RR 1.31, 95% CI 1.08–1.60), ovulation rate (RR 1.31, 95% CI 1.07–1.59), and insulin resistance (IR) (MD –0.68, 95% CI –1.01 to 0.35) were improved by acupuncture combined with metformin [58]. An RCT conducted by Dong *et al*. discovered that the weight, body mass index (BMI), hip circumference, waist-hip ratio (WHR), fasting glucose, insulin sensitivity, visfatin, and HDL-C in the acupuncture group were decreased, while visfatin was also reduced in the sham acupuncture group during the treatment [59].

Anxiety and depression

In addition, acupuncture has a therapeutic effect in improving patients' anxiety and depression. In 2019, Wang *et al*. investigated the effects of EA on anxiety and depression in unmarried PCOS patients. They concluded that the Zung-SAS and Zung-SDS scores ($P = 0.007$, $P = 0.027$), and the level of 5-HT ($P = 0.023$) were lower after intervention in the acupuncture group, while the serum norepinephrine ($P = 0.028$), the SF-36 domain scores for mental health, vitality, social functioning, general health, and health transition, the total score of CHQOL, and the scores of PCOSQOL infertility and body hair dimensions ($P < 0.05$) were increased. This confirmed that acupuncture has a positive effect on anxiety, depression, and quality of life in PCOS patients [60]. Another RCT demonstrated that acupuncture could improve the scores of depression and anxiety of PCOS women [61]. We have listed some relevant RCTs in Table 2.

Mechanism

Hyperandrogenism and anovulation

The pathogenesis of PCOS is complex, involving genetic, epigenetic, and maternal-fetal environmental factors. Androgen excess and IR are considered to be the crucial pathogenesis of this syndrome [62,63]. One underlying mechanism through which acupuncture exerts its effects in the treatment of PCOS might be its capacity to alter the hyperandrogenic environment. Many studies have confirmed this and reached similar conclusions. The possible mechanism for this lies in acupuncture's ability to activate the nerve growth factor/TrkA-mediated downstream signaling pathway, thereby contributing to the EA-mediated improvement in the circulating and adipose tissue concentrations of androgens [64]. Moreover, EA can break the vicious cycle initiated by excessive androgen secretion by enhancing the expression of ovarian granular cell layer P450 aromatase and decreasing the expression of theca cell layer P450C17α, androgen receptor, and Connexin 43 [65,66]. It is worth noting that a study carried out by Feng *et al*. not only confirmed that EA treatment of PCOS is mediated by central opioid receptors, but showed that manual acupuncture can also reduce androgen levels by regulating steroid hormone/peptide receptors [67].

Glucose and lipid metabolism

Hyperinsulinemia, another hallmark of PCOS induced by IR, can reduce the hepatic synthesis of sex hormone binding globulin (SHBG) and stimulate the production of androgen by ovarian thecal cells [63]. It was discovered that insulin-mediated glucose disposal was significantly reduced by 35% to 40%, possibly due to a decrease in insulin receptor signaling caused by serine hyperphosphorylation of insulin receptors and IRS-1 [68,69]. LF-EA activates many pathways, including metabolic adaptation and sympathetic nerve activation, in a similar manner to those activated by exercise. Also, the activation of the autonomic nervous system mediates an increase in systemic glucose uptake. These notions were confirmed by the study of Benrick *et al*., who found that EA can increase systemic glucose uptake in overweight and obese women and can induce various transcriptional

Table 2 The RCTs of acupuncture for PCOS

Ref. ID	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
53	RCT	84	Twice weekly for 2 weeks, once weekly for 6 weeks, and once every other week for 8 weeks, for a total of 14 sessions over 16 weeks	LF-EA: CV3, CV6, ST29, SP6, SP9 stimulated electrically with LF-EA of 2 Hz and LI4, Neiguan (PC6) stimulated manually Physical exercises: brisk walking, cycling, or any other aerobic exercise at least 30 min for no less than 3 days per week No active intervention: received oral information about the benefits of regular physical exercise	LF-EA and physical exercise improved hyperandrogenism and menstrual frequency more effectively than no intervention in PCOS patients. LF-EA was superior to physical exercise in treating hyperandrogenism and oligo/amenorrhea	The variability of sham methods, the location and depth of needling, and the number and duration of treatments
54	RCT	54	Twice a week, with each session separated by an interval of 2–4 days for a total of 32 sessions over 16 weeks	Acupuncture group: Set 1: CV3, CV6, SP6, ST29, Yinlingquan (SP9), LI4, and Baihui (GV20). Set 2: Tianshu (ST25), ST29, CV3, SP9, LI4, GV20, LR3, and PC6 Control group: shallow acupoints through EA without electricity at 4 non-meridian points in the shoulders and upper arms	The treatment of PCOS by acupuncture may be beneficial in improving glucose and lipid metabolism. Sham acupuncture may also improve several aspects of glucose and lipid metabolism through the placebo effect	Some heterogeneities in the results such as body weight; small sample size
55	RCT	1000	Twice a week, with a maximum of 32 acupuncture treatments	Active acupuncture protocol includes Set 1 and Set 2 which was alternated every other treatment. Set 1: GV20, CV6, CV3, ST29, SP9, SP6; Set 2: GV20, ST27, ST29, CV6, CV3, PC6, SP6, LR3 with low- frequency (2 Hz) Sham acupuncture protocol is using the thin needles 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 Clomiphene or placebo: patients started with an initial oral dose of 1 pill of clomiphene (50 mg) from days 3 to 7 of the menstrual cycle. The dosage of oral medication was increased by 1 pill in the absence of ovulation or maintained in the presence of ovulation. The maximum dosage of clomiphene didn't exceed 150 mg per day or 750 mg per cycle. The treatment could be repeated for up to 4 cycles Group A: active acupuncture plus clomiphene Group B: control acupuncture plus clomiphene Group C: active acupuncture plus placebo Group D: control acupuncture plus placebo	Among Chinese women with PCOS, the use of acupuncture with or without clomiphene, compared with control acupuncture and placebo, did not increase live births	–
57	RCT	32	Twice a week for 10–13 weeks, with two sets of 11 and 13 acupoints alternating every other treatment	Acupuncture group: Set 1: CV3, CV6, ST29, SP6, SP9, LI4, GV20. Set 2: CV3, CV6, ST25, ST29, SP6, LR3, PC6, GV20 Control group: visited the same physical therapists, twice weekly for 10–13 weeks	The treatment with acupuncture can reduce the levels of ovarian and adrenal sex steroid, thereby improving the ovulation rate of lean/overweight PCOS patients	Small sample size; no reporting of adverse events; no use of placebo or sham needles
58	RCT	54	30 min per session for a total of 16 weeks	The treatment protocol was consistent with that of Ref. 54	EA can improve anxiety/depression and quality of life and may influence levels of NE and 5-HT in PCOS patients	Small sample size; no reporting of adverse events
59	RCT	72	Twice weekly for 2 weeks, once weekly for 6 weeks, and once every other week for 8 weeks (14 treatments over 16 weeks)	Acupuncture:CV3, CV6, ST29, SP6, SP9 stimulated electrically with LF-EA of 2 Hz, and LI4, PC6 stimulated manually Exercises: brisk walking, cycling, or any other aerobic exercise at least 30 min, no less than 3 days per week No active intervention: received oral information about the benefits of regular physical exercise No intervention: –	There was a modest improvement in depression and anxiety scores in women treated with acupuncture, and improved HRQoL scores were noted in both intervention groups	The variability of sham methods, location and depth of needling, and the number and duration of treatments

and epigenetic changes in adipose tissue [70,71]. Further study found that the decreased levels of MSX1 and SRNX1, which are involved in glucose homeostasis, could be increased by EA treatment in muscle tissue of women with PCOS [72]. Moreover, by downregulating miR-32-3p levels and upregulating the expression of PLA2G4A, which is vital in the pathogenesis of PCOS and diabetes, acupuncture can inhibit the progression of PCOS and diabetes [73]. Another study found that daily administration of EA can regulate metabolic disorders and improve reproductive function in PCOS-like rats via the regulation of visceral fat, brown fat, and the intestinal flora [74].

Anxiety and depression

In addition, neurotransmitter changes are likely to be a major factor in PCOS patients accompanied with anxiety and depression, and numerous studies have shown that acupuncture directly or indirectly regulates neurotransmitters such as β-endorphin, serotonin, acetylcholine, 5-HT, dopamine, and acetylcholine and thus might be of therapeutic benefit [60,75,76].

To summarize, these findings support that acupuncture has a positive effect on the hyperandrogenism, ovulation disorders, glucose and lipid metabolism dysfunctions, and anxiety and depression in PCOS patients.

Infertility undergoing *in-vitro* fertilization/embryo transfer (IVF-ET)

Overview

The occurrence of assisted reproductive technique brings hope for infertile women who are failure to conventional treatment including pharmacotherapy and/or surgery. Nevertheless, the live birth rates do little increase even if the implantation is up to 90% as the advance of technique [77]. Although many efforts have been inputted, little change is achieved, and how to improve the live birth rate has become a big challenge. In recent years, the complement and alternative medicine are introduced to proving adjuvant therapy, including yoga, herbal medicine, and acupuncture, etc. Among them, herbal medicine and acupuncture are crucial components of TCM. Within the classical book "The Yellow Emperor's Inner Classic," infertility is attributed to the "kidney qi deficiency" incorporating the "Seven-Seven Theory." Based on meridian theory, acupuncture can regulate the function of "kidney qi" to improving reproductive function via stimulating acupoints located on specific meridian. Acupuncture has been demonstrated to have distinct benefits at multiple aspects for patients who are undergoing IVF-ET, including controlled ovarian hyperstimulation (COH), oocyte retrieval, ET, and live birth.

Clinical efficacy

Controlled ovarian hyperstimulation (COH)

Accumulating evidence supports that acupuncture benefits patients undergoing COH. In a clinical study [78], Hong *et al*. found that the rate of ovarian hyperstimulation syndrome (OHSS) and transplant cycle cancellation in the EA group were considerably lower than in the control group. In addition, there were significant differences in the days of gonadotropin (Gn) usage (MD = 0.47, 95% CI 0.00–0.94, $P = 0.05$) between the two groups. However, there was no statistical differences for the clinical pregnancy rate, fertilization rate, or high-quality embryo rate. Further, a meta-analysis [79] showed that compared with COH alone, acupuncture combined with COH could significantly increase the implantation rate (RR = 2.13, 95% CI 1.08–4.21), the number of oocytes retrieved (MD = 1.02, 95% CI 0.72–1.32) and the antral follicle count (MD = 1.52, 95% CI 1.08–1.95), and reduce follicle-stimulating hormone (FSH) levels (MD = −1.52, 95% CI −2.41 to −0.62). Ten studies (including 715 women) were included in a meta-analysis that showed that both acupuncture and acupuncture as an adjunct therapy could significantly improve ovulation [80].

Oocyte retrieval

Up to now, the analgesia of acupuncture is widely accepted and used in clinical practice. In an RCT, Stener-Victorin *et al*. found that the two treatments of EA and intravenous alfentanil had equivalent effects in terms of pain directly connected with oocyte aspiration, the sufficiency of anesthesia during oocyte aspiration, abdominal pain, and the degree of nausea [81]. A meta-analysis [82] showed that EA without pre-medication can be recommended in paracervical block for pain relief during oocyte retrieval. In addition, the analgesic effect of mixed frequency and fixed frequency EA were comparable when utilized for short-duration EA [83]. Moreover, the use of acupuncture has been shown to increase the rate of live births among women undergoing IVF [84].

ET

Reproductive outcomes

A multicenter RCT indicated that clinical pregnancy rate was higher in the TEAS group than in the controls (55.1% vs. 46.7%, $P = 0.03$) [85]. Moreover, in women older

than 35 years, the clinical pregnancy rates (30.8 vs. 13.9%) and embryo implantation rates (48.9% vs. 23.7%) were higher in the TEAS than the control group. There were no significant differences for the live births, biochemical pregnancy, or embryo implantation between the two groups. A meta-analysis [86] showed the significant effects of acupuncture adjuvant to frozen–thawed ET on the outcomes of clinical pregnancy rate (RR = 1.54, 95% CI 1.28–1.85), biochemical pregnancy rate (RR = 1.51, 95% CI 1.21–1.89), endometrial thickness (MD = 0.97, 95% CI 0.43–1.51), and endometrial pattern (RR = 1.41, 95% CI 1.13–1.75; 7 trials), without statistically significant effects for live birth rate (RR = 1.48, 95% CI 0.90–2.43, 4 trials).

Anxiety and quality of life associated with ART

It is estimated that over 80% of infertile women, to some extent, experience anxiety [87], and this in turn would have a negative impact on pregnancy outcomes. Therefore, it is crucial to manage the psychosomatic disorders for infertile women during the IVF process. After ET, patients who undergo acupuncture reported considerably less anxiety than the control subjects, enjoyed their treatments more, and felt more relaxed [88,89]. Acupuncture also produced a positive effect on the general health MOS Short Form 36 (SF36) following ET, despite that the benefit was no longer significant (MD 0.1, 95% CI −2.7 to 2.9) at 14 weeks after treatment.

Acupuncture treatment cross several IVF stages

Acupuncture or EA can improve reproductive outcomes among patients undergoing IVF-ET. A single-blind RCT [90] found that the pregnancy rate (31% vs. 23%) and the ongoing pregnancy rate (28% vs. 18%) at 18 weeks were higher in the acupuncture than the control, although the differences were not statistically significant. Similar, TEAS was superior to the control for improving the clinical pregnancy rate, embryo implantation rate, high-quality embryo rate, live birth rate, and biochemical pregnancy rate [91,92]. In addition, no serious adverse events associated with TEAS were reported [92], while high-quality evidence is still required to generalize the usage of acupuncture in these disorders. Table 3 summarizes the RCTs of the effect of infertility undergoing acupuncture on IVF-ET.

Mechanism

COH

COH impairs endometrial receptivity during the implantation window, resulting in a lower pregnancy rate and a higher abortion rate. A recent study conclude that high frequency electroacupuncture (HF-EA) could effectively improve endometrial receptivity and blastocyst implantation amount through significantly reducing the protein expression of the E-cadherin, β-catenin, and CLDN1 adhesion molecules and markedly enhancing the LIF/STAT3 signaling pathway in COH rats [93]. In addition, acupuncture may regulate angiogenesis of the endometrium and the number and the activity of uterus dendritic cells (uDCs) in COH rats during the peri-implantation phase [94]. Both VEGF and FGF-2 protein and mRNA levels were significantly lower on day 4 and higher on day 6 and day 8 of pregnancy compared with COH model rats. *In vitro*, acupuncture regulated the levels of VEGF, IL-15, and IL-18 secreted by uDCs but not the secretion of soluble sFLT-1. EA can also facilitate embryo implantation in COH rats by activating the VEGFR2/PI3K/AKT and VEGFR2/ERK signaling pathways, which have a positive relationship with endometrial angiogenesis [95].

Oocyte retrieval

Acupuncture is recognized as an analgesic technique in the realm of pathological pain, including inflammatory and neuropathic pain. Prior laboratory findings have revealed that acupuncture can mobilize opioid peptides, and electrical stimulation involves the biological activation of endogenous pain-inhibiting systems by releasing endogenous opioids and oxytocin, which appear to be essential for inducing functional changes in various organ systems [96,97]. Furthermore, other studies have proved that signal integrators such as transient receptor potential vanilloid type 1 and purinergic receptor P2X3 are crucial in acupuncture's analgesic effects [98,99]. Both low- and high-frequency stimulation have been found to produce endorphin-induced analgesia, and the types of endorphins produced depend on the stimulation pattern [100,101]. Moreover, cumulative analgesic effects may be achieved by longer electric stimulation periods [102].

ET

Reproductive outcomes

On the embryo implantation day, better developed endometrial pinopodes, elevated endometrial integrin α1β1/αVβ3, elevated leukemia inhibitory factor, and elevated serum progesterone levels were found in the TEAS group compared with controls [85]. Increased ovary and endometrial focal blood flow [103–105] and modulation of chemokines, integrins, and growth factors were found to maintain normal endometrial receptivity [106]. Thus, acupuncture might improve fertility outcomes by enhancing endometrial function during the

Table 3 The RCTs of acupuncture for infertility undergoing IVF-ET

Ref. ID	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
79	RCT	150	One session at least 30 min before oocyte aspiration	EA group: LI4, Waiguan (TE5), ST29, GV20, and ST36 Control group: 0.25–0.5 mg alfentanil and 0.25 mg atropine	EA has similar anesthetic properties as alfentanil during oocyte aspiration and thus can be an alternative option during oocyte aspiration	Non-blinded; no reporting of adverse events; small sample size
82	RCT	848	Three times, with the first session given after 6–8 days of follicle stimulation, and two sessions given prior to and after ET	Acupuncture group: first treatment: ST29, CV4, Qihai (CV6), SP6 and SP10; 1 h prior to ET: ST29, SP8, SP10, LR3, CV4, one point from Shenmen (HT7), PC6, or GV29, and auricular point Zhigong; following ET: GV20, KI3, ST36, SP6, PC6, and auricular point Shenmen (MA-TF1) Sham acupuncture group: non-insertive acupuncture	Acupuncture at the time of ovarian stimulation and ET resulted in no significant difference in live birth rates	Did not achieve the planned sample size; single blinding; non-identical eligibility criteria
83	RCT	739	Two sessions, with 2 Hz applied for 30 min at 24 h before ET and 30 min after ET	TEAS: 24 h before ET: SP8, ST29, EX-CA1, and SP10 30 min after ET: ST36, Zhongwan (CV12), BL23, CV4, and KI3 Control: IVF treatment	TEAS can increase the pregnancy rate in women undergoing IVF-ET, especially in older women; TEAS can improve endometrial receptivity	Not blinded; no reporting of adverse events
86	RCT	150	Two sessions, 25 min before and after ET	Acupuncture group: body acupoints before ET: PC6, SP8, LR3, GV20, and ST29; after ET: ST36, SP6, SP10, and LI4; and auricular acupuncture: MA-TF1, Zhigong, Neifenmi, and Naodian Control group: lying quietly	Acupuncture during IVF does not increase pregnancy rates, but can make patients more relaxed and optimistic	Single-blinded; small sample size; no reporting of adverse events
87	RCT	848	The same as Ref. 82	The treatment protocol was consistent with that of Ref. 82	Acupuncture can reduce anxiety during ET. Women have reduced emotional well-being 3 months following the IVF cycle, highlighting ongoing unmet psychosocial needs	The same as Ref. 82.
88	RCT	228	Three sessions, including injection on day 9 and immediately before and after ET	Acupuncture group: the acupuncture protocol was consistent with that of Ref. 86 Sham acupuncture group: using sham acupoints that were located close to but not on real acupoints	Acupuncture has a small effect on pregnancy and live birth rates that is not statistically significant, and it is safe for women undergoing ET	Single-blindness; no reporting of adverse events

Note: IVF-ET *in-vitro* fertilization/embryo transfer; TEAS, transcutanclus electrical acupoint stimulation.

peri-implantation stage.

Anxiety and quality of life

Acupuncture plays a role in increasing the release of β-endorphin, endomorphins, enkephalins, serotonin, and other neurochemical substances to relieve pain and mental stress and reduce anxiety and/or depression of patients [96,107,108].

In summary, acupuncture has multiple benefits in the setting of IVF, including increased oocyte retrieval, optimization of the uterine environment, alleviation of discomfort during and after operations, and stress reduction. However, further evidence-based research is still needed to completely understand the advantages, processes, and optimal usage of acupuncture in IVF.

Nausea and vomiting of pregnancy

Overview

Nausea and vomiting of pregnancy (NVP) affecting up to 80% of pregnant women is often ignored, due to a lack of effective and safe treatment [3]. Hyperemesis gravidarum (HG), an extreme situation of NVP, is the leading cause of termination of a wanted pregnancy in a woman, even if its incidence is less than 1% in pregnant women [109]. In some conditions, NVP/HG can lead to serious maternal and fetal outcomes, including dehydration, electrolyte imbalance, hospitalization, and even termination of a wanted pregnancy [110]. As few drugs is effective and safe, together with the fear of potential teratogenic risks on the fetal, the desire of alleviating symptoms in this population is far from satisfied by practitioners. Recently, strong evidence indicates that acupuncture is effective on symptoms improvement of NVP, providing another option for pregnant women who are unwilling to taking medicine, due to the fear of teratogenic risk.

Clinical efficacy

Previously, a placebo-controlled, randomized, single-blind, crossover trial was carried out by Carlsson *et al*. to evaluate the effects of acupuncture on symptoms improvement of women with HG. The results of that study indicated that based on the intravenous fluid, active acupuncture on Neiguan (PC6) could help patients recover more quickly than placebo acupuncture [111]. Later, a multicenter RCT was also carried out by Caroline Smith *et al*. to evaluate acupuncture effect on NVP-affected women, results indicated that acupuncture was an effective treatment compared with the no acupuncture for women who experience nausea and the dry retching score also decreased in the acupuncture group by the end of the third week (RR 0.72, 95% CI 0.56–0.93, $P < 0.01$) [112]. Meanwhile, Fatemeh Tara *et al*. evaluated the efficacy of acupressure on PC6 in women with NVP, they found that four times per day for 15 consecutive days could alleviate the severity of nausea, vomiting, and retching [113]. However, a study showed that in the first trimester of pregnancy, acupressure therapy does not work any better than vitamin B6 at reducing nausea and vomiting in symptomatic women [114]. In addition, a study found that for women with NVP who received auriculotherapy on Shenmen, the score of nausea and vomiting was significantly lower [115]. However, a systematic review found limited benefit with acupressure and no benefit in acupuncture or nerve stimulation in the treatment of NVP [116], as included studies have serious methodological flaws, including small sample sizes, inadequate blinding of participants and investigators, and lack of adequate control conditions [117]. Recently, a randomized, controlled, and 2 × 2 factorial trial was conducted by Wu and colleagues to assess the effect of acupuncture combined with doxylamine-pyridoxine on the moderate and severe NVP. The findings indicated that after treatment, active acupuncture (MD −0.7, 95% CI −1.3 to −0.1), doxylamine-pyridoxine (MD −1.0, 95% CI −1.6 to −0.4) and their combination (MD, −1.6, 95% CI −2.2 to −0.9) produced a greater reduction in Pregnancy-Unique Quantification of Emesis (PUQE) scores compared to their respective control groups and could reduce the amount of antiemetics [118]. This study provided evidence for the establishment of a pregnancy-safe treatment regimen together with an integrative guideline for managing severe NVP and added new evidence for the safety and efficacy of acupuncture as a complementary treatment. In addition, a systematic review and meta-analysis summarized the most frequently used acupoints for the treatment of NVP, including PC6, Waiguan (TE5), ST36, Xinshu (CV17), Zhongwan (CV12), and Gongsun (SP4) [119]. The RCTs described above are listed in Table 4.

Mechanism

Nausea and vomiting, a reflex phenomenon, is caused by the contraction of gastric smooth muscles, which forces food out of the stomach and into the esophagus and throat before vomiting out of the mouth. It is well-known that the sensory fibers from sympathetic nerves that innervate the stomach go through the celiac ganglion and superior cervical ganglion to the spinal cord. Approximately 90% of the vagus nerve fibers are afferent, and their signals are processed by the medulla and transmit stimuli from the intestine to the brain. It has been demonstrated that using gastric motility in rats, acupuncture activates somatic A-β fibers, which transmit the stimulus to the spinal cord and modulate visceral and other sensory inputs at the spinal level via somatic visceral reflexes [120], and vagotomy,

Table 4 The RCTs of acupuncture for NVP

Ref. ID	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
109	RCT	33	3 times a day, 30 min each time, for 7 consecutive days	Group A: deep acupuncture at PC6 on days 1, 2, 5, and 6 and acupuncture at PC6 on days 3 and 4 Group B: superficial acupuncture at PC6 on days 1, 2, 5, and 6 and deep acupuncture at PC6 on days 3 and 4	In comparison with placebo, acupuncture at PC6 may help HG patients recover better and faster	Small sample size; single-blindness; no reporting of adverse events
110	RCT	593	The first week was treated twice, then once a week for a total of 4 weeks	Traditional acupuncture: the liver qi stagnation pattern for CV12, PC6, Yanglingquan (GB34), Shangwan (CV13), Youmen (KI21), Liangqiu (ST34), ST36; the stomach or spleen qi deficiency pattern for ST36, PC6, CV12; the stomach heat pattern for Neiting (ST44), Jianli (CV11), ST34, Liangmen (ST21), PC6 and Quze (PC3); the phlegm pattern for ST40,SP9, Burong (ST19), Pishu (BL20), KI21; the heart qi deficiency pattern for Tongli (HE5), PC6, ST36, Juque (CV14); the heart fire pattern for PC6, CV14, Xinshu (BL15) P6 acupuncture: PC6 Sham acupuncture: acupuncture needles inserted into an area close to, but not on, acupuncture points Control group: no acupuncture	Acupuncture is an effective treatment for women who experience nausea and dry retching in early pregnancy. A time-related placebo effect was found for some women	Single-blindness; no reporting of adverse events
111	RCT	90	4 times a day, 10 min each time for 5 consecutive days	The acupressure group: PC6 pressure The sham acupressure group: pressure at TE5 The medication group: vitamin B6 (tab 40 mg, oral) 1/2 tab every 8 h and metoclopramide (tab 5 mg, oral) 5 mg every 8 h	It seems that PC6 acupoint pressure can reduce the severity of nausea, vomiting, and retching in pregnant women	Small sample size; single-blindness; no reporting of adverse events
112	RCT	66	7 days	The acupressure group: SeaBands on PC6 point and identical looking tablets were used as placebo in the same regimen as vitamin B6 The vitamin B6 group: SeaBands on the dummy point and 50 mg tablets of vitamin B6 were prescribed every 12 h for 5 days	Acupressure therapy is not more effective than vitamin B6 in reducing nausea and vomiting in symptomatic women in the first trimester of pregnancy	Single-blindness; not reported adverse events
113	RCT	128	Three times a day, for 30 s for 4 days	Auriculotherapy group: point zero, stomach, sympathetic autonomic, Shen Men cardia The sham control group: the points where these magnetic seeds were placed (e.g., the vision, knee, shoulder, and eyes) had no effects on the nausea and vomiting	Pregnant women who experience nausea may achieve relief with the proper application of effective points on the ears to manage nausea and vomiting as a supplementary and alternative therapy	Not reported adverse events
116	RCT	352	Acupuncture treatment for 30 min per day, up to 14 sessions over 2 weeks	Placebo plus acupuncture group: the core points were PC6 and ST36, and adjuvant points included the liver heat pattern for LR3, the stomach deficiency pattern for CV12, and the phlegm-dampness pattern for Fenglong (ST40) Doxylamine–pyridoxine plus sham acupuncture group: sham acupuncture was a pragmatic placebo needle on sham acupoints with the same acupuncture protocol Acupuncture plus doxylamine–pyridoxine group Placebo plus sham acupuncture group	Both acupuncture and doxylamine–pyridoxine alone was efficacious for moderate to severe NVP. Their combination may yield a potentially greater benefit than each alone	–

Note: NVP, nausea and vomiting during pregnancy; HG, hyperemesis gravidarum.

regional nerve block, local acupoint anesthesia, and brainstem injury can eliminate the effect of acupuncture on gastrointestinal motility [121]. Possible mechanisms for the effect of acupuncture treatment on NVP/HG mainly focus on its antiemetic and gastrointestinal functions [122]. Due to the increased heart rate, respiratory rate, and metabolic demand that occur with NVP, there is a decrease in the parasympathetic capacity needed to organize the neurological regulatory responses. Acupuncture can regulate gastrointestinal motility by stimulating the reflexes of the vagus and sympathetic nerves [123]. The study carried out by Su *et al*. found that stimulating CV12 could inhibit gastric motility via the efferent sympathetic pathway and the TRPV1 receptor [124]. Therefore, one possible mechanism through which acupuncture might affect the endogenous opioid system and 5-hydroxytryptamine transmission is by activating 5-hydroxytryptamine and noradrenergic fibers, thus affecting the afferent stimulation of the central nervous system on the vomiting center and relieving nausea and vomiting [108,125]. In addition, EA at PC6 could significantly inhibit the frequency of transient lower esophageal sphincter relaxations triggered by gastric distension [126], which could be another mechanism through which acupuncture might relieve NVP by affecting gastric emptying via somatic visceral reflexes.

In summary, acupuncture can alleviate NVP with only mild adverse reactions. In addition, the combination of acupuncture and western medicine has a synergistic effect and may reduce the need for medication. For patients who are unwilling to take medication for treatment, acupuncture may be a suitable option.

Perinatal complications

Overview

The period of pregnancy and labor is a very challenging phase for both mothers and newborns, and the severe case might be life-threatening. The pharmacological treatment of these obstetric complications is often restricted due to prioritizing the safety of fetuses and newborns and breastfeeding and due to the different maternal and perinatal side effects. Numerous evidence has indicated that acupuncture, a non-pharmacologic method, is beneficial for obstetric disorders and complications and can be used in conjunction with pharmacologic agents to reduce medication requirements [125], for example postpartum urinary retention (PUR).

Clinical efficacy

Acupuncture is an effective option for PUR. A prospective randomized case-controlled trial conducted by Lauterbach *et al*. suggested that 92% of participants who underwent acupuncture achieved spontaneous micturition within 1 h [128]. Subsequently, Qu *et al*. assessed whether acupoint hot compress could reduce the incidence of PUR, result indicated that compared with participants who received routine postpartum care, participants who received routine postpartum care together with acupoint hot compress had significantly decreased incidence of PUR (RR 0.58, 95% CI 0.35–0.98); improved postpartum uterine contraction pain at 6.5 h (median score, 1 vs. 2), 28.5 h (1 vs. 1), 52.5 h (1 vs. 1), and 76.5 h (0 vs. 0) after delivery; reduced depressive symptoms (RR 0.73, 95% CI 0.54–0.98); and increased breastfeeding milk volume at 28.5, 52.5, and 76.5 h after delivery [129]. A Chinese scholar compiled a list of acupoints often utilized in the treatment of PUR, including SP6, Zhongji (CV3), Guanyuan (CV4), ST36, Qihai (CV6), Yinlingquan (SP9), Shuidao (ST23), and Weiyang (CV3) [130]. The relevant RCTs are listed in Table 5.

Mechanism

The elevated progesterone during pregnancy and immediately postpartum suppresses smooth muscle tone and detrusor contraction, and impaired detrusor muscles together with a relaxed urethra can be a part of the mechanism of PUR [131]. Damage to the pelvic, hypogastric, and pudendal nerves during labor may be another mechanism for PUR. Usually, urinary retention due to sympathetic and parasympathetic nerve injuries is transient and will be restored within 3 months postpartum. In addition, the ischemic nerve injury caused by the extension of the second stage of labor and the direct partial or complete nerve transection caused by spontaneous or surgical delivery trauma can lead to urinary retention. The mechanism of acupuncture in the treatment of PUR may accelerate urination by lowering the bladder urination threshold, improving the excitability of bladder urination muscles and pelvic cavity and perineal nerve muscles, and improving the internal pressure of the bladder, and these effects may be realized by promoting the contraction of urination muscles, relaxing and opening the urethral sphincter, removing the inhibition from the brain on the spinal cord urination center, inducing a urination reflex, and reducing or even eliminating residual urine [132]. The study conducted by Zhang *et al*. have shown that acupuncture can induce the contraction of bladder detrusor muscles through nerve reflex and parasympathetic efferent impulses, which increase bladder pressure and the relaxation of the internal sphincter, thus regulating the urination function of women with PUR [133].

In conclusion, acupuncture has a significant effect on obstetric diseases such as PUR, with fewer side effects. However, although acupuncture can also treat other

Table 5 The RCTs of acupuncture for perinatal complications

Ref. ID	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
126	RCT	55	Not mentioned	Acupuncture group: 5–7 acupoints for each session, namely Pangguangshu (BL28), BL32, Lieque (LU7), KI6, GV20, HT7, and SP6 The control group: catheterization	Acupuncture is an excellent alternative to catheterization in treatment of women with postpartum urinary retention	Small sample size; no report of treatment sessions; lack of sham acupoints
127	RCT	1200	3 sessions of a 4-h acupoint hot compress at 30 min, 24 h, and 48 h after delivery	Intervention group: received routine postpartum care plus 3 sessions of acupoint hot compress administered at Shenque (RN8), Baliao including Shangliao (BL31), BL32, Zhongliao (BL33), BL34, and Yongquan (KI1) for time point 1 and at RN8 for time points 2 and 3 Control group: received routine postpartum care	Acupoint hot compresses after vaginal delivery decreased postpartum urinary retention, and thus may be considered as an adjunctive intervention in postnatal care that meets patient self-care needs	Failure to adopt personalized intervention protocols based on different syndromes in the subjects; not double-blinded; not applied to those with multiparas or complications

obstetric complications, the evidence level is insufficient due to the poor quality of clinical trials and small sample size.

Menopausal transition

Overview

Typically, menopause occurs between the ages of 45 to 56 and is caused by the loss of ovarian activity. During the menopausal transition, approximately 50% to 75% of women experience vasomotor symptoms like hot flashes and night sweats, around 30% have postmenopausal osteoporosis, and nearly 40% suffer from insomnia or mental trouble, resulting in a reduced quality of life [134–136]. Currently, HT is the main protocol for the treatment of menopausal transition, while a systematic review including 22 studies involving 43 637 women suggested that HT might be inappropriate for women at high risk of cardiovascular disease, thromboembolic disease, and some types of cancer [137]. When it comes to high risks of stroke and venous thromboembolism (VTE), HT substantially increases the incidence of dementia and venous thrombosis [138]. The clear efficacy and few adverse effects of acupuncture treatment in menopausal symptom improvement suggests that it could be a viable alternative therapy, particularly for high-risk women [139].

Clinical evidence

Evidence from recent RCTs supports acupuncture treatment in improving menopausal symptoms and quality of life. In a pragmatic RCT, Avis *et al*. found that the frequency of vasomotor symptoms declined by 36.7% after 6 months in the acupuncture group but increased by 6.0% in the control group [140]. Another trial indicated that acupuncture was superior to sham acupuncture in reducing hot flash frequency and severity and in decreasing scores on the Menopause Rating Scale (MRS) II [141]. Meanwhile, acupuncture significantly reduce day and night sweats in women with moderate-to-severe menopausal symptoms [142]. Moreover, acupuncture also performed well in improving quality of life for menopausal women, including perimenopausal insomnia (8.03 vs. 1.29, $P < 0.05$) [143]. A systematic review indicated that the effect of acupuncture treatment on depression relief was equivalent to antidepressants, with no significant difference in the Hamilton Rating Scale of Depression (HRSD) scores between the two groups [144]. In addition, at the week 8 of treatment, the reduction from baseline in the MRS total score was 6.3 in the EA group and 4.5 in the sham EA group, providing a between-group difference of 1.8 (95% CI 0.9–2.8) [145]. Meanwhile, an RCT that evaluated the value of laser acupuncture (LA) on postmenopausal osteoporosis found that LA combined with calcium and vitamin D3 supplements performed better in bone mineral density (BMD) and pain score than drug only [146]. All the RCTs mentioned above are listed in Table 6.

Mechanism

The mechanisms through which acupuncture improves menopausal symptoms have been studied for several years. A study found that hot flash status had a positive tendency toward increased levels of circulating IL-6 (P-trend = 0.049), IL-8 (P-trend < 0.001), TNF-α (P-trend = 0.008), and macrophage inflammatory protein-1β (P-trend = 0.04), suggesting that hot flashes might be related to low-grade systemic inflammation [147], and acupuncture can regulate the release of the innate immune cytokines and adaptive immunity cytokines [148]. Li *et al*. found that acupuncture could modulate the serum

Table 6 The RCTs of acupuncture for menopausal transition

Ref. ID	Design	Sample size	Number of treatments	Interventions	Conclusion	Limitation
138	RCT	209	20 sessions decided by the acupuncturist and patient within the first 6 months (acupuncture group) or within the second 6 months (waitlist control group)	Acupuncture needling based on anatomical location	Acupuncture treatments was associated with significant reduction in VMS and several quality-of-life measures compared with no acupuncture, and the clinical benefit persisted for at least 6 months after treatment	No reporting of specific acupoints; potential unreliability and risk of bias associated with self-reporting of VMS
139	RCT	40	Acupuncture for 12 weekly treatments and three capsules of Chinese medicine orally with water twice per day	TCM acupoints: CV4, GV20, PC6, ST36, SP6, LI4, KI3, and Fengchi (GB20) and 7–10 supplementary acupoints based on individual's TCM syndrome type as determined by TCM practitioners, i.e., kidney yang with spleen yang deficiency: Pishu (BL20), BL23, SP9, CV6; kidney yin with liver yin deficiency: Ganshu (BL18), BL23, Yinxi (HT6), KI6, LR3 Sham acupoint: needles were inserted superficially into seven bilateral sites that did not correspond to established TCM acupoints	TCM acupoints were superior to sham acupoint and verum CHM in reducing menopausal symptoms, whereas verum CHM showed no significant improvements when compared with placebo CHM	Small sample size; did not take into account TCM treatment principles
140	RCT	70	One treatment per week for five consecutive weeks	The intervention group: CV3, CV4, Ququan (LR8), SP6, and SP9 for the first 5 weeks The control group: the same protocol as the intervention group after 6 weeks	The standardized and brief acupuncture treatment produced a fast and clinically relevant reduction in moderate-to-severe menopausal symptoms during the six-week intervention	Small sample size; lack of placebo; no correct acupuncture technique training; not double-blinded
141	RCT	76	3 times per week for 10 times sessions	Acupuncture group: BL23 and BL18 with unilateral Qimen (LR14) and Jingmen (GB25) Placebo-acupuncture group: Streitberger needles at the same acupoints	Acupuncture can contribute to improvement in the short term treatment of PMI, both subjectively and objectively	Small sample size
143	RCT	360	24 sessions, 30 min each session, over 8 weeks (3 times per week)	EA group: CV4 and ST25, EX-CA1, SP6 Sham EA group: nonacupoints laterally and horizontally 1–2 cun (approximately 1–2 inches) away from the corresponding acupoints	Although it seemed to improve the quality of life, 8 weeks of EA might not relieve menopausal symptoms among women during menopause transition	Small sample size
144	RCT	68	One tablet once daily and 3 sessions per week of LA for 12 weeks	Drug group: oral calcium and vitamin D3 supplement containing fluoride Drug/LA group: oral calcium and vitamin D3 supplement containing fluoride plus LA including CV4, Mingmen (GV4) and bilaterally Dazhu (BL11), BL18, BL20, BL23, ST36, SP6, GB25, Yanglingquan (GB34), and Xuanzhong (GB39)	LA in combination with calcium and vitamin D supplementation containing fluoride is an effective modality for improving forearm BMD and reducing pain in osteoporotic post-menopausal women	Small sample size; lack of follow-up to assess the lasting effect of LA on BMD and pain; non-blinded

Note: VMS, vasomotor symptoms; TCM, traditional Chinese medicine; CHM, Chinese herbal medicine; PMI, perimenopausal insomnia; LA, laser acupuncture.

levels of E_2, corticotropin releasing hormone, adrenocorticotropic hormone, and corticosterone and improve BMD and bone mineral content in ovariectomized (OVX) rats [149]. EA alleviated osteoporosis secondary to ovariectomy by regulating the osteoprotegerin (OPG)/receptor activator of nuclear factor-κB ligand (RANKL) and Wnt/β-catenin signaling pathways [150]. In the OVX rats, it was demonstrated

that EA at CV4 could significantly increase serum alkaline phosphatase (ALP) and bone gla protein (BGP) levels, enhance the maximum and fracture loads, increase BMD, and activate the Wnt-β-catenin signaling pathway, which improved the osteoporotic morphological changes [151]. Another study also showed that EA treatment increased levels of osteocalcin and the BMD of lumbar vertebrae, decreased levels of tartrate-resistant acid phosphatase 5b, and improved bone microstructure in the femur of OVX rats. The ratio of OPG to RANKL and the levels of LRP5, β-catenin, and Runx2 were significantly upregulated after EA, while the expression of phosphorylated (p)-p38 and p-JNK were downregulated in the EA-treated groups compared with the OVX group [152].

The current evidence suggests that acupuncture is beneficial in improving menopause-related symptoms including hot flashes, sleep disturbances, and depression and quality-of-life. Nevertheless, the mechanism of acupuncture treating menopause remains unclear, further studies are needed.

Conclusions

Acupuncture, one of the important components of TCM, has been used to maintain women health with a long history in China and now widespread to around the world. Acupuncture provides proven benefit for many obstetric and gynecological diseases, including PD, CGP, PCOS, IVF, NVP, prenatal complication, and perimenopausal syndrome. Until now, effort devoted into both biological and clinical research on acupuncture has a few decades [153], numerous acupuncture studies emerged [154]. However, how acupuncture work and what's the underlying biochemical mechanism are still myth.

This narrow review analyzes the high-quality clinical trials of acupuncture in the treatment of obstetrical and gynecological diseases, to summarize the current evidence and provides brief review for biological mechanism and clinical effects to articulate a more instructive set of recommendations in the future. For basic experiment, we can explore complex molecular pathways underlying its efficacy including multiomics. For clinician, in view of the rapid growth of evidences, clear, actionable, trustworthy, and patient-centered acupuncture clinical practice guidelines should be formulated by incorporating them into mainstream regiments to improve the quality of women's health. In the future, women related diseases on which acupuncture have shown great effect in real world but with a low or very low level of evidence are the main priorities for scientific world.

Despite that proven evidence indicated that the acupuncture significantly improves pain relevant disorders, PCOS and NVP, the underlying mechanisms are not fully understood. While due to flaws of methodology and heterogeneity of acupuncture protocol, stronger evidence is still needed to support the usage of acupuncture in IVF-ET, infertility, prenatal complication, and menopausal transition, and the behind mechanisms are also deserved to be elucidated. In fact, therapeutic effects of acupuncture interventions are influenced by many factors including depth of needling, number and locations of acupoints, and De Qi and patients' expectation, etc. Until recently, an extension of CONSORT was defined for these factors in details by the guidance of Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA). With the advantages of being easy to perform, self-controllable, cost effective, and non-invasive, acupuncture will play an important role in maintaining women' health.

Acknowledgements

This work was supported by grants from the National Key R&D Program of China (No. 2019YFC1709500), the Project of Heilongjiang Province "TouYan" Innovation Team and the Project of Traditional Chinese Medicine Evidence-Based Capacity Improvement in 2023.

Compliance with ethics guidelines

Conflicts of interest Huichao Qin, Jiaxing Feng, and Xiaoke Wu declare that they have no conflict of interest.

This manuscript is a review article and does not involve a research protocol requiring approval by the relevant institutional review board or ethics committee.

References

1. Blumenthal SJ. Critical women's health issues in the 21st century. JAMA 2000; 283(5): 667
2. Stuenkel CA, Manson JE. Women's health—traversing medicine and public policy. N Engl J Med 2021; 384(22): 2073–2076
3. Fejzo MS, Trovik J, Grooten IJ, Sridharan K, Roseboom TJ, Vikanes Å, Painter RC, Mullin PM. Nausea and vomiting of pregnancy and hyperemesis gravidarum. Nat Rev Dis Primers 2019; 5(1): 62
4. O'Heney J, McAllister S, Maresh M, Blott M. Fetal monitoring in labour: summary and update of NICE guidance. BMJ 2022; 379: o2854
5. Duralde ER, Sobel TH, Manson JE. Management of perimenopausal and menopausal symptoms. BMJ 2023; 382: e072612
6. Qiu J. China plans to modernize traditional medicine. Nature 2007; 446(7136): 590–591
7. Williams H, Sweet L, Graham K. Acupuncture during pregnancy and the perinatal period: women's attitudes, beliefs and practices. Women Birth 2020; 33(3): e286–e294

8. Kaptchuk TJ. Acupuncture: theory, efficacy, and practice. Ann Intern Med 2002; 136(5): 374–383
9. Chang S. The meridian system and mechanism of acupuncture—a comparative review. Part 1: the meridian system. Taiwan J Obstet Gynecol 2012; 51(4): 506–514
10. Reverby SM. Acupuncture's radical roots and political branches. Am J Public Health 2021; 111(5): 760–761
11. WHO. WHO global report on traditional and complementary medicine 2019. 2019. Available at the website of WHO (accessed September 11, 2023)
12. Chen T, Zhang WW, Chu YX, Wang YQ. Acupuncture for pain management: molecular mechanisms of action. Am J Chin Med 2020; 48(4): 793–811
13. Feng J, Wang J, Zhang Y, Zhang Y, Jia L, Zhang D, Zhang J, Han Y, Luo S. The efficacy of complementary and alternative medicine in the treatment of female infertility. Evid Based Complement Alternat Med 2021; 2021: 6634309
14. Lu L, Zhang Y, Tang X, Ge S, Wen H, Zeng J, Wang L, Zeng Z, Rada G, Ávila C, Vergara C, Tang Y, Zhang P, Chen R, Dong Y, Wei X, Luo W, Wang L, Guyatt G, Tang C, Xu N. Evidence on acupuncture therapies is underused in clinical practice and health policy. BMJ 2022; 376: e067475
15. Zuarez-Easton S, Erez O, Zafran N, Carmeli J, Garmi G, Salim R. Pharmacologic and nonpharmacologic options for pain relief during labor: an expert review. Am J Obstet Gynecol 2023; 228(5 5S): S1246–S1259
16. Fletcher SG, Zimmern PE. Differential diagnosis of chronic pelvic pain in women: the urologist's approach. Nat Rev Urol 2009; 6(10): 557–562
17. Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. Hum Reprod Update 2015; 21(6): 762–778
18. Sinaii N, Cleary SD, Younes N, Ballweg ML, Stratton P. Treatment utilization for endometriosis symptoms: a cross-sectional survey study of lifetime experience. Fertil Steril 2007; 87(6): 1277–1286
19. Teal S, Edelman A. Contraception selection, effectiveness, and adverse effects: a review. JAMA 2021; 326(24): 2507–2518
20. Taylor HS, Kotlyar AM, Flores VA. Endometriosis is a chronic systemic disease: clinical challenges and novel innovations. Lancet 2021; 397(10276): 839–852
21. Shipman PL. Why is human childbirth so painful? American Scientist 2013; 101(6): 426
22. Smith CA, Collins CT, Levett KM, Armour M, Dahlen HG, Tan AL, Mesgarpour B. Acupuncture or acupressure for pain management during labour. Cochrane Database Syst Rev 2020; 2(2): CD009232
23. Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 177: obstetric analgesia and anesthesia. Obstet Gynecol 2017; 129(4): e73–e89
24. Bucstain C, Garmi G, Zafran N, Zuarez-Easton S, Carmeli J, Salim R. Risk factors and peripartum outcomes of failed epidural: a prospective cohort study. Arch Gynecol Obstet 2017; 295(5): 1119–1125
25. Armour M, Dahlen HG, Zhu X, Farquhar C, Smith CA. The role of treatment timing and mode of stimulation in the treatment of primary dysmenorrhea with acupuncture: an exploratory randomised controlled trial. PLoS One 2017; 12(7): e0180177
26. Ma YX, Ye XN, Liu CZ, Cai PY, Li ZF, Du DQ, Guo G, Chen SZ, Zhao JP, Liu JJ, Yi HQ, Gao SZ. A clinical trial of acupuncture about time-varying treatment and points selection in primary dysmenorrhea. J Ethnopharmacol 2013; 148(2): 498–504
27. Wade C, Wang L, Zhao WJ, Cardini F, Kronenberg F, Gui SQ, Ying Z, Zhao NQ, Chao MT, Yu J. Acupuncture point injection treatment of primary dysmenorrhoea: a randomised, double blind, controlled study. BMJ Open 2016; 6(1): e008166
28. Li PS, Peng XM, Niu XX, Xu L, Hung Yu Ng E, Wang CC, Dai JF, Lu J, Liang RN. Efficacy of acupuncture for endometriosis-associated pain: a multicenter randomized single-blind placebo-controlled trial. Fertil Steril 2023; 119(5): 815–823
29. Armour M, Cave AE, Schabrun SM, Steiner GZ, Zhu X, Song J, Abbott J, Smith CA. Manual acupuncture plus usual care versus usual care alone in the treatment of endometriosis-related chronic pelvic pain: a randomized controlled feasibility study. J Altern Complement Med 2021; 27(10): 841–849
30. Jin Y, Yu X, Hu S, Liu L, Wang B, Feng Y, Li Y, Xiong B, Wang L. Efficacy of electroacupuncture combined with intravenous patient-controlled analgesia after cesarean delivery: a randomized clinical trial. Am J Obstet Gynecol MFM 2023; 5(2): 100826
31. Usichenko TI, Henkel BJ, Klausenitz C, Hesse T, Pierdant G, Cummings M, Hahnenkamp K. Effectiveness of acupuncture for pain control after cesarean delivery: a randomized clinical trial. JAMA Netw Open 2022; 5(2): e220517
32. Wu L, Zhao H, Zhang Z, Huang M, Wu S, Fang C, Wang R, Li S, Yi W, Zhou A. Combined spinal-epidural anesthesia with acupoint injection for labor anesthesia reduces IL-1β/IL-10 ratio in maternal peripheral blood, umbilical cord blood and improves the labor outcomes: a prospective randomized controlled trial. Clin Immunol 2022; 236: 108935
33. Bishop KC, Ford AC, Kuller JA, Dotters-Katz S. Acupuncture in obstetrics and gynecology. Obstet Gynecol Surv 2019; 74(4): 241–251
34. Kho KA, Shields JK. Diagnosis and management of primary dysmenorrhea. JAMA 2020; 323(3): 268–269
35. Horne AW, Missmer SA. Pathophysiology, diagnosis, and management of endometriosis. BMJ 2022; 379: e070750
36. Lee JH, Jang KJ, Lee YT, Choi YH, Choi BT. Electroacupuncture inhibits inflammatory edema and hyperalgesia through regulation of cyclooxygenase synthesis in both peripheral and central nociceptive sites. Am J Chin Med 2006; 34(6): 981–988
37. Liu S, Wang Z, Su Y, Qi L, Yang W, Fu M, Jing X, Wang Y, Ma Q. A neuroanatomical basis for electroacupuncture to drive the vagal-adrenal axis. Nature 2021; 598(7882): 641–645
38. Mingfu L, Xiaotong D, Xiaojing S, Jin J, Jinling Z, Ying H. Study on the dynamic compound structure composed of mast cells, blood vessels, and nerves in rat acupoint. Evid Based Complement Alternat Med 2013; 2013: 160651
39. Li Y, Yu Y, Liu Y, Yao W. Mast cells and acupuncture analgesia. Cells 2022; 11(5): 860
40. Boadas-Vaello P, Castany S, Homs J, Álvarez-Pérez B, Deulofeu M, Verdú E. Neuroplasticity of ascending and descending pathways after somatosensory system injury: reviewing knowledge to identify neuropathic pain therapeutic targets. Spinal Cord 2016; 54(5): 330–340
41. Hu ML, Zhou FY, Liu JJ, Ding Y, Zhong JM, Ding MX.

Electroacupuncture inhibits the activation of p38MAPK in the central descending facilitatory pathway in rats with inflammatory pain. Evid Based Complement Alternat Med 2017; 2017: 7531060

42. Lyu Z, Guo Y, Gong Y, Fan W, Dou B, Li N, Wang S, Xu Y, Liu Y, Chen B, Guo Y, Xu Z, Lin X. The role of neuroglial crosstalk and synaptic plasticity-mediated central sensitization in acupuncture analgesia. Neural Plast 2021; 2021: 8881557
43. Huang T, Yang L, Jia S, Mu X, Wu M, Ye H, Liu W, Cheng X. Capillary blood flow in patients with dysmenorrhea treated with acupuncture. J Tradit Chin Med 2013; 33(6): 757–760
44. Ma YX, Ma LX, Liu XL, Ma YX, Lv K, Wang D, Liu JP, Xing JM, Cao HJ, Gao SZ, Zhu J. A comparative study on the immediate effects of electroacupuncture at Sanyinjiao (SP6), Xuanzhong (GB39) and a non-meridian point, on menstrual pain and uterine arterial blood flow, in primary dysmenorrhea patients. Pain Med 2010; 11(10): 1564–1575
45. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. Cochrane Database Syst Rev 2018; 5: CD000331
46. Wang JJ, Yang FG, Tsai CC, Chao AS. The neural basis of pain during labor. Am J Obstet Gynecol 2023; 228(5 5S): S1241–S1245
47. Wang W, Sung N, Gilman-Sachs A, Kwak-Kim J. T helper (Th) cell profiles in pregnancy and recurrent pregnancy losses: Th1/Th2/Th9/Th17/Th22/Tfh Cells. Front Immunol 2020; 11: 2025
48. Yu WY, Ma LX, Tian Y, Mu JD, Zhang Z, Sun TY, Qian X, Wang JX. Acupuncture alleviates menstrual pain in rat model via suppressing eotaxin/CCR3 axis to weak EOS-MC activation. Evid Based Complement Alternat Med 2022; 2022: 4571981
49. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nat Rev Endocrinol 2018; 14(5): 270–284
50. Palomba S. Is fertility reduced in ovulatory women with polycystic ovary syndrome? An opinion paper Hum Reprod 2021; 36(9): 2421–2428
51. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JSE, Legro RS, Lizneva D, Natterson-Horowtiz B, Teede HJ, Yildiz BO. Polycystic ovary syndrome. Nat Rev Dis Primers 2016; 2(1): 16057
52. Calcaterra V, Verduci E, Cena H, Magenes VC, Todisco CF, Tenuta E, Gregorio C, De Giuseppe R, Bosetti A, Di Profio E, Zuccotti G. Polycystic ovary syndrome in insulin-resistant adolescents with obesity: the role of nutrition therapy and food supplements as a strategy to protect fertility. Nutrients 2021; 13(6): 1848
53. Jedel E, Labrie F, Odén A, Holm G, Nilsson L, Janson PO, Lind AK, Ohlsson C, Stener-Victorin E. Impact of electro-acupuncture and physical exercise on hyperandrogenism and oligo/amenorrhea in women with polycystic ovary syndrome: a randomized controlled trial. Am J Physiol Endocrinol Metab 2011; 300(1): E37–E45
54. Johansson J, Redman L, Veldhuis PP, Sazonova A, Labrie F, Holm G, Johannsson G, Stener-Victorin E. Acupuncture for ovulation induction in polycystic ovary syndrome: a randomized controlled trial. Am J Physiol Endocrinol Metab 2013; 304(9): E934–E943
55. Wu XK, Stener-Victorin E, Kuang HY, Ma HL, Gao JS, Xie LZ, Hou LH, Hu ZX, Shao XG, Ge J, Zhang JF, Xue HY, Xu XF, Liang RN, Ma HX, Yang HW, Li WL, Huang DM, Sun Y, Hao CF, Du SM, Yang ZW, Wang X, Yan Y, Chen XH, Fu P, Ding CF, Gao YQ, Zhou ZM, Wang CC, Wu TX, Liu JP, Ng EHY, Legro RS, Zhang H; PCOSAct Study Group. Effect of acupuncture and clomiphene in Chinese women with polycystic ovary syndrome: a randomized clinical trial. JAMA 2017; 317(24): 2502–2514
56. Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, Christman GM, Huang H, Yan Q, Alvero R, Haisenleder DJ, Barnhart KT, Bates GW, Usadi R, Lucidi S, Baker V, Trussell JC, Krawetz SA, Snyder P, Ohl D, Santoro N, Eisenberg E, Zhang H; NICHD Reproductive Medicine Network. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med 2014; 371(2): 119–129
57. Legro RS, Barnhart HX, Schlaff WD, Carr BR, Diamond MP, Carson SA, Steinkampf MP, Coutifaris C, McGovern PG, Cataldo NA, Gosman GG, Nestler JE, Giudice LC, Leppert PC, Myers ER; Cooperative Multicenter Reproductive Medicine Network. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med 2007; 356(6): 551–566
58. Chen X, Lan Y, Yang L, Liu Y, Li H, Zhu X, Zhao Y, Long C, Wang M, Xie Q, Li Z, Wu J. Acupuncture combined with metformin versus metformin alone to improve pregnancy rate in polycystic ovary syndrome: a systematic review and meta-analysis. Front Endocrinol (Lausanne) 2022; 13: 978280
59. Dong HX, Wang Q, Wang Z, Wu XK, Cheng L, Zhou ZM, Yang L, Yi P, Huang DM. Impact of low frequency electro-acupuncture on glucose and lipid metabolism in unmarried PCOS women: a randomized controlled trial. Chin J Integr Med 2021; 27(10): 737–743
60. Wang Z, Dong H, Wang Q, Zhang L, Wu X, Zhou Z, Yang L, Huang D. Effects of electroacupuncture on anxiety and depression in unmarried patients with polycystic ovarian syndrome: secondary analysis of a pilot randomised controlled trial. Acupunct Med 2019; 37(1): 40–46
61. Stener-Victorin E, Holm G, Janson PO, Gustafson D, Waern M. Acupuncture and physical exercise for affective symptoms and health-related quality of life in polycystic ovary syndrome: secondary analysis from a randomized controlled trial. BMC Complement Altern Med 2013; 13(1): 131
62. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, Janssen OE, Legro RS, Norman RJ, Taylor AE, Witchel SF; Task Force on the Phenotype of the Polycystic Ovary Syndrome of The Androgen Excess and PCOS Society. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril 2009; 91(2): 456–488
63. Stener-Victorin E, Deng Q. Epigenetic inheritance of polycystic ovary syndrome—challenges and opportunities for treatment. Nat Rev Endocrinol 2021; 17(9): 521–533
64. Stener-Victorin E, Maliqueo M, Soligo M, Protto V, Manni L, Jerlhag E, Kokosar M, Sazonova A, Behre CJ, Lind M, Ohlsson C, Højlund K, Benrick A. Changes in HbA_{1c} and circulating and adipose tissue androgen levels in overweight-obese women with polycystic ovary syndrome in response to electroacupuncture. Obes Sci Pract 2016; 2(4): 426–435

65. Xu G, Zhang A, Liu J, Wang X, Feng J, Chen Y. Effects of electroacupuncture on ovarian expression of the androgen receptor and connexin 43 in rats with letrozole-induced polycystic ovaries. Evid Based Complement Alternat Med 2020; 2020: 3608062
66. Sun J, Jin C, Wu H, Zhao J, Cui Y, Liu H, Wu L, Shi Y, Zhu B. Effects of electro-acupuncture on ovarian P450arom, P450c17α and mRNA expression induced by letrozole in PCOS rats. PLoS One 2013; 8(11): e79382
67. Feng Y, Johansson J, Shao R, Mannerås-Holm L, Billig H, Stener-Victorin E. Electrical and manual acupuncture stimulation affect oestrous cyclicity and neuroendocrine function in an 5α-dihydrotestosterone-induced rat polycystic ovary syndrome model. Exp Physiol 2012; 97(5): 651–662
68. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev 2012; 33(6): 981–1030
69. Dunaif A, Segal KR, Shelley DR, Green G, Dobrjansky A, Licholai T. Evidence for distinctive and intrinsic defects in insulin action in polycystic ovary syndrome. Diabetes 1992; 41(10): 1257–1266
70. Kokosar M, Benrick A, Perfilyev A, Nilsson E, Källman T, Ohlsson C, Ling C, Stener-Victorin E. A single bout of electroacupuncture remodels epigenetic and transcriptional changes in adipose tissue in polycystic ovary syndrome. Sci Rep 2018; 8(1): 1878
71. Benrick A, Kokosar M, Hu M, Larsson M, Maliqueo M, Marcondes RR, Soligo M, Protto V, Jerlhag E, Sazonova A, Behre CJ, Højlund K, Thorén P, Stener-Victorin E. Autonomic nervous system activation mediates the increase in whole-body glucose uptake in response to electroacupuncture. FASEB J 2017; 31(8): 3288–3297
72. Benrick A, Pillon NJ, Nilsson E, Lindgren E, Krook A, Ling C, Stener-Victorin E. Electroacupuncture mimics exercise-induced changes in skeletal muscle gene expression in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2020; 105(6): 2027–2041
73. Wu J, Chen X. Acupuncture therapy protects PCOS patients with diabetes by regulating miR-32-3p/PLA2G4A pathway. Am J Transl Res 2021; 13(8): 8819–8832
74. Zhang F, Ma T, Tong X, Liu Y, Cui P, Xu X, Shi J, Hu W, Lu W, Pei Z, Xu M, Li X, Xu C, Feng Y. Electroacupuncture improves metabolic and ovarian function in a rat model of polycystic ovary syndrome by decreasing white adipose tissue, increasing brown adipose tissue, and modulating the gut microbiota. Acupunct Med 2022; 40(4): 347–359
75. Zhang HL, Huo ZJ, Wang HN, Wang W, Chang CQ, Shi L, Li D, Li R, Qiao J. Acupuncture ameliorates negative emotion in PCOS patients: a randomized controlled trial. Chin Acupunct Moxibustion (Zhongguo Zhen Jiu) 2020; 40(4): 385–390 (in Chinese)
76. Chaudhari N, Dawalbhakta M, Nampoothiri L. GnRH dysregulation in polycystic ovarian syndrome (PCOS) is a manifestation of an altered neurotransmitter profile. Reprod Biol Endocrinol 2018; 16(1): 37
77. Busnelli A, Reschini M, Cardellicchio L, Vegetti W, Somigliana E, Vercellini P. How common is real repeated implantation failure? An indirect estimate of the prevalence. Reprod Biomed Online 2020; 40(1): 91–97
78. Hong YL, Tan Y, Yin YY, Zou YJ, Guo YH, Nie XW. Effect of electro-acupuncture on clinical outcomes and ovarian hyperstimulation syndrome in *in vitro* fertilization and embryo transplantation. Chin J Integr Tradit West Med (Zhongguo Zhong Xi Yi Jie He Za Zhi) 2014; 34(11): 1292–1296 (in Chinese)
79. Wang RR, Su MH, Liu LY, Lai YY, Guo XL, Gan D, Zheng XY, Yang H, Yu SY, Liang FR, Wei W, Zhong Y, Yang J. Systematic review of acupuncture to improve ovarian function in women with poor ovarian response. Front Endocrinol (Lausanne) 2023; 14: 1028853
80. Liu X, Shi W, Liu Z, Shi S, Ke C, Zhang P, Tan Z, Zhang W. Effects of acupuncture on luteinized unruptured follicle syndrome: a meta-analysis of randomized controlled trials. Complement Ther Med 2020; 49: 102319
81. Stener-Victorin E, Waldenström U, Nilsson L, Wikland M, Janson PO. A prospective randomized study of electro-acupuncture versus alfentanil as anaesthesia during oocyte aspiration in *in-vitro* fertilization. Hum Reprod 1999; 14(10): 2480–2484
82. Stener-Victorin E. The pain-relieving effect of electro-acupuncture and conventional medical analgesic methods during oocyte retrieval: a systematic review of randomized controlled trials. Hum Reprod 2005; 20(2): 339–349
83. Humaidan P, Brock K, Bungum L, Stener-Victorin E. Pain relief during oocyte retrieval—exploring the role of different frequencies of electro-acupuncture. Reprod Biomed Online 2006; 13(1): 120–125
84. Smith CA, de Lacey S, Chapman M, Ratcliffe J, Norman RJ, Johnson NP, Boothroyd C, Fahey P. Effect of acupuncture vs sham acupuncture on live births among women undergoing *in vitro* fertilization: a randomized clinical trial. JAMA 2018; 319(19): 1990–1998
85. Feng X, Zhu N, Yang S, Wang L, Sun W, Li R, Gong F, Han S, Zhang R, Han J. Transcutaneous electrical acupoint stimulation improves endometrial receptivity resulting in improved IVF-ET pregnancy outcomes in older women: a multicenter, randomized, controlled clinical trial. Reprod Biol Endocrinol 2022; 20(1): 127
86. Zhu C, Xia W, Huang J, Zhang X, Li F, Yu X, Ma J, Zeng Q. Effects of acupuncture on the pregnancy outcomes of frozen-thawed embryo transfer: a systematic review and meta-analysis. Front Public Health 2022; 10: 987276
87. Ramezanzadeh F, Aghssa MM, Abedinia N, Zayeri F, Khanafshar N, Shariat M, Jafarabadi M. A survey of relationship between anxiety, depression and duration of infertility. BMC Womens Health 2004; 4(1): 9
88. Domar AD, Meshay I, Kelliher J, Alper M, Powers RD. The impact of acupuncture on *in vitro* fertilization outcome. Fertil Steril 2009; 91(3): 723–726
89. Smith CA, de Lacey S, Chapman M, Ratcliffe J, Norman RJ, Johnson NP, Fahey P. The effects of acupuncture on the secondary outcomes of anxiety and quality of life for women undergoing IVF: a randomized controlled trial. Acta Obstet Gynecol Scand 2019; 98(4): 460–469
90. Smith C, Coyle M, Norman RJ. Influence of acupuncture stimulation on pregnancy rates for women undergoing embryo transfer. Fertil Steril 2006; 85(5): 1352–1358
91. Zhu F, Zhao B, Wu J, Yin S, Ma T, Li Z, Zhu X, Wang T, Yang

B, Che D. Effect of transcutaneous electrical acupoint stimulation on pregnancy outcomes in women with *in vitro* fertilization-embryo transfer: a systematic review and meta-analysis. Front Cell Dev Biol 2022; 10: 1068894
92. Yang H, Hu WH, Xu GX, Yin ZH, Yu SY, Liu JJ, Xiao ZY, Zheng XY, Yang J, Liang FR. Transcutaneous electrical acupoint stimulation for pregnancy outcomes in women undergoing *in vitro* fertilization-embryo transfer: a systematic review and meta-analysis. Front Public Health 2022; 10: 892973
93. You F, Du X, Zhang T, Wang Y, Lv Y, Zeng L. High-frequency electroacupuncture improves endometrial receptivity via regulating cell adhesion molecules and leukemia inhibitory factor/signal transducer and activator of transcription signaling pathway. Bioengineered 2021; 12(2): 10470–10479
94. Dong H, Zhong Z, Chen W, Wu X, Zhang Q, Huang G, Yang W. Effect of acupuncture on endometrial angiogenesis and uterus dendritic cells in COH rats during peri-implantation period. Evid Based Complement Alternat Med 2017; 2017: 3647080
95. Chen W, Chen J, Xu M, Zhong Z, Zhang Q, Yang W, Huang G. Electroacupuncture facilitates implantation by enhancing endometrial angiogenesis in a rat model of ovarian hyperstimulation. Biol Reprod 2019; 100(1): 268–280
96. Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. Trends Neurosci 2003; 26(1): 17–22
97. Andersson S, Lundeberg T. Acupuncture—from empiricism to science: functional background to acupuncture effects in pain and disease. Med Hypotheses 1995; 45:
98. Jiang YL, Yin XH, Shen YF, He XF, Fang JQ. Low frequency electroacupuncture alleviated spinal nerve ligation induced mechanical allodynia by inhibiting TRPV1 upregulation in ipsilateral undamaged dorsal root ganglia in rats. Evid Based Complement Alternat Med 2013; 2013: 170910
99. Xu GY, Li G, Liu N, Huang LYM. Mechanisms underlying purinergic P2X3 receptor-mediated mechanical allodynia induced in diabetic rats. Mol Pain 2011; 7: 60
100. Tang NM, Dong HW, Wang XM, Tsui ZC, Han JS. Cholecystokinin antisense RNA increases the analgesic effect induced by electroacupuncture or low dose morphine: conversion of low responder rats into high responders. Pain 1997; 71(1): 71–80
101. White PF, Craig WF, Vakharia AS, Ghoname E, Ahmed HE, Hamza MA. Percutaneous neuromodulation therapy: does the location of electrical stimulation effect the acute analgesic response? Anesth Analg 2000; 91(4): 949–954
102. Ghoname ES, Craig WF, White PF, Ahmed HE, Hamza MA, Gajraj NM, Vakharia AS, Noe CE. The effect of stimulus frequency on the analgesic response to percutaneous electrical nerve stimulation in patients with chronic low back pain. Anesth Analg 1999; 88(4): 841–846
103. Ho M, Huang LC, Chang YY, Chen HY, Chang WC, Yang TC, Tsai HD. Electroacupuncture reduces uterine artery blood flow impedance in infertile women. Taiwan J Obstet Gynecol 2009; 48(2): 148–151
104. Chang R, Chung PH, Rosenwaks Z. Role of acupuncture in the treatment of female infertility. Fertil Steril 2002; 78(6): 1149–1153
105. Stener-Victorin E, Waldenström U, Andersson SA, Wikland M. Reduction of blood flow impedance in the uterine arteries of infertile women with electro-acupuncture. Hum Reprod 1996; 11(6): 1314–1317
106. Kim J, Shin KH, Na CS. Effect of acupuncture treatment on uterine motility and cyclooxygenase-2 expression in pregnant rats. Gynecol Obstet Invest 2000; 50(4): 225–230
107. Han JS, Chen XH, Sun SL, Xu XJ, Yuan Y, Yan SC, Hao JX, Terenius L. Effect of low- and high-frequency TENS on Met-enkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF. Pain 1991; 47(3): 295–298
108. Han JS, Terenius L. Neurochemical basis of acupuncture analgesia. Annu Rev Pharmacol Toxicol 1982; 22(1): 193–220
109. Niebyl JR. Clinical practice. Nausea and vomiting in pregnancy. N Engl J Med 2010; 363(16): 1544–1550
110. Jarvis S, Nelson-Piercy C. Management of nausea and vomiting in pregnancy. BMJ 2011; 342(jun17 1): d3606
111. Carlsson CP, Axemo P, Bodin A, Carstensen H, Ehrenroth B, Madegård-Lind I, Navander C. Manual acupuncture reduces hyperemesis gravidarum: a placebo-controlled, randomized, single-blind, crossover study. J Pain Symptom Manage 2000; 20(4): 273–279
112. Smith C, Crowther C, Beilby J. Acupuncture to treat nausea and vomiting in early pregnancy: a randomized controlled trial. Birth 2002; 29(1): 1–9
113. Tara F, Bahrami-Taghanaki H, Amini Ghalandarabad M, Zand-Kargar Z, Azizi H, Esmaily H, Azizi H. The effect of acupressure on the severity of nausea, vomiting, and retching in pregnant women: a randomized controlled trial. Complement Med Res 2020; 27(4): 252–259
114. Jamigorn M, Phupong V. Acupressure and vitamin B6 to relieve nausea and vomiting in pregnancy: a randomized study. Arch Gynecol Obstet 2007; 276(3): 245–249
115. Negarandeh R, Eghbali M, Janani L, Dastaran F, Saatchi K. Auriculotherapy as a means of managing nausea and vomiting in pregnancy: a double-blind randomized controlled clinical trial. Complement Ther Clin Pract 2020; 40: 101177
116. McParlin C, O'Donnell A, Robson SC, Beyer F, Moloney E, Bryant A, Bradley J, Muirhead CR, Nelson-Piercy C, Newbury-Birch D, Norman J, Shaw C, Simpson E, Swallow B, Yates L, Vale L. Treatments for hyperemesis gravidarum and nausea and vomiting in pregnancy: a systematic review. JAMA 2016; 316(13): 1392–1401
117. Roscoe JA, Matteson SE. Acupressure and acustimulation bands for control of nausea: a brief review. Am J Obstet Gynecol 2002; 186(5 Suppl 2): S244–S247
118. Wu XK, Gao JS, Ma HL, Wang Y, Zhang B, Liu ZL, Li J, Cong J, Qin HC, Yang XM, Wu Q, Chen XY, Lu ZL, Feng YH, Qi X, Wang YX, Yu L, Cui YM, An CM, Zhou LL, Hu YH, Li L, Cao YJ, Yan Y, Liu L, Liu YX, Liu ZS, Painter RC, Ng EHY, Liu JP, Mol BWJ, Wang CC. Acupuncture and doxylamine-pyridoxine for nausea and vomiting in pregnancy : a randomized, controlled, 2 × 2 factorial trial. Ann Intern Med 2023; 176(7): 922–933
119. Tan MY, Shu SH, Liu RL, Zhao Q. The efficacy and safety of complementary and alternative medicine in the treatment of nausea and vomiting during pregnancy: a systematic review and meta-analysis. Front Public Health 2023; 11: 1108756
120. Sato A, Sato Y, Suzuki A, Uchida S. Neural mechanisms of the reflex inhibition and excitation of gastric motility elicited by

acupuncture-like stimulation in anesthetized rats. Neurosci Res 1993; 18(1): 53–62
121. Li Y, Tougas G, Chiverton SG, Hunt RH. The effect of acupuncture on gastrointestinal function and disorders. Am J Gastroenterol 1992; 87(10): 1372–1381
122. Lu H, Zheng C, Zhong Y, Cheng L, Zhou Y. Effectiveness of acupuncture in the treatment of hyperemesis gravidarum: a systematic review and meta-analysis. Evid Based Complement Alternat Med 2021; 2021: 2731446
123. Lu MJ, Yu Z, He Y, Yin Y, Xu B. Electroacupuncture at ST36 modulates gastric motility via vagovagal and sympathetic reflexes in rats. World J Gastroenterol 2019; 25(19): 2315–2326
124. Su YS, He W, Wang C, Shi H, Zhao YF, Xin JJ, Wang XY, Shang HY, Hu L, Jing XH, Zhu B. "Intensity-response" effects of electroacupuncture on gastric motility and its underlying peripheral neural mechanism. Evid Based Complement Alternat Med 2013; 2013: 535742
125. Takeshige C, Sato T, Mera T, Hisamitsu T, Fang J. Descending pain inhibitory system involved in acupuncture analgesia. Brain Res Bull 1992; 29(5): 617–634
126. Zou D, Chen WH, Iwakiri K, Rigda R, Tippett M, Holloway RH. Inhibition of transient lower esophageal sphincter relaxations by electrical acupoint stimulation. Am J Physiol Gastrointest Liver Physiol 2005; 289(2): G197–G201
127. Nutaitis AC, Meckes NA, Madsen AM, Toal CT, Menhaji K, Carter-Brooks CM, Propst KA, Hickman LC. Postpartum urinary retention: an expert review. Am J Obstet Gynecol 2023; 228(1): 14–21
128. Lauterbach R, Ferrer Sokolovski C, Rozenberg J, Weissman A. Acupuncture for the treatment of post-partum urinary retention. Eur J Obstet Gynecol Reprod Biol 2018; 223: 35–38
129. Zhu Y, Wang F, Zhou J, Gu S, Gong L, Lin Y, Hu X, Wang W, Zhang A, Ma D, Hu C, Wu Y, Guo L, Chen L, Cen L, He Y, Cai Y, Wang E, Chen H, Jin J, Huang J, Jin M, Sun X, Ye X, Jiang L, Zhang Y, Zhang J, Lin J, Zhang C, Shen G, Jiang W, Zhong L, Zhou Y, Wu R, Lu S, Feng L, Guo H, Lin S, Chen Q, Kong J, Yang X, Tang M, Liu C, Wang F, Hu XM, Lee HW, Xu X, Zhang R, Robinson N, Lee MS, Han J, Qu F. Effect of acupoint hot compress on postpartum urinary retention after vaginal delivery: a randomized clinical trial. JAMA Netw Open 2022; 5(5): e2213261
130. Li D, Wu X, Xiao S. Study on the regularity of acupoint selection for acupuncture treatment of postpartum urinary retention. Guiding J Tradit Chin Med Pharm (Zhong Yi Yao Dao Bao) 2021; 27: 151–154, 159 (in Chinese)
131. Perú Biurrun G, Gonzalez-Díaz E, Fernández Fernández C, Fernández Corona A. Post partum urinary retention and related risk factors. Urology 2020; 143: 97–102
132. Chen PD, Yang ZX, Zhou C, Wu QX, Liu F, Ning Y. Clinical research thinking of acupuncture and moxibustion intervention on postpartum urinary retention. West J Tradit Chin Med (Xi Bu Zhong Yi Yao) 2019; 32(9): 38–40 (in Chinese)
133. Zhang YJ. Clinical research progress of acupuncture in treating postpartum urinary retention. Shanghai J Acupunct Moxibustion (Shanghai Zhen Jiu Za Zhi) 2011; 30: 504–507 (in Chinese)
134. Zhang JP, Wang YQ, Yan MQ, Li ZA, Du XP, Wu XQ. Menopausal symptoms and sleep quality during menopausal transition and postmenopause. Chin Med J (Engl) 2016; 129(7): 771–777
135. Crandall CJ, Mehta JM, Manson JE. Management of menopausal symptoms: a review. JAMA 2023; 329(5): 405–420
136. Tang SS, Yin XJ, Yu W, Cui L, Li ZX, Cui LJ, Wang LH, Xia W. Prevalence of osteoporosis and related factors in postmenopausal women aged 40 and above in China. Chin J Epidemiol (Zhonghua Liu Xing Bing Xue Za Zhi) 2022; 43(4): 509–516 (in Chinese)
137. Farquhar C, Marjoribanks J, Lethaby A, Suckling JA, Lamberts Q. Long term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev 2009; (2), CD004143
138. Flores VA, Pal L, Manson JE. Hormone therapy in menopause: concepts, controversies, and approach to treatment. Endocr Rev 2021; 42(6): 720–752
139. Pan M, Pan X, Zhou J, Wang J, Qi Q, Wang L. Update on hormone therapy for the management of postmenopausal women. Biosci Trends 2022; 16(1): 46–57
140. Avis NE, Coeytaux RR, Isom S, Prevette K, Morgan T. Acupuncture in Menopause (AIM) study: a pragmatic, randomized controlled trial. Menopause 2016; 23(6): 626–637
141. Nedeljkovic M, Tian L, Ji P, Déglon-Fischer A, Stute P, Ocon E, Birkhäuser M, Ausfeld-Hafter B. Effects of acupuncture and Chinese herbal medicine (Zhi Mu 14) on hot flushes and quality of life in postmenopausal women: results of a four-arm randomized controlled pilot trial. Menopause 2014; 21(1): 15–24
142. Lund KS, Siersma V, Brodersen J, Waldorff FB. Efficacy of a standardised acupuncture approach for women with bothersome menopausal symptoms: a pragmatic randomised study in primary care (the ACOM study). BMJ Open 2019; 9(1): e023637
143. Fu C, Zhao N, Liu Z, Yuan LH, Xie C, Yang WJ, Yu XT, Yu H, Chen YF. Acupuncture improves peri-menopausal insomnia: a randomized controlled trial. Sleep 2017; 40(11):
144. Di YM, Yang L, Shergis JL, Zhang AL, Li Y, Guo X, Xue CC, Lu C. Clinical evidence of Chinese medicine therapies for depression in women during perimenopause and menopause. Complement Ther Med 2019; 47: 102071
145. Liu Z, Ai Y, Wang W, Zhou K, He L, Dong G, Fang J, Fu W, Su T, Wang J, Wang R, Yang J, Yue Z, Zang Z, Zhang W, Zhou Z, Xu H, Wang Y, Liu Y, Zhou J, Yang L, Yan S, Wu J, Liu J, Liu B. Acupuncture for symptoms in menopause transition: a randomized controlled trial. Am J Obstet Gynecol 2018; 219(4): 373.e1–373.e10
146. Hassan ES, Maged AM, Kotb A, Fouad M, El-Nassery N, Kamal WM. Effect of laser acupuncture on pain and density of bone in osteoporotic postmenopausal women: a randomized controlled trial. Menopause 2023; 30(5): 545–550
147. Huang WY, Hsin IL, Chen DR, Chang CC, Kor CT, Chen TY, Wu HM. Circulating interleukin-8 and tumor necrosis factor-α are associated with hot flashes in healthy postmenopausal women. PLoS One 2017; 12(8): e0184011
148. Xu Y, Hong S, Zhao X, Wang S, Xu Z, Ding S, Zhang K, Zhang Y, Xu L, Yu N, Zhao T, Yan Y, Yang F, Liu Y, Yu K, Liu B, Guo Y, Pang G. Acupuncture alleviates rheumatoid arthritis by immune-network modulation. Am J Chin Med 2018; 46(5): 997–1019
149. Li X, Wu K, Dong Q, Chen H, Li C, Ren Z, Liu F, Yue X, Xia C, Wang Y, Luo Y, Li L, Zhao R, Wang Z, Qin D. Overall adjustment acupuncture improves osteoporosis and exerts an

endocrine-modulating effect in ovariectomized rats. Front Endocrinol (Lausanne) 2022; 13: 1074516

150. Zheng X, Wu G, Nie Y, Lin Y. Electroacupuncture at the governor vessel and bladder meridian acupoints improves postmenopausal osteoporosis through osteoprotegerin/RANKL/RANK and Wnt/β-catenin signaling pathways. Exp Ther Med 2015; 10(2): 541–548
151. Fan H, Ji F, Lin Y, Zhang M, Qin W, Zhou Q, Wu Q. Electroacupuncture stimulation at CV4 prevents ovariectomy-induced osteoporosis in rats via Wnt-β-catenin signaling. Mol Med Rep 2016; 13(3): 2485–2491
152. Zheng X, Nie Y, Sun C, Wu G, Cai Q, Huang S, Lin Y. Long-term electroacupuncture stimulation prevents osteoporosis in ovariectomised osteopaenic rats through multiple signalling pathways. Acupunct Med 2018; 36(3): 176–182
153. Priebe T, Stumpf SH, Zalunardo R. Can a science-based definition of acupuncture improve clinical outcomes? J Integr Med 2017; 15(3): 165–171
154. No authors listed. Acupuncture. NIH Consens Statement 1997; 15(5): 1–34