

# BMJ Open Efficacy and safety of acupuncture for postpartum hypogalactia: protocol for a systematic review and meta-analysis

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## ABSTRACT

**Introduction** Breast milk is recognised as the best natural food for neonates, but many women experience postpartum hypogalactia (PH). Randomised trials have found that acupuncture exert therapeutic effect on women with PH. However, systematic reviews on the efficacy and safety of acupuncture are still lacking; therefore, this systematic review aims to evaluate the efficacy and safety of acupuncture for PH.

**Methods and analysis** Six English databases (PubMed, Cochrane Library, EMBASE, EBSCO, Scopus, and Web of Science) and four Chinese databases (China National Knowledge Infrastructure, Wan-Fang, Chinese Biomedical Literature and Chinese Scientific Journal) will be systematically searched from their establishment to 1 September 2022. Randomised controlled trials of the efficacy of acupuncture for PH will be reviewed. The study selection, data extraction and research quality evaluation will be conducted independently by two reviewers. The primary outcome is the change in serum prolactin level from baseline to the end of treatment. Secondary results include milk secretion volume, total effectiveness rate, degree of mammary fullness, rate of exclusive breast feeding, and adverse events. A meta-analysis will be performed using RevMan V.5.4 statistical software. Otherwise, a descriptive analysis will be conducted. The risk of bias will be assessed using the revised Cochrane risk-of-bias tool.

**Ethics and dissemination** This systematic review protocol does not require ethical approval because it does not include private information/data of the participants. This article will be published in peer-reviewed journals. **PROSPERO registration number** CRD42022351849.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study will be the first systematic review to evaluate the efficacy and safety of acupuncture for postpartum hypogalactia (PH) by including available clinical trials that have been published in the past.
- ⇒ The quality of the included trials will be assessed using the Revised Cochrane Risk of Bias Tool (RoB2) for Randomised Trials.
- ⇒ This study will provide more reliable evidence for clinical management because most randomised controlled trials on acupuncture for PH have small sample sizes.
- ⇒ This study will include only English and Chinese trials, which may lead to missing studies in other languages.

29%, respectively.<sup>3 4</sup> Many investigators have reported that PH is the most common cause of breastfeeding failure.<sup>5-7</sup> Breast milk has been identified as the gold standard to provide nutritional support for all infants and prevent infant morbidity and mortality.<sup>8-10</sup> For mothers, breast feeding can decrease the risk of breast cancer, ovarian cancer and type 2 diabetes.<sup>11</sup> Thus, if a mother's own milk is insufficient, it poses challenges not only to mothers who desire to provide milk for their babies, but also to infants who need optimal nutrition. Additionally, the cost of not breastfeeding can cause heavy financial burden to households and society; the total global costs of not breast feeding were estimated at 694 322 lives lost annually and economic losses of US\$341.3 billion.<sup>12</sup> Therefore, as the biggest breastfeeding obstacle, PH is a global health priority that needs focused attention and solutions.

Factors contributing to PH include caesarean section, maternal overweight and poor maternal physical and mental health.<sup>13</sup> Presently, there are pharmacological and non-pharmacological treatments for PH. The most commonly used pharmacological are galactagogues such as metoclopramide,

## INTRODUCTION

Postpartum hypogalactia (PH) is a common condition that greatly affects healthy growth and development of babies. It is characterised by little or no breast milk during the lactation period. The WHO recommended that infants should be exclusively breastfed in the first 6 months.<sup>1</sup> However, only 38% of infants aged under 6 months are exclusively breastfed worldwide, which is lower than the target of 50% in 2025.<sup>2</sup> In China and Europe, the rate is just 13%–39% and



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domperidone and sulpiride,<sup>14</sup> which are not recommended by the Academy of Breastfeeding Medicine,<sup>15</sup> may increase milk volume with low-certainty evidence,<sup>16</sup> and are associated with multiple side effects.<sup>17</sup> Other than drugs, PH can be treated by relaxation techniques, skin-to-skin holding, hand expression, etc,<sup>18–20</sup> but the role of these methods in augmenting breast milk might be unsatisfactory. Consequently, it is critical to seek new safe and effective therapies for treating PH.

Acupuncture, a complementary and alternative medicine technique, has been used to treat PH in China for more than 2000 years.<sup>21</sup> In western countries, acupuncture is one of the most frequently recommended interventions to increase maternal milk production.<sup>22</sup> Acupuncture involves insertion of fine needles into certain acupoints on the surface of the body, with specific operational methods to restore the balance or harmony of the individual and thereby restore health.<sup>23</sup> A recent overview<sup>24</sup> found that acupuncture showed a large effect in increasing lactation success rate post-delivery. Furthermore, several studies have demonstrated that acupuncture is an effective treatment for PH. For instance, Suwikrom *et al*<sup>25</sup> found that acupuncture was superior to conventional treatment for boosting breast milk production in women with PH. Moreover, Su *et al*<sup>26</sup> found that electroacupuncture can markedly improve the breast milk volume and nutrient composition level in women with PH. The mechanisms underlying the effects of acupuncture may involve adjusting microbial and hormonal signals and regulating the activity of the hypothalamic dopamine system and norepinephrine system.<sup>27</sup> Thus, acupuncture may be a viable option for women with PH.

Many previous randomised controlled trials (RCTs) on acupuncture for PH exist.<sup>25 26 28–30</sup> However, the clinical outcomes reported vary and the quality of evidence derived from RCTs is unclear, which may lead to inconsistent consensus and risk of bias. Taking these limitations into account, we will conduct a systematic review and meta-analysis of RCTs evaluating acupuncture in PH treatment to solve the above issues and provide more reliable evidence for clinical application and reference for future research.

## METHODS

### Study registration

This study has been registered on PROSPERO (No. CRD42022351849). This protocol is developed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) statement.<sup>31</sup>

### Criteria for inclusion of studies in this review

#### Types of studies

All RCTs of acupuncture therapy for PH will be included in the review without any limitations on language and publication time. Non-RCTs, quasi-RCTs, case series, comments, conference abstracts, guides, letters, notes,

book sections, editorials, reviews and animal experimental studies, as well as expert experiences will be excluded.

#### Types of participants

RCTs involving participants with PH, including primipara and multipara participants, will be included without restrictions on age and parity. Studies that include participants with other disorders, such as breast engorgement, mastitis and breast abscess, will be excluded.

#### Types of interventions

Acupuncture is defined as needle insertion at acupuncture points, Ashi points or meridian locations and includes manual acupuncture, electroacupuncture, auricular acupuncture and plum-blossom needle. Studies with interventions that do not use needles to penetrate the skin, such as transcutaneous electrostimulation or acupressure, will be excluded.

#### Types of comparator (s)/control

The following comparative studies will be included:

1. Acupuncture versus placebo acupuncture.
2. Acupuncture versus conventional treatment.
3. Acupuncture versus Chinese medicine.
4. Acupuncture in addition to other therapy versus other therapy alone.

Studies comparing the clinical efficacy between different acupoints, different acupuncture methods or comparing acupuncture with other complementary and alternative therapies will be excluded.

#### Types of outcome measures

##### Primary outcome

Changes in serum prolactin levels from baseline to the end of treatment will be measured.

##### Secondary outcomes

1. Milk secretion volume.
2. Total effectiveness rate.
3. Degree of mammary fullness.
4. Rate of exclusive breast feeding.
5. Adverse events.

### Search methods for identification of studies

#### Electronic search

The following 10 databases will be searched from their inception to 1 September 2022: PubMed, Cochrane Library, EMBASE, EBSCO, Scopus, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Chinese Scientific Journal Database (VIP Database) and Wan-Fang Database. The following medical search headings (MeSH) will be used: “acupuncture,” “acupuncture therapy,” “acupuncture points,” “electroacupuncture,” “lactation,” “lactation disorder,” “milk, human,” “milk ejection,” “breast feeding,” “postpartum period,” “randomized controlled trial,” “controlled clinical trial” and “random allocation.” Chinese databases will be searched using the

**Table 1** Search strategy for PubMed

No.	Search terms
#1	Acupuncture. Mesh
#2	Acupuncture. ti, ab
#3	Acupuncture therapy. Mesh
#4	Acupuncture therapy. ti, ab
#5	Acupuncture points. Mesh
#6	Acupuncture points. ti, ab
#7	electroacupuncture. Mesh
#8	electroacupuncture. ti, ab
#9	(body acupuncture or manual acupuncture or auricular acupuncture) . ti, ab
#10	#1 or #2–9
#11	Lactation. Mesh
#12	Lactation disorder. Mesh
#13	Milk, human. Mesh
#14	Milk ejection. Mesh
#15	Breast feeding. Mesh
#16	Postpartum period. Mesh
#17	(lactation or milk or breast feeding or breastfeeding or hypogalactia or galactosis or colostrum or postpartum or postnatal or puerperal). ti, ab
#18	#11 or #12–17
#19	randomized controlled trial. pt
#20	controlled clinical trial. pt
#21	random allocation. Mesh
#22	clinical trial. pt
#23	randomized. ti,ab
#24	randomly. ti,ab
#25	trial. ti
#26	#19 or #20–25
#27	#10 and #18 and #26

Chinese translations of these search terms. The search strategy for PubMed is shown in [table 1](#).

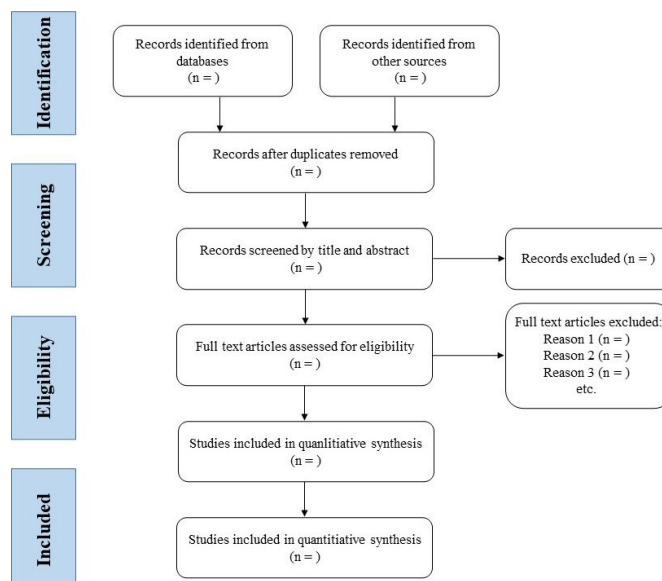
### Searching other resources

Potential eligible studies will be manually searched by screening the conference papers and the reference lists of the relevant reviews and the included articles.

### Data collection and analysis

#### Selection of studies

First, all retrieved articles will be imported into EndNote (V.X9). After removing duplicates, two reviewers (Q-NB and Y-FZ) will independently screen the titles and abstracts of all studies to filter out articles that meet the inclusion criteria. Then, the same two reviewers will independently read full text of these articles to determine eligibility; studies that have been excluded will be documented with the reasons for their exclusion. When multiple articles describe the same trial, only the study with the most

**Figure 1** Flow diagram of the study selection process.

complete data will be included. Last, the selection results will be cross-checked by the same two reviewers. If there are any disagreements in the process, the final decision will be arbitrated by a third reviewer (Z-HY). The primary selection process is shown in the PRISMA flow chart ([figure 1](#)).

### Data extraction and management

Two reviewers (Q-NB and Y-FZ) will independently extract predefined information from the included studies by using Microsoft Excel. The predefined information will include: publication year, demographic characteristics of the participants, sample size, randomisation, allocation concealment, blinding methods, funding, diagnostic criteria, inclusion/exclusion criteria, details of the intervention and control, outcome measurement methods, follow-up duration, adverse events and outcomes. If the reported data are missing or unclear, the reviewers will contact the corresponding author to make the supplementation or clarification. Then the same two reviewers will cross-check the accuracy of these data. Any disagreements will be resolved through discussion or judged by a third reviewer (Z-HY).

### Assessment for risk of bias

Two investigators (Q-NB and Y-FZ) will independently appraise the methodological quality of the included trials using the Revised Cochrane Risk of Bias (RoB 2) tool for randomised trials.<sup>32</sup> This tool included five domains: randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported results. Each domain corresponds to different signalling questions. According to the signal answer given to different questions, each bias domain will be judged as 'low risk', 'high risk' or 'some concerns', and the overall bias of risk will

be given. A third reviewer (Z-HY) will intervene to reach a consensus if inconsistent results are obtained.

### Measures for the treatment effect

Efficacy data will be synthesised and statistically analysed in RevMan (V.5.4). Dichotomous data will be calculated by the relative risk with 95% CIs, and continuous data will be analysed using the weighted mean difference (WMD) or standardised mean difference (SMD) with 95% CIs. The WMD will be used for the same scale or same assessment tools; SMD will be used for different instruments.

### Assessment of heterogeneity

$\chi^2$  tests will be conducted using RevMan software to investigate the statistical heterogeneity, and a  $p < 0.10$  will be considered significant, in line with the Cochrane Handbook.<sup>33</sup> The  $I^2$  values will be calculated to quantify the percentage of heterogeneity in the outcome measures. When  $I^2$  values  $> 30\%$ ,  $50\%$  and  $75\%$ , the heterogeneity between studies will be considered moderate, significant or considerable, respectively.

### Assessment of reporting bias

A Funnel plot<sup>34</sup> and Egger's test<sup>35</sup> will be performed to detect the publication bias if the number of included studies exceeds 10.

### Data synthesis

We will use RevMan software to conduct data synthesis. The use of a fixed-effects or random-effects model will be determined based on the heterogeneity level. If little or no statistical heterogeneity ( $I^2 \leq 50\%$  and  $p \geq 0.10$ ) is detected among trials, the fixed-effects model will be used for data synthesis. If significant heterogeneity ( $I^2 > 50\%$  and  $p < 0.10$ ) exists, the random-effects model will be used. If there is considerable heterogeneity ( $I^2 \geq 75\%$ ) in the trials, meta-analysis will not be performed, and a descriptive qualitative summary will be provided. If necessary, subgroup analysis will be performed with careful consideration of each subgroup. During the meta-analysis process, a third reviewer (Z-HY) may inspect and monitor the procedures irregularly.

### Subgroup analysis and investigation of heterogeneity

Subgroup analysis and meta-regression will be undertaken to explore potential sources of the heterogeneity in the previous analysis. If the necessary data are available, subgroup analysis will be conducted according to different types of control group and different comparators, meta-regression analysis will be carried out based on sample size and treatment duration.

### Sensitivity analysis

To test the robustness of the meta-analysis results, we will conduct a sensitivity analysis for the primary outcome according to the sample size and the statistical model. The results of the sensitivity analysis will be presented in summary tables and discussed.

### Grading the quality of evidence

Two reviewers (Q-NB and Y-FZ) will independently evaluate evidence quality using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. The GRADE system evaluates five aspects: limitations in study design, inconsistency, indirectness, imprecision and publication bias. The quality of evidence will be graded as 'high', 'moderate', 'low' or 'very low' in accordance with the GRADE rating standards.

### ETHICS AND DISSEMINATION

This study does not require ethical approval, since no private information of participants will be involved. The results of this study will be disseminated in peer-reviewed journals or conference presentations. Important protocol amendments will be documented and updated in PROSPERO.

### Patient and public involvement

Patient priorities, experiences and preferences were not involved in the development of the research question, outcome measures, study design or the conduct of this review. The results will not be disseminated to participants.

### DISCUSSION

PH is a public health priority that requires efforts to explore more effective treatments. Many RCTs have indicated that acupuncture is effective in promoting breast milk production of women with PH. However, no systematic review in this field has been published. Consequently, it is necessary to conduct a comprehensive review by adding relevant studies into the analysis. The aim of this review is to provide more robust evidence for acupuncture in the treatment of PH and to inform clinical practice and acupuncture research. Inevitably, this study has some limitations. First, diverse treatment courses, acupoints and methods of milk measurement used in different studies may run a high risk of heterogeneity. Second, only English and Chinese trials will be selected, which may lead to publication bias.

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**Contributors** Q-NB contributed to the concept of the study, and Y-FZ developed the protocol methodology. H-BZ is responsible for planning the statistical analysis. Z-YZ and F-RL will monitor protocol implementation. The original manuscript was completed by Q-NB and was edited by QB. Q-NB and Y-FZ will independently screen potential studies and extract data from the included studies. Q-NB and Y-FZ will assess the risk of bias and perform the data synthesis. Z-HY will arbitrate any conflicts between reviewers and perform quality checks at all stages of review. All authors have read, provided feedback and approved the final manuscript.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

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## REFERENCES

- World Health Organization. Global strategy for infant and young childfeeding. Geneva, Switzerland, 2003. Available: [https://2001.media.tghn.org/articles/WHO\\_UNICEF\\_2003.pdf](https://2001.media.tghn.org/articles/WHO_UNICEF_2003.pdf)
- Almohanna AA, Win KT, Meedya S. Effectiveness of Internet-based electronic technology interventions on breastfeeding outcomes: systematic review. *J Med Internet Res* 2020;22:e17361.
- Theurich MA, Weikert C, Abraham K, et al. Breastfeeding rate and promotion in selected European countries. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2018;61:926–36.
- Wang Y, Zhou C. China should take more measures to raise its breastfeeding rate. *Biosci Trends* 2019;13:358–60.
- Fu C-Y, Tang X-J, Pan L-P, et al. Exclusive breastfeeding rate and related factors among mothers within maternal health WeChat groups in Jiaxing, Zhejiang Province, China: a cross-sectional survey. *Int Breastfeed J* 2022;17:80.
- Chan K, Labonté JM, Francis J, et al. Breastfeeding in Canada: predictors of initiation, exclusivity, and continuation from the 2017–2018 Canadian community health survey. *Appl Physiol Nutr Metab* 3, 2023.
- Geddes D, Perrella S. Breastfeeding and human lactation. *Nutrients* 2019;11:802.
- de Halleux V, Peltain C, Senterre T, et al. Use of donor milk in the neonatal intensive care unit. *Semin Fetal Neonatal Med* 2017;22:23–9.
- Cartagena D, Penny F, McGrath JM, et al. Differences in neonatal outcomes among premature infants exposed to mother's own milk versus donor human milk. *Adv Neonatal Care* 2022;22:539–49.
- Obeng C, Jackson F, Nsiah-Asamoah C, et al. Human milk for vulnerable infants: breastfeeding and milk sharing practice among Ghanaian women. *Int J Environ Res Public Health* 2022;19:16560.
- Westerfield KL, Koenig K, Oh R. Breastfeeding: common questions and answers. *Am Fam Physician* 2018;98:368–73.
- Walters DD, Phan LTH, Mathisen R. The cost of not breastfeeding: global results from a new tool. *Health Policy Plan* 2019;34:407–17.
- Segura-Pérez S, Richter L, Rhodes EC, et al. Risk factors for self-reported insufficient milk during the first 6 months of life: a systematic review. *Matern Child Nutr* 2022;18 Suppl 3:e13353.
- Asztalos EV. Supporting mothers of very preterm infants and breast milk production: a review of the role of galactagogues. *Nutrients* 2018;10:600.
- Brodrribb W. ABM clinical protocol # 9: use of galactagogues in initiating or augmenting maternal milk production, second revision 2018. *Breastfeed Med* 2018;13:307–14.
- Foong SC, Tan ML, Foong WC, et al. Oral galactagogues (natural therapies or drugs) for increasing breast milk production in mothers of non-hospitalised term infants. *Cochrane Database Syst Rev* 2020;5:CD011505.
- McBride GM, Stevenson R, Zizzo G, et al. Use and experiences of galactagogues while breastfeeding among Australian women. *PLoS One* 2021;16:e0254049.
- Mohd Shukri NH, Wells J, Eaton S, et al. Randomized controlled trial investigating the effects of a breastfeeding relaxation intervention on maternal psychological state, breast milk outcomes, and infant behavior and growth. *Am J Clin Nutr* 2019;110:121–30.
- Vila-Candel R, Duke K, Soriano-Vidal FJ, et al. Affect of early skin-to-skin mother-infant contact in the maintenance of exclusive breastfeeding: experience in a health department in Spain. *J Hum Lact* 2018;34:304–12.
- Becker GE, Smith HA, Cooney F. Methods of milk expression for lactating women. *Cochrane Database Syst Rev* 2016;9:CD006170.
- Zheng XY, Mu X, Yuan CK, et al. Research progress of acupuncture therapy in treating few postpartum lactation. *Zhen Jiu Lin Chuang Za Zhi* 2021;37:97–101.
- Winterfeld U, Meyer Y, Panchaud A, et al. Management of deficient lactation in Switzerland and Canada: a survey of midwives' current practices. *Breastfeed Med* 2012;7:317–8.
- Zhang B, Shi H, Cao S, et al. Revealing the magic of acupuncture based on biological mechanisms: a literature review. *Biosci Trends* 2022;16:73–90.
- Lu L, Zhang Y, Ge S, et al. Evidence mapping and overview of systematic reviews of the effects of acupuncture therapies. *BMJ Open* 2022;12:e056803.
- Suwikrom S, Jaisamuth N, Poonsawad P. Acupuncture to boost breast milk in postpartum hypogalactia: randomized controlled trial. *J Med Assoc Thai* 2021;104:1930–6.
- Su WW, Gao XA, Tian JS. Effect of electroacupuncture at shaoze (Si 1) on breast milk volume and composition in postpartum hypogalactia. *Zhongguo Zhen Jiu* 2020;40:13–6.
- Sheng PL, Xie QW. Relationship between effect of acupuncture on prolactin secretion and central catecholamine and R-aminobutyric acid. *Zhen Ci Yan Jiu* 1989;14:446–51.
- Maged AM, Hassanin ME, Kamal WM, et al. Effect of low-level laser therapy versus electroacupuncture on postnatal scanty milk secretion: a randomized controlled trial. *Am J Perinatol* 2020;37:1243–9.
- Liu MF, Bi XX, Geng DD, et al. Observation on clinical effect and safety of meridional flow injection combined with syndrome differentiation acupuncture in treatment of postpartum lactation. *Zhonghua Zhong Yi Yao Xue Kan* 2021;39:245–8.
- Zhao R, Wang XX, Li YE, et al. Clinical observation of acupuncture plus electroacupuncture for postpartum hypogalactia. *Shanghai Zhen Jiu Za Zhi* 2018;37:1160–4.
- Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;350:g7647.
- Eldridge S, Campbell M, Campbell M. Revised Cochrane risk of bias tool for randomized trials (RoB 2.0): additional considerations for cluster-randomized trials. 2016. Available: <https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool> [Accessed 13 Jun 2022].
- Higgins J, Green S. Cochrane handbook for systematic reviews of interventions: wiley online library. 2008. Available: <https://www.wiley.com/en-gb/Cochrane+Handbook+for+Systematic+Reviews+of+Interventions,+2nd+Edition-p-9781119536628> [Accessed 26 Jan 2023].
- Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. *J Clin Epidemiol* 2001;54:1046–55.
- Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.