

## STUDY PROTOCOL

# Acupuncture for treating attention deficit hyperactivity disorder in children: A protocol for systematic review and meta-analysis

Jung Tae Kim<sup>1,2</sup>, Kibong Kim<sup>1,3</sup>, Lin Ang<sup>4</sup>, Hye Won Lee<sup>5</sup>, Jun-Yong Choi<sup>6</sup>, Myeong Soo Lee<sup>4\*</sup>

**1** Department of Korean Pediatrics, School of Korean Medicine, Pusan National University, Yangsan, Republic of Korea, **2** IMOM Korean Medicine Clinic, Jeju, Republic of Korea, **3** Department of Korean Pediatrics, School of Korean Medicine & Korean Medicine Hospital, Pusan National University, Yangsan, Republic of Korea, **4** KM Science Research Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea, **5** KM Convergence Research Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea, **6** Department of Korean Internal Medicine, School of Korean Medicine & Korean Medicine Hospital, Pusan National University, Yangsan, Republic of Korea

☞ These authors contributed equally to this work.

\* [drmslee@gmail.com](mailto:drmslee@gmail.com)



## OPEN ACCESS

**Citation:** Kim JT, Kim K, Ang L, Lee HW, Choi J-Y, Lee MS (2022) Acupuncture for treating attention deficit hyperactivity disorder in children: A protocol for systematic review and meta-analysis. PLoS ONE 17(10): e0275504. <https://doi.org/10.1371/journal.pone.0275504>

**Editor:** Christine Nardini, National Research Council: Consiglio Nazionale delle Ricerche, ITALY

**Received:** June 21, 2022

**Accepted:** September 16, 2022

**Published:** October 10, 2022

**Peer Review History:** PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0275504>

**Copyright:** © 2022 Kim et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Data Availability Statement:** No datasets were generated or analysed during the current study. All relevant data from this study will be made available upon study completion.

## Abstract

### Background

Attention deficit hyperactivity disorder (ADHD) patients often use complementary and alternative medicine to treat symptoms, and acupuncture is one option. This systematic review aims to assess whether acupuncture is an effective treatment for attention deficit hyperactivity disorder (ADHD).

### Methods

We will search nine databases from their inception: PubMed, AMED, CINAHL, EMBASE, the Cochrane Central Register of Controlled Trials, RISS, KoreaMed, KISS, and the China National Knowledge Infrastructure database. Two investigators will independently review the selected studies, extract the data, and analyze them. The Cochrane Risk of Bias Assessment Tool will be used to assess the risk of bias.

### Discussion

Because this is a systematic review, no ethical approval is needed. The systematic review will be published in a peer-reviewed journal and disseminated both electronically and in print. The review will be updated to support health policy and practice.

### Trial registration number

Reviewregistry1345.

**Funding:** No external funding was supported. LA, HWL and MSL were funded internally by the Korea Institute of Oriental Medicine (KSN2021210) (<https://www.kiom.re.kr/eng/>). The authors alone are responsible for the writing and content of paper. The funders had and will not have a role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing interests:** NO authors have competing interests.

## Introduction

Attention deficit hyperactivity disorder (ADHD) is a disorder with symptoms of inattention, hyperactivity, and impulsivity. The estimated prevalence of ADHD is 7.2% in children and adolescents worldwide [1]. The prevalence of ADHD in children is 7.8%–9.5% in the United States [2] and 6.27% in China [3]. The drug treatment for children with ADHD includes stimulant medication, atomoxetine, and antidepressants in combination with behavioral therapies [4]. However, these therapies are not free of side effects, including abdominal pain, headache, cardiovascular risk, irritability, and insomnia [5].

The reported use of complementary and alternative medicine for ADHD ranges from 12% to 64% [6]. Nutritional interventions, herbal preparations, massage, mind–body medicine, and acupuncture are most commonly used [6]. Acupuncture involves inserting needles for therapeutic or preventive purposes into the skin tissue and underlying tissues at specific points on the body, called acupuncture points [7]. These points can also be stimulated with electricity, lasers, pressure, heat, and ultrasonic waves [7]. Acupuncture is widely used in Asia for managing a variety of conditions, including cardiovascular diseases, infertility, pain and mental health [8–11]. In the cerebral cortex, acupuncture can stimulate the growth and development of nerve fibers, neural nerve regeneration and brain connectivity [12–14]. It has been hypothesized that acupuncture can improve attention, especially active attention, in children with ADHD [15, 16]. To date, the use of acupuncture for ADHD has been investigated in three systematic reviews (SRs) in English [17–19]. One of these three were Cochrane reviews, but they found no eligible studies [19]. The other two reviews indicated limited evidence that acupuncture may be beneficial for the treatment of ADHD [17, 18]. Further, the authors combined the studies regardless of control treatments and ignored clinical heterogeneities, resulting in potentially biased or inaccurate conclusions [17]. They are also outdated and may miss several newly published studies [17, 18]. Therefore, this systematic review will aim to provide an up-to-date evaluation on the effects of acupuncture on children with ADHD.

## Methods

### Study registration

The protocol is registered at reviewregistry1345 (<https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/625ffb6ceccdb1001efe3598/>) [20].

### Criteria for considering studies in this review

**Types of studies.** We will include prospective randomized controlled trials (RCTs). Observational, cohort, qualitative, uncontrolled, laboratory, and case-control studies and case series will be excluded. Language restrictions will not apply.

**Types of participants.** Children with ADHD will be included regardless of sex or nationality.

**Types of interventions and controls.** We will include studies that investigated invasive acupuncture with or without electrical stimulation on body, ear and head. Other methods of stimulating acupuncture points without needle insertion (acupressure, pressure buttons, laser stimulation, etc.) will be excluded. Treatments that may be used as control interventions include general conventional treatments (medications), sham treatments (interventions that mimic acupuncture/real treatment in some aspects but differ in others, such as skin penetration or point location), and waiting lists. The acceptance of sham acupuncture as a valid control is highly controversial [21–23], and we will analyze the results using subgroup and

sensitivity analyzes. In addition to acupuncture and another active treatment, we will also include studies that compared the active treatment with acupuncture, as well as studies that combined the active treatment with acupuncture. We will exclude RCTs comparing two different forms of acupuncture or using other types of alternative therapies including cupping, herbal medicines, exercise and etc.

**Type of outcome measures.** *Primary outcomes.* Improvement in ADHD symptoms [24]: DSM-IV-based scales (Conners' Rating Scales (Parent and teacher), Disruptive Behavior Rating Scale, ADHD-RS (Parent, Teacher, and Investigator)) or Global assessment scales (Clinical Global Impression-Improvement or Severity scale, Children's and Parent's Global Assessment Scales).

Secondary outcomes

1. Total treatment efficacy
2. Quality of life
3. Adverse events (AEs)

## Search method for identifying studies

**Electronic searches.** The electronic database searches will be conducted in PubMed, AMED, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), three Korean databases—KoreaMed, the Research Information Service System (RISS), the Korean Studies Information Service System (KISS), and the China National Knowledge Infrastructure (CNKI) database. We will use English for the search terms of all eight databases. In addition, we will use Korean for RISS and KISS and Chinese for CNKI.

Additional studies will be identified by searching the reference lists of the selected studies. We will also search the World Health Organization's International Clinical Trial Registration Platform (ICTRP) (<http://apps.who.int/trialsearch>), ClinicalTrials.gov (<http://clinicaltrials.gov/>), and The Clinical Research Information Service (CRIS) (<https://cris.nih.go.kr/cris/index/index.do>). In addition to the studies located in the database searches, we will include relevant SRs and articles by searching the reference lists of these studies. In addition, dissertations and abstracts will be included in the search.

**Search strategy.** The search strategy will use the following terms: (acupuncture OR acup\* OR electroacupuncture OR ear acupuncture) AND (attention deficit OR attention OR hyperactivity\* or ADHD).

## Data collection, extraction, and analysis

**Selection of studies.** Two reviewers (JTK, KK) will independently evaluate the titles and abstracts of the studies identified in the searches and select appropriate studies based on the predefined criteria. Disagreements in study selection will be resolved by another reviewer (MSL). A Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)-compliant flowchart will be used to document and summarize the study selection [25, 26].

**Data extraction.** The selected articles will be reviewed by two independent reviewers (JTK and LA), who will extract data from the articles based on the predefined criteria. The extracted data will include the acupuncture intervention, the control intervention, the main outcomes, and adverse effects, as well as the author(s) name, year of publication, country, sample size, age, and sex of the study participants. We will tabulate the extracted data for further analysis. GRADE software will be used to assess the strength of evidence based on the

Cochrane Handbook for Systematic Reviews of Interventions, and a table summarizing the results will be produced.

Based on the revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [27], details of the acupuncture method and control interventions will be extracted. In cases where studies do not meet standards (lack of STRICTA protocol, insufficient information), we will email or call the authors for additional information and note the results in the final publication. We will also report the case where it is not possible to contact the PI of the study and obtain the full information. While all studies that meet the search criteria will be included, those that do not meet the proposed standards will be listed separately and the reason for exclusion is noted. Only those studies that meet the inclusion criteria and none of the exclusion criteria will be included in the results tables.

**Assessment of risk of bias.** We will assess the risk of bias based on the Risk of Bias Assessment Tool (RoB 2.0) developed by the Cochrane Collaboration [28]. Five aspects will be examined: randomization, deviations from planned interventions, missing outcome data, measurement of outcomes, and selection of reported outcomes. Risk of bias will be graded as "low risk of bias," "some concern," or "high risk of bias" for each area of each study. Disagreements will be resolved by involving a third reviewer when necessary.

## Data analysis

The data analysis will be carried out using the Cochrane Collaboration's Review Manager (RevMan) software, version 5.4 for Windows (Nordic Cochrane Center, Copenhagen, Denmark). Comparisons of the intervention and control groups will be performed. The assessment of clinical effectiveness will be based on the risk ratio for the categorical data and the mean difference (MD) for the continuous data. Efficacy values will accompany categorical and continuous variables with 95% confidence intervals. We will use the standardized MD rather than the weighted MD for variables with different scales. When heterogeneity was detected by chi-square or Higgins  $I^2$  tests, we will perform subgroup analyses to determine the cause of clinical heterogeneity. Due to the variety of interventions, study designs, and other factors involved in the included studies, a random-effects model will be used to assess the combined effect sizes of the efficacy variables. The Egger regression method and funnel plots will be used to assess publication bias. We will contact the investigators of the original study if we discover missing or incomplete data.

A subgroup analysis will be conducted according to different control interventions (acupuncture vs. sham acupuncture, acupuncture vs. conventional intervention, acupuncture combined with conventional intervention vs. conventional intervention) and stimulation type (manual vs. electrical). The meta-analysis results will be subjected to sensitivity analyses, where appropriate, to determine their robustness.

We will provide all data underlying the results of this study in the article and supplementary materials.

## Ethics and dissemination

The protocol for this systematic review does not require ethical approval. In addition to peer-reviewed publications and conference presentations, the results of this review will be widely disseminated.

## Discussion

Clinicians may be able to utilize the results of this systematic review and meta-analysis on the evidence related to the safety and effectiveness of acupuncture for treating ADHD in children.

## Supporting information

**S1 Checklist. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.**

(DOC)

**S2 Checklist. Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) checklist (<https://stricta.info/checklist/>).**

(PDF)

## Author Contributions

**Conceptualization:** Jung Tae Kim, Kibong Kim, Myeong Soo Lee.

**Data curation:** Lin Ang, Hye Won Lee.

**Formal analysis:** Jung Tae Kim, Lin Ang.

**Investigation:** Jung Tae Kim, Kibong Kim, Myeong Soo Lee.

**Methodology:** Jung Tae Kim, Myeong Soo Lee.

**Project administration:** Hye Won Lee.

**Resources:** Jun-Yong Choi.

**Supervision:** Kibong Kim, Myeong Soo Lee.

**Validation:** Hye Won Lee, Jun-Yong Choi.

**Writing – original draft:** Jung Tae Kim, Kibong Kim, Myeong Soo Lee.

**Writing – review & editing:** Lin Ang, Hye Won Lee, Jun-Yong Choi.

## References

1. Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-analysis. *Pediatrics*. 2015; 135(4):e994–e1001. <https://doi.org/10.1542/peds.2014-3482> PMID: 25733754
2. Centers for Disease Control and Prevention (CDC). Mental health in the United States. Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder—United States, 2003. *MMWR Morb Mortal Wkly Rep*. 2005; 54(34):842–7. PMID: 16138075.
3. Wang T, Liu K, Li Z, Xu Y, Liu Y, Shi W, et al. Prevalence of attention deficit/hyperactivity disorder among children and adolescents in China: a systematic review and meta-analysis. *BMC Psychiatry*. 2017; 17(1):32. <https://doi.org/10.1186/s12888-016-1187-9> PMID: 28103833
4. Wolraich M. Attention deficit hyperactivity disorder in children. <https://bestpractice.bmj.com/topics/en-gb/142>. Last accessed 10 June 2022. *BMJ Best Practice*. Sept 2021.
5. Dynamed. Attention deficit hyperactivity disorder (ADHD) in children and adolescents.
6. Feldman HM, Reiff MI. Attention Deficit–Hyperactivity Disorder in Children and Adolescents. *New England Journal of Medicine*. 2014; 370(9):838–46. <https://doi.org/10.1056/NEJMcp1307215> PMID: 24571756.
7. World Health Organization. Acupuncture: Review and analysis of reports on controlled clinical trials. Geneva: World Health Organization; 2002.
8. National Center for Complementary and Integrative Health. Acupuncture: in depth. <https://www.nccih.nih.gov/health/acupuncture-in-depth>. Accessed 10th June, 2022.
9. Pan W, Li F-x, Wang Q, Huang Z-q, Yan Y-m, Zhao L, et al. A randomized sham-controlled trial of manual acupuncture for infertile women with polycystic ovary syndrome. *Integrative Medicine Research*. 2022; 11(2):100830. <https://doi.org/10.1016/j.imr.2021.100830> PMID: 35059289
10. Qi W-C, Fu H-J, Sun R-R, Li X, Cai D-J, Wang C, et al. Effectiveness and safety of acupuncture for angina pectoris: An overview of systematic reviews. *Integrative Medicine Research*. 2022; 11(3):100864. <https://doi.org/10.1016/j.imr.2022.100864> PMID: 35535308

11. Vickers AJ, Cronin AM, Maschino AC, Lewith G, MacPherson H, Foster NE, et al. Acupuncture for Chronic Pain: Individual Patient Data Meta-analysis. *Archives of Internal Medicine*. 2012; 172(19):1444–53. <https://doi.org/10.1001/archinternmed.2012.3654> PMID: 22965186
12. Hu L-n, Tian J-x, Gao W, Zhu J, Mou F-f, Ye X-c, et al. Electroacupuncture and moxibustion promote regeneration of injured sciatic nerve through Schwann cell proliferation and nerve growth factor secretion. *Neural Regeneration Research*. 2018; 13(3). <https://doi.org/10.4103/1673-5374.228731> PMID: 29623933
13. Park J-Y, Cho S-J, Lee S-H, Ryu Y, Jang J-H, Kim S-N, et al. Peripheral ERK modulates acupuncture-induced brain neural activity and its functional connectivity. *Scientific Reports*. 2021; 11(1):5128. <https://doi.org/10.1038/s41598-021-84273-y> PMID: 33664320
14. Zhao L, Liu J-W, Kan B-H, Shi H-Y, Yang L-P, Liu X-Y. Acupuncture accelerates neural regeneration and synaptophysin production after neural stem cells transplantation in mice. *World journal of stem cells*. 2020; 12(12):1576–90. <https://doi.org/10.4252/wjsc.v12.i12.1576> PMID: 33505601.
15. Chai TQ. Observation on therapeutic effects of 155 cases of child attentional deficit hyperactivity disorder treated with acupuncture and moxibustion. *Chin Acupunct Mox*. 1999; 19:5–7.
16. Loo M. CHAPTER 13—Attention-Deficit Hyperactivity Disorder. In: Loo M, editor. *Integrative Medicine for Children*. Saint Louis: W.B. Saunders; 2009. p. 178–92.
17. Chen YC, Wu LK, Lee MS, Kung YL. The Efficacy of Acupuncture Treatment for Attention Deficit Hyperactivity Disorder: A Systematic Review and Meta-Analysis. *Complementary Medicine Research*. 2021; 28(4):357–67. <https://doi.org/10.1159/000513655> PMID: 33508834
18. Lee MS, Choi TY, Kim JI, Kim L, Ernst E. Acupuncture for treating attention deficit hyperactivity disorder: a systematic review and meta-analysis. *Chin J Integr Med*. 2011; 17(4):257–60. Epub 2011/04/22. <https://doi.org/10.1007/s11655-011-0701-7> PMID: 21509667.
19. Li S, Yu B, Zhou D, He C, Kang L, Wang X, et al. Acupuncture for Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents. *Cochrane Database of Systematic Reviews*. 2011;(4). CD007839. <https://doi.org/10.1002/14651858.CD007839.pub2> PMID: 21491402
20. Kim JT, Lee MS. reviewregistry1345. Acupuncture for treating attention deficit/hyperactivity disorder in children: a systematic review and meta-analysis. <https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/625ffb6ceccdb1001efe3598/>. Accessed on 10th June, 2022. 2022.
21. Birch S, Lee MS, Kim T-H, Alraek T. On defining acupuncture and its techniques: A commentary on the problem of sham. *Integrative Medicine Research*. 2022; 11(2):100834. <https://doi.org/10.1016/j.imr.2022.100834> PMID: 35111572
22. Birch S, Lee MS, Kim T-H, Alraek T. Historical perspectives on using sham acupuncture in acupuncture clinical trials. *Integrative Medicine Research*. 2022; 11(1):100725. <https://doi.org/10.1016/j.imr.2021.100725> PMID: 34458094
23. Lee I-S, Chae Y. Cognitive components of acupuncture treatment. *Integrative Medicine Research*. 2021; 10(4):100754. <https://doi.org/10.1016/j.imr.2021.100754> PMID: 34336595
24. Woods D, Wolraich M, Pierce K, DiMarco L, Muller N, Sachdeva R. Considerations and evidence for an ADHD outcome measure. *Acad Pediatr*. 2014; 14(5 Suppl):S54–60. <https://doi.org/10.1016/j.acap.2014.06.011> PMID: 25169459.
25. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021; 372:n71. <https://doi.org/10.1136/bmj.n71> PMID: 33782057
26. Wang X, Chen Y, Liu Y, Yao L, Estill J, Bian Z, et al. Reporting items for systematic reviews and meta-analyses of acupuncture: the PRISMA for acupuncture checklist. *BMC Complementary and Alternative Medicine*. 2019; 19(1):208. <https://doi.org/10.1186/s12906-019-2624-3> PMID: 31405367
27. MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, et al. Revised STAndards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement. *PLoS Med*. 2010; 7(6):e1000261. Epub 20100608. <https://doi.org/10.1371/journal.pmed.1000261> PMID: 20543992.
28. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019; 366:l4898. <https://doi.org/10.1136/bmj.l4898> PMID: 31462531