International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Comparative Efficacy of Myopia Control Interventions in Children at 1-Year and 2-Year Follow-up: A Systematic Review and Network Meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202670068

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 July 2026 and was last updated on 18 July 2026.

INTRODUCTION

Review question / Objective To compare the efficacy of myopia control interventions (atropine at various concentrations, OK, DIMS, MFCLs, RLRL, and combination therapies) in children with myopia, assessed at two time points (1-year and 2-year follow-up), through parallel network meta-analyses. The primary outcome is the mean change in axial length (AL, mm). Secondary outcomes include change in spherical equivalent refraction (SER, D) and adverse events.

Rationale Myopia is a growing public health concern worldwide, with early-onset myopia increasing the risk of high myopia and associated ocular complications. Multiple interventions—including low-concentration atropine, orthokeratology (OK), defocus incorporated multiple segments (DIMS) spectacle lenses, multifocal contact lenses (MFCLs), and repeated low-level red-light (RLRL) therapy—have demonstrated efficacy in slowing myopia progression in children. However, existing network meta-analyses (NMAs) have predominantly focused on 1-year outcomes. Whether the comparative efficacy ranking changes at 2-year follow-up and which interventions provide the most sustained effect remain unclear. This evidence gap limits clinicians' ability to make evidence-based decisions regarding initial treatment selection and timing of regimen switching.

Condition being studied Not reported.

METHODS

Search strategy PubMed search strategy (adapted for other databases):
("myopia"[MeSH Terms] OR "myopia"[Title/Abstract] OR "myopic"[Title/Abstract]
OR "axial elongation"[Title/Abstract] OR "axial length"[Title/Abstract]
OR "refractive error"[Title/Abstract])
AND

("atropine"[Title/Abstract] OR "orthokeratology"[Title/Abstract]
OR "ortho-k"[Title/Abstract] OR "OK lens"[Title/Abstract]
OR "corneal reshaping"[Title/Abstract] OR "contact lens"[Title/Abstract]
OR "multifocal"[Title/Abstract] OR "DIMS"[Title/Abstract]
OR "defocus incorporated"[Title/Abstract] OR "peripheral defocus"[Title/Abstract]
OR "red light"[Title/Abstract] OR "low-level light"[Title/Abstract]
OR "RLRL"[Title/Abstract] OR "bifocal"[Title/Abstract]
OR "progressive addition"[Title/Abstract] OR "combination therapy"[Title/Abstract]
OR "combined therapy"[Title/Abstract])
AND
("randomized controlled trial"[Publication Type] OR "randomized"[Title/Abstract]
OR "randomised"[Title/Abstract] OR "RCT"[Title/Abstract]
OR "controlled clinical trial"[Publication Type])
AND
("child"[MeSH Terms] OR "children"[Title/Abstract]
OR "pediatric"[Title/Abstract]
OR "paediatric"[Title/Abstract] OR "school-age"[Title/Abstract]
OR "adolescent"[MeSH Terms])
Date limit: Inception to 18 July 2026.

Participant or population Children aged 6–14 years with myopia defined as cycloplegic spherical equivalent refraction (SER) ≤ −0.50 diopters (D).

Intervention Atropine eye drops (any concentration), orthokeratology (OK) contact lenses, defocus incorporated multiple segments (DIMS) spectacle lenses, multifocal soft contact lenses (MFCLs), peripheral defocus spectacle lenses, repeated low-level red-light (RLRL) therapy, or combination therapies (e.g., atropine + OK).

Comparator Single-vision spectacle lenses (SVL), placebo, or any other myopia control intervention listed above.

Study designs to be included Randomized controlled trials (RCTs) or randomized crossover trials (first-phase data only).

Eligibility criteria
Exclusion criteria: Non-randomized designs (cohort, case-control, retrospective, before-after, case series). Studies enrolling exclusively adults (≥18 years) or children with high myopia only (> −6.00 D) without a low-to-moderate group. Studies not reporting AL data. Studies with follow-up duration <1 year or not reporting both 1-year and 2-year data. Reviews, meta-analyses, conference abstracts, editorials, letters, or grey literature.

Information sources
Databases will be searched from inception to 18 July 2026:
• PubMed/MEDLINE
• Embase
• Cochrane Central Register of Controlled Trials (CENTRAL)
• Web of Science
• CNKI (China National Knowledge Infrastructure)
• Wanfang Data

Clinical trial registries: ClinicalTrials.gov, Chinese Clinical Trial Registry (ChiCTR).

Main outcome(s) Reported axial length (AL) change (mean ± SD or SE) at both 1-year (12 ± 3 months) and 2-year (24 ± 3 months) follow-up.

Data management Data management: All records will be imported into reference management software (EndNote or Zotero). Deduplication will be performed.

Selection process: Two reviewers will independently screen titles and abstracts against eligibility criteria. Full texts of potentially eligible studies will be retrieved and assessed independently by two reviewers. Disagreements will be resolved by consensus or a third reviewer.

Data collection: A standardized data extraction form will be used by two independent reviewers. Discrepancies will be resolved by discussion.
Data Items
For each included study, the following will be extracted:
• Study characteristics: author, year, journal, country, study design, sample size, funding
• Participant characteristics: age (mean ± SD), age range, baseline SER, baseline AL, sex distribution, ethnicity
• Intervention details: type, concentration/dose, frequency, duration
• Outcome data at 1-year (±3 months) and 2-year (±3 months): AL change (mean ± SD) and SER change (mean ± SD) for each group; number of participants analyzed at each time point
• Risk of bias items
Outcomes and Prioritisation
Primary outcome:
• Change in axial length (AL, mm) from baseline to 1-year and 2-year follow-up

Secondary outcomes:

• Change in spherical equivalent refraction (SER, D) from baseline to 1-year and 2-year follow-up
• Incidence of adverse events (photophobia, allergic conjunctivitis, blurred vision, corneal staining).

Quality assessment / Risk of bias analysis Two reviewers will independently assess risk of bias using the Cochrane Risk of Bias 2.0 tool (RoB 2) for randomized trials. Domains include: (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result. Each domain will be rated as "low risk," "some concerns," or "high risk." Disagreements will be resolved by consensus.

Strategy of data synthesis Network geometry: A network diagram will be generated for each time point (1-year and 2-year), with nodes representing interventions and edges representing direct comparisons.

Statistical analysis: Random-effects network meta-analysis will be conducted separately for 1-year and 2-year AL change data using a frequentist approach (R package netmeta). The pooled effect size will be reported as mean difference (MD) with 95% confidence intervals (CIs).

Heterogeneity: Global I^2 statistic for the network will be reported. If substantial heterogeneity (I^2 > 50%) is detected, prespecified subgroup analyses will explore sources.

Inconsistency: Local inconsistency will be assessed using node-splitting analysis. Global inconsistency will be assessed using the design-by-treatment interaction model.

Ranking: Treatment hierarchy will be presented using P-scores (frequentist analogue of SUCRA) for each outcome at each time point.

Subgroup and sensitivity analyses (if data permit):
• By baseline age (≤10 vs >10 years)
• By baseline myopia severity (low: −0.50 to −3.00 D vs moderate: >−3.00 to −6.00 D)
• By study region (Asia vs non-Asia)
• Leave-one-out sensitivity analysis
• Excluding studies with high risk of bias

Minimum data requirements: At least 5 studies per time point forming a connected network are required for NMA. For each intervention node, at least 2 studies are required.
Meta-bias(es)

Publication bias will be assessed using comparison-adjusted funnel plots and the Egger's test for asymmetry (where ≥10 studies are available per outcome).
Confidence in Cumulative Estimate
The confidence in the evidence for each NMA estimate will be evaluated using the Confidence in Network Meta-Analysis (CINeMA) framework, which considers within-study bias, across-studies bias, indirectness, imprecision, heterogeneity, and incoherence.

Subgroup analysis Not reported.

Sensitivity analysis Not reported.

Language restriction English or Chinese.

Country(ies) involved China.

Appendix: Key Information Summary

Search end date	18 July 2026
Primary outcome	Axial length (AL) change at 1 and 2 years
Analysis method	Frequentist random-effects NMA
Software	R (netmeta, meta)
Risk of bias	Cochrane RoB 2
Evidence quality	CINeMA
Contact	18608775531@163.com

Keywords Myopia; Network meta-analysis; Axial length; Atropine.

Contributions of each author
Author 1 – Wenji Wang – Guarantor; Protocol drafting; Search strategy development; Data extraction; Statistical analysis.