INPLASY PROTOCOL

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None declared.

Comparative Efficacy of 50 Interventions for Myopia Prevention and Control in Children: a Systematic Review and Network Meta-analysis

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Review question / Objective: **The purpose of this study was to analyze and compare the efficacy of different interventions for myopia prevention and control in children.**
Eligibility criteria: **Inclusion Criteria(1) Subjects aged 6 to 18 years old; (2) The language of the literature is limited to Chinese and English; (3) No restrictions are made on the ethnicity, course and refractive status of the subjects; (4) Interventions to delay the progression of myopia in children; (5) Outcomes: mean annual change in axial length and spherical equivalent; (6) The follow-up time is at least 1 year, and the longest follow-up years are taken for those greater than 1 year; (7) RCTs.Exclusion Criteria(1) Repeated publication, no full text found; (2) Review, experience, case report, conference, meta-analysis; (3) Failure to provide data suitable for meta-analysis; (4) Subjects aged < 6 years old or > 18 years old at the time of trial participation; (5) Non-randomized controlled trials.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 September 2022 and was last updated on 17 September 2022 (registration number INPLASY202290079).

INTRODUCTION

Review question / Objective: **The purpose of this study was to analyze and compare the efficacy of different interventions for myopia prevention and control in children.**

Condition being studied: **Myopia is a disease affecting nearly a quarter of the world's population, and the prevalence of myopia is expected to double by 2050. Approximately 100 million people in the United States are myopic, most of whom have been myopic since childhood. In some urban areas of East and South-East Asia, 80% to 90% of high school graduates**

suffer from myopia and approximately 20% from high myopia. Myopic populations in Europe and the Middle East also appear to be increasing, albeit at a slower pace. The rapid growth of the population of myopia raises concerns in the world.

In addition to decreased visual function due to optical defocus, myopia is associated with an increased risk of irreversible blindness, such as myopic macular degeneration, retinal detachment, and glaucoma. The risk of these complications increases with degrees of myopia. In addition, myopia has a substantial financial burden. For example, the spending on spectacles and contact lenses in the United States is up to $2 billion annually.

In many East and Southeast Asian countries, including China, there is a tendency for early-onset myopia in childhood under educational pressure. More than half of school-aged children are about 80% myopic by the end of school. Early-onset myopia often leads to faster progression and a longer duration of myopia. Thus early-onset myopia increases the risk of high myopia and sight-threatening complications in later life. Myopic macular degeneration is predicted to cause irreversible visual impairment and even blindness in 55.7 million people worldwide in 2050. Therefore, it is important to delay myopia progression in childhood.

It can be seen that the widespread prevalence and incidence of myopia are increasing, resulting in the occurrence of related diseases affecting vision and the accompanying decline in the quality of life, as well as the huge cost incurred to correct myopia, which has made myopia a major public health problem.

At present, there is no effective way to prevent the occurrence of myopia. The main methods to control myopia include spectacles (bifocal spectacles, prism bifocal spectacles, progressive multi-focal spectacles, peripheral defocus spectacles), contact lenses (nightwear orthokeratology, multi-focal soft contact lenses), outdoor activities, drugs and low-level red light mainly. These studies were based on clinical observations, myopic animal models, or both. Trials of such interventions provided a substantial evidence base. However, most studies are of a single intervention versus controls, lacking direct head-to-head comparisons. There are many inconsistencies among trials studying the same intervention. Conventional meta-analyses enable comparisons between two interventions only, do not enable comparisons between multiple treatments, and most meta-analyses give statistical advice only on the efficacy of a single intervention. In clinic, two or more combined measures are often combined to treat myopia, especially myopia progressing rapidly. Previously, the additive effect of combined intervention in preventing and controlling myopia has been proposed. However, its conclusion still needs to be supported by a large amount of evidence. Therefore, this network meta-analysis directly or indirectly compared the efficacy of 50 interventions, including combined interventions, and ranked them to provide more comprehensive and reliable evidence-based medical recommendations for preventing and controlling myopia in children.

METHODS

Participant or population: Subjects aged 6 to 18 years old; No restrictions are made on the ethnicity, course and refractive status of the subjects.

Intervention: Interventions to delay the progression of myopia in children.

Comparator: Blank control, placebo, single vision spectacle lenses or single vision corneal contact lenses were designated as controls in this study.

Study designs to be included: RCT.

Eligibility criteria: Inclusion Criteria(1) Subjects aged 6 to 18 years old; (2) The language of the literature is limited to Chinese and English; (3) No restrictions are made on the ethnicity, course and refractive status of the subjects; (4) Interventions to delay the progression of

myopia in children; (5) Outcomes: mean annual change in axial length and spherical equivalent; (6) The follow-up time is at least 1 year, and the longest follow-up years are taken for those greater than 1 year; (7) RCTs.Exclusion Criteria(1) Repeated publication, no full text found; (2) Review, experience, case report, conference, meta-analysis; (3) Failure to provide data suitable for meta-analysis; (4) Subjects aged < 6 years old or > 18 years old at the time of trial participation; (5) Non-randomized controlled trials.

Information sources: A systematically electronic literature search was conducted using the databases of PubMed, Cochrane Library, Web of Science and EMBASE and ClinicalTrials.gov in English and the CNKI (http://www-cnki-net-s.vpn.uestc.edu.cn:8118/), Wan-Fang (http://www-wanfangdata-com-cn-s.vpn.uestc.edu.cn:8118/index.html), VIP (http://qikan.cqvip.com/), Chinese Biomedical Literature Service System (http://www.sinomed.ac.cn/index.jsp) and Chinese Clinical Registry in Chinese (up to July 2022). The search strategy is presented in the Appendix. To identify relevant studies, we also examined reference lists from clinical trials, meta-analyses, and systematic review reports.

Main outcome(s): Primary Outcome Measures: The mean annual change in axial length (millimeters/year) and mean annual change in refraction (diopters/year).

Quality assessment / Risk of bias analysis: The quality of the included RCTs was assessed using the Cochrane Collaboration's risk-of-bias method and the modified Jadad scale, respectively, including a description of the method of randomization, allocation concealment, blinding, completeness of data, selective reporting of results, and other sources of bias. The Cochrane Collaboration's risk-of-bias tool rated each item area as having a 'low', 'high', or 'unclear' bias risk; a modified Jadad scale total score of 4-7 was assigned to high-quality studies and 1-3 to low-quality studies. In order to ensure the reliability of the screening process and avoid subjective bias, the literature screening and methodological quality evaluation were independently completed and checked by two investigators. Disagreements during the screening process were resolved through negotiation, and if there were differences, they were decided by the tutor (a third party).

Strategy of data synthesis: Network meta-analysis was performed on continuous variable data using Stata17.0 software. Inconsistency tests were used to analyze global inconsistency between direct and indirect evidence, with $P > 0.05$ considered no inconsistency, and a consistency model was fitted, whereas an inconsistency model was fitted. Local inconsistency tests for direct and indirect comparisons were performed using the node splitting method, and $P > 0.05$ was considered no local inconsistency. Measurement data were presented as weighted mean difference (WMD) and its 95% confidence interval (CI). In statistics, $P < 0.05$ indicates a significant difference and vice versa. Intervention efficacy was ranked according to the surface under the cumulative ranking area (SUCRA), with a larger area under the curve indicating better intervention efficacy. Publication bias was assessed using funnel plots when more than 10 included articles, and publication bias was assessed by visual inspection of the symmetry of the distribution of each point on funnel plots.

Subgroup analysis: No subgroup analysis.

Sensitivity analysis: No senstivity analysis.

Language restriction: Search in Chinese and in English.

Country(ies) involved: China.

Keywords: Myopia; Interventions; Prevention; Control; Efficacy.

Contributions of each author:

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