Acupuncture-Related Therapies for Ovulatory Disorders: A Systematic Review and Bayesian Network Meta-Analysis Protocol

Hang Zhou

Chengdu University of Traditional Chinese Medicine

Li Yan

Chengdu University of Traditional Chinese Medicine Affiliated Hospital

Yi Yang

Chengdu University of Traditional Chinese Medicine Affiliated Hospital

ShuGuang Zhang

Chengdu University of Traditional Chinese Medicine Affiliated Hospital

XiaoYan Zheng

Chengdu University of Traditional Chinese Medicine

Huan Wang

Sichuan college of Traditional Chinese Medicine

LinWen Deng (✉ dlwen1982@163.com)

Hospital of Chengdu University of Traditional Chinese Medicine

Protocol

Keywords: Acupuncture and moxibustion therapy, Ovulation disorders, Network Meta-Analysis (NMA)

Posted Date: December 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1172347/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background Ovulation disorders (ODs) are major cause of infertility. Many clinical studies have shown that acupuncture is potentially useful in the treatment of ODs. In this context, the present study aims to evaluate the effectiveness and safety of different acupuncture therapies through systematic review and Bayesian network meta-analysis (NMA).

Methods A comprehensive literature search until June 2021 will be carried out in the following databases: PubMed/MEDLINE, Cochrane Library, Science Net, EBSCO, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang database, VIP database, and China biomedical database (CBM). Randomized controlled trials (RCTs) meeting the eligibility criteria based on PICO elements will be included. The main outcomes will be ovulation rate, pregnancy rate and changes in female reproductive hormones. The secondary outcome will be the prevalence of adverse events directly related to acupuncture. Cochrane bias risk assessment tool (RoB 2.0) will be used to evaluate the quality of the selected literature. Stata, Aggregate Data Drug Information System (ADDIS) and BUGS will be used to manage the data.

Discussion: The results of this study can provide evidence to the effectiveness and safety of acupuncture therapy for ODs. However, large-scale, case-control studies with rigorous designs are required to provide even more accurate evidence.

Systematic review registration: This agreement has been registered in INPLASY <https://inplasy.com/>, the registration ID is INPLASY202160078.

Background

Normal ovulation requires the proper function of the hypothalamus-pituitary-gonadal axis [1]. Any organic lesion or function of this axis can cause temporary or long-term ovarian dysfunction, leading to abnormal ovulation. Ovulation disorders (ODs) have multiple causes including abnormalities of the central nervous system [2], hypothalamus [3], pituitary and ovaries, polycystic ovary syndrome [4,5,6], luteinized unruptured follicle syndrome [7]. Additionally, disorders affecting other endocrine systems, such as thyroid and adrenal cortex dysfunction as well as selected systemic diseases (e.g, severe malnutrition), can affect ovarian function and lead to ovulation dysfunction. Acupuncture is a traditional medical treatment in China. Several studies have shown that acupuncture treatment of ODs has a significant, long-lasting beneficial effects [8,9] and that the adverse reactions are limited [10,11,12,13]. However, other studies questioned that the effectiveness of acupuncture in this setting remains to be demonstrated [14] and that the quality of evidence-based clinical observations is low.

Currently it is not possible to recommend the clinical use of acupuncture in the treatment of ovulatory disorders. Nor it is possible to recommend the best treatment scheme. This is due to several reasons: the variety of acupuncture-related therapies, the different emphasis on efficacy, the inconsistent conclusions of the studies and the lack of direct comparisons between different acupuncture-related therapies.

Therefore, in addition to the conventional meta-analysis method, the present study uses the network meta-analysis method to compare the efficacy of a variety of acupuncture related methods on ovulation rate, pregnancy rate and changes in reproductive hormones of patients with ovulation disorders. The aim of this study is to provide evidence-based medicine for a clinical selection of the best acupuncture related treatment scheme to improve several reproductive indicators in patients with ODs (**Figure 1**).

Network meta-analysis (NMA) [15,16] is a technique suitable for comparing multiple treatments simultaneously in a single analysis. It combines direct and indirect evidence within a network of RCTs by making cross-comparisons. It can also compare the efficacy of at least two interventions by combining data from different trials and by ranking all the included interventions. Therefore, it is also called mixed treatment comparison meta-analysis or multiple treatments meta-analysis. The purpose of this paper is to compare the effects of various acupuncture-related measures on ovulation rate and pregnancy rate of patients with ODs by using the network meta-analysis method, to provide a reference for clinical application (**Figure 2**)

Methods

Eligible criteria

Normative references

The results of this study will be reported following the National Institute for health and care excellence (NICE) network meta-analysis reporting standard.

Research type

Published RCTs of acupuncture-related therapy for ovulation disorders

Research objects

Patients with ODs refer to the disease types published by up-to-date(<https://www.uptodate.com/>) .Combined with World Health Organization (WHO) standards, ODs are divided into four categories(a) WHO I type ovulation disorder: there is hypothalamus or pituitary failure with low level of endogenous estrogen, low level of FSH and LH;(b) WHO II type: normo-gonadotropic, normo-estrogenic anovulation, with possible imbalance in FSH and LH levels, common in patients with polycystic ovary syndrome and hyperprolactinemia;(c) WHO III patients: ovarian failure, FSH and LH levels are increased, estrogen levels are decreased;(d) ODs different from those included in the above categories. Examples are luteinized unruptured follicle syndrome (LUFS). Patients with severe medical conditions were excluded. See **Table 1** for detailed retrieval strategy.

Exclusion criteria

The following are considered not to meet the inclusion criteria: (a) Abstracts, conference papers, dissertations, case reports, animal mechanism studies; (b) Repetitive publications; (c) Publications in which there are no definite diagnostic criteria nor clear criteria to evaluate the efficacy of treatments; (d) Absence of a widely accepted method of randomization; (e) The intervention does not include acupuncture related treatment; (f) Articles that are not available after having requested them to the authors; (i) Articles published belonging to the same study. Refer to **Table 2** for the draft qualification criteria for inclusion and exclusion.

Types of interventions

The treatment group is formed by women treated with all kinds of acupuncture-related therapies, including electroacupuncture, auricular acupuncture, warm acupuncture, auricular point sticking and pressing, moxibustion, acupoint catgut embedding. The control group is formed by women treated with Western medicine or placebo, The frequency of acupoint use and the frequency of intervention measures are counted and displayed by histogram. We show the possible patterns of different intervention methods on the acupuncture points related to ovulation disorders, Using Cytoscape (version 3.8.0) to construct the network framework diagram of "acupuncture-method-acupoint-ODs type" (**Figure3**), and reveal the degree of acupuncture points for different diseases and different acupuncture programs.

Outcome measures

Main outcome measures: Ovulation rate, pregnancy rate and changes in reproductive hormones. Different ODs will be discussed separately.

Secondary indicators The prevalence of adverse events directly related to interventions will be considered as secondary outcome.

Literature retrieval strategy

PubMed, EMBASE, Cochrane Library, CBM, CNKI, Wan Fang, and VIP database will be searched by computer. All the available literature will be searched until June 2021. In addition, the references of the included literature are traced to supplement the relevant literature. The retrieval is carried out by combining subject words with free words.

Literature screening and data extraction

Two researchers will independently screen, extract, and cross-check the literature. In case of disagreement, both parties shall reach an agreement through discussion or a third researcher shall assist

in the exclusion process. Data will be extracted by a unified data extraction table, including title, author, sample size, average age, gender, course of the disease, intervention measures, course of treatment, outcome indicators. The selection process will be performed in the PRISMA flowchart (see checklist in **Additional file 1**), as shown in **Figure 4**.

Bias risk assessment of included studies

Two researchers will evaluate the included studies according to the bias risk assessment tool recommended in Cochrane Handbook 5.1. (a)Random sequence generation; (b)Allocation concealment; (c)Blinding of participants and personnel; (d)Blinding of outcome assessment; (e)Incomplete outcome data; (f)Selective outcome reporting; (g) Assessing risk of bias from other sources. If the two sides do not agree, they will discuss with the third researcher to reach an agreement.

Data analyses

Quality assessment

The included literature will be assessed according to the recommended levels of evaluation development and evaluation (grading) guidelines to assess the quality of evidence. An assessment and grading of the quality of the included literature will be performed according to the recommendations of the guideline (quote). The guidelines classify the quality of evidence as high, medium, and low. The entire study flow is reported in **Figure 5**. Funnel plots and the Egger regression test will be performed to examine potential publish bias. In addition, sensitivity analysis will be carried out by sequentially deleting trials to check the stability of the primary outcomes.

Subgroup analysis

If the relevant studies are sufficient, the following characteristics will be considered for subgroup analysis: (a) RCT studies on the same type of ovulation disorder but with different diseases or causes; (b) RCT studies on different acupuncture intervention methods for the same disease; (c) RCT studies on different acupuncture points for the same treatment method.

Pairwise meta-analysis

The premise of Pairwise Meta-analysis is the law of similarity, which means that the meta-analysis can be carried out only when the included studies meet a certain degree of similarity, we state that no less than 3 studies of the same interventions and outcome indicators can make sense in pairwise meta-analysis. By using Stata 14.0, odds ratio (OR) and 95% confidence interval (CI) will be adopted. I^2 test will

be applied to assess heterogeneity and select a model. A random-effect model will be adopted if $I^2 > 50\%$ while a fixed-effect model will be adopted for I^2 values $\leq 50\%$. Before selecting a model, sensitivity analysis will be performed properly to delete high-heterogeneity studies. Employing Begg's testing, public bias will be estimated by symmetry of the funnel plot if more than 10 pairwise comparison studies are included.

Bayesian analysis

WinBUGS 1.4.3 software is used for statistical analysis. When drawing the evidence network diagram, the test with three arm trials or more is divided into all the double arm trials of all possible combinations [17]. The average effect of all pairing comparisons and the contribution to the whole network are calculated. Next, we make a comparison-correction funnel chart to evaluate whether the included studies have a small sample effect [15]. Inconsistency factors (if) and 95% CI are used to evaluate the consistency of each closed loop. The Markov chain Monte Carlo (MCMC) random effect model will be analyzed through the WinBUGS program, using four chains to simulate and set the number of iterations to 50000 [18]. The area under the cumulative ranking probability graph (Sucra) will be drawn to predict the efficacy ranking of each treatment measure [19].

Ethics and informed consents

Because this is a systematic literature research program, ethical approval can be skipped. At the same time, the agreement has been registered in INPLASY <https://inplasy.com/>. The registration ID is INPLASY202160078.

Patient and Public Involvement

This subject of this study is the second article, and no patients or the public participated in this study.

Strengths and limitations of this study

- This protocol permitted the design of a multi-dimensional network map of research involving acupuncture and moxibustion for the treatment of different ovulation disorders (ODs).
- By applying network analysis and Constructing the network of "acupuncture-methods-acupoints-ODstype", this protocol comprehensively evaluates the efficacy, safety, and best treatment combinations involving needle massage for the treatment of ODs.
- This protocol applied the WHO classification system to classify ODs to provide a research report with contemporary clinical significance. This work provides significant guidance for researchers engaged in acupuncture and evidence-based moxibustion research.

- Due to the global and multilingual aspects of this study, consensus discussion will be limited with only a select number of individuals.

Discussion

ODs are an important cause of infertility [20], with a considerable impact on the psychological health of the women affected as well as on their familial relationships. The wide application of acupuncture and moxibustion in clinical practice led to a rapid expansion of the research on their effects in the treatment of ODs [21, 22, 23, 24]. The therapeutic results of complementary and alternative medicine are promising. Even though the mechanism of action of acupuncture is still uncompleted understood, modern technology has shown that acupuncture can regulate the neuroendocrine-immune system [25], with potential benefit for patients with ODs. However, the clinical application of acupuncture and moxibustion is complex. The increasing knowledge on acupuncture and moxibustion and the development of new instruments make the therapeutic decision difficult, since it has not yet clearly determined which is the best treatment.

It is well known that there are many different diseases causing ovulation disorders and various treatment approaches. Therefore, we divided ODs into four categories according to the World Health Organization (WHO) standards with little modifications. To our knowledge, so far there is only one published systematic review and Bayesian analysis on acupuncture in the treatment of ODs, and it is limited to PCOS [26]. The standardized evaluation of acupuncture treatment of ovulation disorders, including acupoints, treatment time, intervention frequency, and the understanding of different types of diseases still need to be further studied. Therefore, how to develop a reasonable and effective treatment plan is an urgent, still unresolved problem. This is the reason for which we decided to carry out a network meta-analysis. If enough data will be available, we will also perform subgroup analysis. The results of the program will be published in relevant journals and updated quickly when and if needed.

Abbreviations

ODs: Ovulation disorders;

NMA: network meta-analysis

CNKI: China National Knowledge Infrastructure

CBM: China biomedical database

RCT: Randomized controlled trials

ADDIS: Aggregate Data Drug Information System

NICE: National Institute for health and care excellence

WHO: World Health Organization

LUFS: luteinized unruptured follicle syndrome

OR: odds ratio

CI: confidence interval

IF: Inconsistency factors

MCMC: Markov chain Monte Carlo

Declarations

Acknowledgements

The authors would like to express their gratitude to EditSprings (<https://www.editsprings.com/>) for the expert linguistic services provided.

Authors' contributions

ZH participated in the design of the review and drafted the protocol, DLW provided methodological support for the design of the review and contributed in drafting the protocol. YL developed the inclusion criteria. ZSG and WH wrote the first draft of the protocol, YY and ZXY have drafted the work and revised it. All authors contributed to the writing and refining the protocol and will be involved in the review. DLW is the corresponding author. The authors read and approved the final manuscript.

Funding

This study is not supported by any fundings.

Availability of data and materials

Not applicable

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

References

1. Benevides R, Vale CC, Fontelles J, França LM, Teófilo TS, Silva SN, et al. Syzygium cumini (L.) Skeels improves metabolic and ovarian parameters in female obese rats with malfunctioning hypothalamus-pituitary-gonadal axis. *Journal of ovarian research*. 2019;12(1), 13.
<https://doi.org/10.1186/s13048-019-0490-8>
2. Vieyra-Valdez E, Linares-Culebro R, Rosas-Gavilán G, Ramírez-Hernández D, Domínguez-Casalá R, Morales-Ledesma L. Roles of the cholinergic system and vagal innervation in the regulation of GnRH secretion and ovulation: Experimental evidence. *Brain Res Bull*. 2020;165:129-138.
<http://doi.org/10.1016/j.brainresbull.2020.09.009>.
3. Talaulikar V, Yasmin E, WHO type 1 anovulation: an update on diagnosis, management and implications for long-term health. *The Obstetrician & Gynaecologist*. 2020;22(3).doi:10.1111/tog.12665.
4. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, Carmina E, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertility and sterility*. 2012;97(1), 28–38.e25.
<https://doi.org/10.1016/j.fertnstert.2011.09.024>
5. Yang Y, Xia Y, Peng X, Xie J, Liu H, Ni X. Tanshinone for polycystic ovary syndrome: A protocol of systematic review and meta-analysis. *Medicine*. 2021;100(3), e24287.
<https://doi.org/10.1097/MD.00000000000024287>
6. Rosenfield RL, Ehrmann DA. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. *Endocrine reviews*. 2016;37(5), 467–520. <https://doi.org/10.1210/er.2015-1104>
7. Liu X, Shi W, Liu Z, Shi S, Ke C, Zhang P, et al. Effects of acupuncture on Luteinized Unruptured Follicle Syndrome: A meta-analysis of randomized controlled trials. *Complementary therapies in medicine*. 2020;49, 102319. <https://doi.org/10.1016/j.ctim.2020.102319>
8. Gao Y, Xu S, Shen Y, Liao T, Hu S, Zhou S, et al. Metformin and acupuncture for polycystic ovary syndrome: A protocol for a systematic review and meta-analysis. *Medicine*. 2020;99(14), e19683.
<https://doi.org/10.1097/MD.00000000000019683>
9. Yun L, Liqun W, Shuqi Y, Chunxiao W, Liming L, Wei, Y. Acupuncture for infertile women without undergoing assisted reproductive techniques (ART): A systematic review and meta-analysis. *Medicine*. 2019;98(29), e16463. <https://doi.org/10.1097/MD.00000000000016463>
10. Stener-Victorin E, Jedel E, Mannerås L. Acupuncture in polycystic ovary syndrome: current experimental and clinical evidence. *Journal of neuroendocrinology*. 2008; 20(3), 290–298.
<https://doi.org/10.1111/j.1365-2826.2007.01634.x>
11. Lim CE, Ng RW, Xu K, Cheng NC, Xue CC, Liu JP, et al. Acupuncture for polycystic ovarian syndrome. *The Cochrane database of systematic reviews*. 2016;(5), CD007689.
<https://doi.org/10.1002/14651858.CD007689.pub3>

12. Johansson J, Stener-Victorin E. (2013). Polycystic ovary syndrome: effect and mechanisms of acupuncture for ovulation induction. Evidence-based complementary and alternative medicine ;eCAM. 2013, 762615. <https://doi.org/10.1155/2013/762615>
13. Wu XK, Stener-Victorin E, Kuang HY, Ma HL, Gao JS, Xie LZ, et al. Effect of Acupuncture and Clomiphene in Chinese Women With Polycystic Ovary Syndrome: A Randomized Clinical Trial. JAMA. 2017;317(24), 2502–2514. <https://doi.org/10.1001/jama.2017.7217>
14. Gu S, Fan AY. Controversial conclusions from two randomized controlled trials for acupuncture's effects on polycystic ovary syndrome or in vitro fertilization support. Journal of integrative medicine. 2020;18(2), 89–91. <https://doi.org/10.1016/j.joim.2020.01.007>
15. Dias S, Welton NJ, Sutton AJ, A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials." *Med Decis Making*, 2014, 33(5): 607-617.<http://doi.org/10.1177/0272989X12458724>
16. Ades AE, Caldwell DM, Reken S, Welton NJ, Sutton AJ, et al. Evidence synthesis for decision making 7: a reviewer's checklist. Medical decision making : an international journal of the Society for Medical Decision Making. 2013;33(5), 679–691. <https://doi.org/10.1177/0272989X13485156>
17. Zhang C, Y JZ, Sun F, et al., "Differentiation and Handling of Homogeneity in Network Meta-analysis." *Chin J Evid-based Med*. 2014, 14(07): 884-888.doi:10.7507/1672-2531.20140146.
18. Wu T, Fu C, Deng Y, Huang W, Li X, Jiao Y. Acupuncture therapy for radiotherapy-induced adverse effects: a protocol for systematic review and Bayesian network meta-analysis. Annals of palliative medicine. 2021;10(2), 2254–2259. <https://doi.org/10.21037/apm-20-1747>
19. Mavridis D, Salanti G. A practical introduction to multivariate meta-analysis. Statistical methods in medical research. 2013;22(2), 133–158. <https://doi.org/10.1177/0962280211432219>
20. Gao R, Guo B, Bai J, Wu Y, Wu K. Acupuncture and clomiphene citrate for anovulatory infertility: a systematic review and meta-analysis. Acupuncture in medicine : journal of the British Medical Acupuncture Society.2020;38(1), 25–36. <https://doi.org/10.1136/acupmed-2017-011629>
21. Rashidi BH, Tehrani ES, Hamedani NA, Pirzadeh L. Effects of acupuncture on the outcome of in vitro fertilisation and intracytoplasmic sperm injection in women with polycystic ovarian syndrome. Acupuncture in medicine : journal of the British Medical Acupuncture Society. 2013;31(2), 151–156. <https://doi.org/10.1136/acupmed-2012-010198>
22. Hong M, Quan X, Cai W, et al., "PCOS-induced anxiety disorder treated mainly with acupuncture therapy: a randomized controlled trial." *Acta Medica*. 2016, 32(3):1155-1158.
23. Arentz S, Smith CA, Abbott J, Fahey P, Cheema BS, Bensoussan A. Combined Lifestyle and Herbal Medicine in Overweight Women with Polycystic Ovary Syndrome (PCOS): A Randomized Controlled Trial. Phytotherapy research : PTR. 2017;31(9), 1330–1340. <https://doi.org/10.1002/ptr.5858>
24. Zhu S, Wang Y, Chang X, Chen H, Jin X. The Protective Effect of Pre-Moxibustion on Reproductive Hormones Profile of Rats with Tripterygium Glycosides-Induced Ovarian Damage. Complementary medicine research. 2020;27(6), 401–409. <https://doi.org/10.1159/000506434>

25. Xu ZF, Hong SH, Wang SJ, et al., "Neuroendocrine-immune regulating mechanisms for the anti-inflammatory and analgesic actions of acupuncture." World Journal of Traditional Chinese Medicine.2020,6(4). doi:10.4103/wjtcn.wjtcn_41_20
26. Song YJ, Liang FX, Wu S, Yang HS, Chen L, Huang Q, et al. Network meta-analysis on the effects of the acupuncture-related therapy on ovulation rate and pregnancy rate in patients with polycystic ovary syndrome Zhongguo zhen jiu = Chinese acupuncture & moxibustion.2019;39(7), 792–798. <https://doi.org/10.13703/j.0255-2930.2019.07.029>

Tables

Table 1 Search strategy for PubMed.

#1	"Acupuncture"[Mesh]
#2	"Acupuncture Therapy"[Mesh]
#3	Electroacupuncture"[Mesh]
#4	"Acupuncture Points"[Mesh]
#5	"Acupuncture, Ear"[Mesh]
#6	#1 OR #2 OR #3 OR #4 OR #5
#7	Acupuncture Treatment[Title/Abstract]
#8	Acupuncture[Title/Abstract]
#9	Acupuncture Treatments[Title/Abstract]
#10	Treatment,Acupuncture[Title/Abstract]
#11	Therapy,Acupuncture[Title/Abstract]
#12	Acupotomy[Title/Abstract]
#13	Acupotomies[Title/Abstract]
#14	electroacupuncture[Title/Abstract]
#15	electroacupuncturing[Title/Abstract]
#16	Plum-blossom needle[Title/Abstract]
#17	percussopunctator[Title/Abstract]
#18	plum acupuncture[Title/Abstract]
#19	pyonex[Title/Abstract]
#20	Catgut embedding at acupoints[Title/Abstract]
#21	imbedding needle[Title/Abstract]
#22	Acupoint embedding[Title/Abstract]
#23	Warm needling[Title/Abstract]
#24	Heat sensitive moxibustion[Title/Abstract]
#25	Acupunctures, Ear[Title/Abstract]
#26	Ear Acupunctures[Title/Abstract]
#27	Auricular Acupuncture[Title/Abstract]
#28	Ear Acupuncture[Title/Abstract]
#29	Acupuncture, Auricular[Title/Abstract]

#30	Acupunctures, Auricular[Title/Abstract]
#31	Auricular Acupunctures[Title/Abstract]
#32	Point, Acupuncture[Title/Abstract]
#33	Points, Acupuncture[Title/Abstract]
#34	Acupoints[Title/Abstract]
#35	Acupoint[Title/Abstract]
#36	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35
#37	#6 OR #36
#38	"Polycystic Ovary Syndrome"[Mesh]
#39	"Hypogonadism"[Mesh]
#40	"Primary Ovarian Insufficiency"[Mesh]
#41	"Hyperprolactinemia"[Mesh]
#42	#38 OR #39 OR #40 OR #41
#43	Polycystic Ovary Syndrome[Title/Abstract]
#44	Ovary Syndrome, Polycystic[Title/Abstract]
#45	Syndrome, Polycystic Ovary[Title/Abstract]
#46	Stein-Leventhal Syndrome[Title/Abstract]
#47	Stein Leventhal Syndrome[Title/Abstract]
#48	Syndrome, Stein-Leventhal[Title/Abstract]
#49	Sclerocystic Ovarian Degeneration[Title/Abstract]
#50	Ovarian Degeneration, Sclerocystic[Title/Abstract]
#51	Sclerocystic Ovary Syndrome[Title/Abstract]
#52	Polycystic Ovarian Syndrome[Title/Abstract]
#53	Ovarian Syndrome, Polycystic[Title/Abstract]
#54	Polycystic Ovary Syndrome[Title/Abstract]
#55	Sclerocystic Ovaries[Title/Abstract]

#56	Ovary, Sclerocystic[Title/Abstract]
#57	Sclerocystic Ovary[Title/Abstract]
#58	hypogonadotropic hypogonadism[Title/Abstract]
#59	Hypogonadism, Isolated Hypogonadotropic[Title/Abstract]
#60	Hypogonadotropic Hypogonadism[Title/Abstract]
#61	Hypogonadism, Hypogonadotropic[Title/Abstract]
#62	Hypergonadotropic Hypogonadism[Title/Abstract]
#63	Hypogonadism, Hypergonadotropic[Title/Abstract]
#64	primary ovarian insufficiency[Title/Abstract]
#65	Ovarian Insufficiency, Primary[Title/Abstract]
#66	Ovarian Failure, Premature[Title/Abstract]
#67	Premature Ovarian Failure[Title/Abstract]
#68	Gonadotropin-Resistant Ovary Syndrome[Title/Abstract]
#69	Gonadotropin Resistant Ovary Syndrome[Title/Abstract]
#70	Resistant Ovary Syndrome[Title/Abstract]
#71	Hypergonadotropic Ovarian Failure, X-Linked[Title/Abstract]
#72	Hypergonadotropic Ovarian Failure, X Linked[Title/Abstract]
#73	X-Linked Hypergonadotropic Ovarian Failure[Title/Abstract]
#74	X Linked Hypergonadotropic Ovarian Failure[Title/Abstract]
#75	Premature Ovarian Failure, X-Linked[Title/Abstract]
#76	Premature Ovarian Failure, X Linked[Title/Abstract]
#77	Fragile X-Associated Primary Ovarian Insufficiency[Title/Abstract]
#78	Fragile X Premature Ovarian Failure[Title/Abstract]
#79	FMR1-Related Primary Ovarian Insufficiency[Title/Abstract]
#80	Primary Ovarian Insufficiency, Fragile X-Associated[Title/Abstract]
#81	Premature Ovarian Failure[Title/Abstract]
#82	hyperprolactinemia[Title/Abstract]

#83	Hyperprolactinemias[Title/Abstract]
#84	Prolactin, Inappropriate Secretion[Title/Abstract]
#85	Inappropriate Secretion Prolactin[Title/Abstract]
#86	Secretion Prolactin, Inappropriate[Title/Abstract]
#87	Inappropriate Prolactin Secretion Syndrome[Title/Abstract]
#88	Prolactin Hypersecretion Syndrome[Title/Abstract]
#89	Hypersecretion Syndrome, Prolactin[Title/Abstract]
#90	Syndrome, Prolactin Hypersecretion[Title/Abstract]
#91	Inappropriate Prolactin Secretion[Title/Abstract]
#92	Prolactin Secretion, Inappropriate[Title/Abstract]
#93	Secretion, Inappropriate Prolactin[Title/Abstract]
#94	lutenized unruptured follicle syndrome[Title/Abstract]
#95	idiopathic hypogonadotrophic hypogonadism[Title/Abstract]
#96	Functional Hypothalamic Amenorrhea[Title/Abstract]
#97	Kallmann syndrome[Title/Abstract]
#98	insensitive ovarian syndrome[Title/Abstract]
#99	Estrogen insensitivity syndrome[Title/Abstract]
#100	Presistent non-ovulation[Title/Abstract]
#101	Anorexia nervosa[Title/Abstract]
#102	Obesity reproductive dysfunction syndrome[Title/Abstract]
#103	Ansosmia syndrome[Title/Abstract]
#104	Nonfunctioning adenomas[Title/Abstract]
#105	Swyer syndrome[Title/Abstract]
#106	Turer syndrome[Title/Abstract]
#107	Sheehan's syndrome[Title/Abstract]
#108	lactational amenorrhea[Title/Abstract]
#109	severe malnutrition[Title/Abstract]
#110	Hyperthyroidism[Title/Abstract]
#111	Hypothyroidism[Title/Abstract]

#112	Congenital adrenal hyperplasia[Title/Abstract]
	#38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR
#113	#53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95
#114	#42 OR #113
#115	#37 AND #114

Table 2 Primary screening

Primary screening 1				
NO	Question	YES	NO	UNCLEAR
1	Is this study a clinical study?			
2	Does this study describe Ovulation disorders?			
3	Does this study employ certain acupuncture therapy?			
4	Does this study relate to Ovulation disorder-induced adverse effects?			
5	Is this study peer-reviewed?			
6	Does this study is written in Chinese or English?			
If you answer NO to any of these questions, the citation/study will be excluded. All other citations will be included.				
Primary screening 2				
NO	Question	YES	NO	UNCLEAR
1	Is this study an RCT?			
2	Do the patients in this study receive regular ovulation induction therapy without other interventions that may cause adverse reactions?			
3	Is acupuncture therapy used as prophylaxis or treatment in this study?			
4	Does this study use acupuncture therapy or combined therapies as an intervention?			
5	Are the results of this study recorded as required, such as ovulation rate, hormones?			
6	Does the sample size of each group in this study ¹⁰ ?			

If you answer NO to any of these questions, the citation/study will be excluded. All other full-text articles will be included.

Supplementary

Additional File 1 is not available with this version

Figures

Figure 1

Figure 2

Systematic review and Bayesian network meta-analysis framework strategy chart of acupuncture related therapy for ovulatory disorders

Figure 3

Intervention acupuncture node ovulation disorder disease network model: (A)Blue dot represents acupuncture mode, yellow dot represents acupuncture point, red represents ovulation disorder-specific disease (B) Histogram, which is used to count the frequency of each point in each acupuncture mode

Figure 4

PRISMA flow diagram of the study selection process

Figure 5

Data analysis flow chart