International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Efficacy of Spleen-Invigorating Compound Formulas on Short Stature in Children: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 June 2026 and was last updated on 12 August 2026.

INTRODUCTION

Review question / Objective Objective: To compare the efficacy/safety of spleen-strengthening traditional Chinese medicine in the treatment of short stature in children.
P: children with short stature.
I: Oral Administration of Spleen-Strengthening Compound Traditional Chinese Medicine.
C: Conventional drugs or placebo.
O: Height, height velocity ,height SDS, bone age, IGF-1, IGFBP-3.
S: RCTs.

Condition being studied Short stature in children is defined as height ≤ −2 standard deviations below the mean for age, sex, and ethnicity, or below the 3rd percentile of the relevant reference population.

METHODS

Participant or population The systematic review and meta-analysis will include children diagnosed with short stature (SS). Participants will comprise children of any gender, age range (based on the pediatric cohort under investigation), and ethnicity.

Intervention Eligible interventions are oral traditional Chinese medicine compound formulas in which spleen invigoration is explicitly the principal therapeutic strategy. This judgement will be based on the treatment principle, formula name, key herbs, formula composition, or the authors' description.
The formula may be used alone or in addition to recombinant human growth hormone (rhGH). Formulas primarily focused on kidney tonification, essence replenishment, yin nourishment, or bone strengthening will be excluded. Formulas with an

unclear balance between spleen and kidney treatment will be considered only in prespecified sensitivity analyses.

Comparator The primary comparison will be an oral spleen-invigorating compound formula plus the same rhGH regimen versus rhGH alone. The rhGH dose, frequency, treatment duration, and background management should be comparable between groups. Studies comparing formula monotherapy with rhGH, placebo, or other treatments will be synthesised separately or narratively and will not be pooled with add-on designs.

Study designs to be included Only randomized controlled trials(RCTs) will be inlcuded in this study.

Eligibility criteria Eligible studies must meet all of the following criteria:

1. Participants are children with short stature.
2. The intervention is an oral traditional Chinese medicine compound formula in which spleen invigoration is the principal therapeutic strategy, used alone or in addition to rhGH.
3. For the primary comparison, the intervention group receives the formula plus rhGH and the control group receives the same rhGH regimen alone. Studies with formula monotherapy versus rhGH, placebo, or other treatments will be considered separately.
4. The study is a randomised controlled trial with a treatment duration of at least 12 weeks.
5. The study reports at least one prespecified growth, endocrine, skeletal, or safety outcome, including height, height velocity, height SDS, bone age, IGF-1, IGFBP-3, or adverse events.

Studies will be excluded if they are non-randomised studies, reviews, case reports, animal or in vitro studies, non-peer-reviewed dissertations, conference abstracts, or reports without usable outcome data. Studies in which oral Chinese medicine is combined with external traditional Chinese medicine therapies, such as acupuncture, massage, or tuina, will be excluded unless the independent effect of the oral formula can be separated. Formulas primarily focused on kidney tonification, essence replenishment, yin nourishment, or bone strengthening will be excluded from the strict primary analysis.

Information sources The following electronic databases will be searched from inception to the final search date: China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database, SinoMed/Chinese Biomedical Literature Database, PubMed, Embase, the Cochrane CENTRAL, and Web of Science Core Collection.

Reference lists of eligible studies and relevant systematic reviews will also be screened to identify additional studies. The full search strategies, dates, and numbers of records retrieved for each database will be documented. Searches will be updated within 1–2 months before manuscript submission.

Main outcome(s) Height, height velocity ,height SDS(HtSDS).

Data management Two reviewers will independently screen studies and extract data using a piloted standardised form. Extracted data will include study characteristics, participant characteristics, diagnostic criteria, intervention and comparator details, rhGH regimen, treatment duration, outcomes, adverse events, and risk-of-bias information. Disagreements will be resolved through discussion or consultation with a third reviewer.

Missing standard deviations or other variance data will not lead to automatic exclusion of an otherwise eligible study. Authors will be contacted where feasible. Where appropriate and reliable, missing standard deviations may be derived from standard errors, confidence intervals, P values, or other reported statistics. Studies with non-derivable data will be excluded only from the relevant quantitative analysis and retained for narrative synthesis.

Potentially overlapping reports will be assessed using author group, study centre, recruitment period, sample size, eligibility criteria, formula composition, intervention regimen, and follow-up duration. If overlap cannot be excluded, only the most complete report will be included in a given meta-analysis. Unreported adverse events will be recorded as “not reported” rather than interpreted as absence of adverse events.

Additional outcome(s) bone age, IGF-1, IGFBP-3.

Quality assessment / Risk of bias analysis The methodological quality of the included randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. Two reviewers will independently evaluate each study. Disagreements will be resolved through discussion, or by consultation with a third reviewer when necessary.

Strategy of data synthesis Meta-analysis will be conducted only when studies are clinically and methodologically comparable. Continuous outcomes will be analysed using mean differences when measured on the same scale and standardised mean differences when different scales are used. Dichotomous outcomes will be analysed using risk ratios. All effect estimates will be presented with 95% confidence intervals.
Outcomes will be grouped by actual follow-up or measurement windows, for example approximately 6 months, 9–12 months, and 12 months. Annualised height velocity derived from different observation windows will not be pooled directly. Height, height velocity, and height SDS will be analysed separately.

A random-effects model will be used as the primary model when at least two sufficiently comparable studies are available; fixed-effect analysis will be considered as a sensitivity analysis. Clinical and methodological comparability will be assessed before statistical pooling. Statistical heterogeneity will be assessed using the I^2 statistic and Cochran's Q test. When substantial heterogeneity cannot be adequately explained, a pooled estimate will not be presented and findings will be narratively synthesised. Publication-bias assessment will be considered only when at least 10 studies are available for an outcome.

Subgroup analysis Subgroup analyses will be conducted only when clinically justified and when sufficient studies are available for a given outcome. Potential exploratory subgroup factors include: (1) spleen-dominant formulas versus borderline spleen-kidney formulas; (2) add-on designs versus formula monotherapy designs; (3) follow-up or measurement window; (4) underlying aetiology of short stature; and (5) risk of bias and data completeness.

All subgroup findings will be interpreted as exploratory and will not be used as the sole basis for clinical conclusions.

Sensitivity analysis Sensitivity analyses will assess the robustness of pooled results by excluding studies with high risk of bias, studies with potentially unreliable or incomplete data, studies with borderline eligibility regarding the principal therapeutic role of spleen invigoration, and studies with potentially overlapping participant populations.

Where applicable, sensitivity analyses will also compare results using random-effects and fixed-effect models, and will assess the influence of individual studies through leave-one-out analyses. Any imputed or statistically derived variance data will be assessed in sensitivity analyses.

Country(ies) involved China.

Keywords Traditional Chinese Medicine (TCM); short stature (SS); spleen-strengthening; randomized controlled trial (RCT); meta-analysis; clinical efficacy.

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