# Observational Study Protocol Template

**Project Title: Study on the Efficacy of Different Intervention Methods for Progressive Myopia After Wearing Orthokeratology Lenses**

## Research protocol version: 1.0, March 9, 2026

## Project Leader: He Meinan

## 1. Research Background and Project Justification

Myopia has become a major global issue affecting the visual health of children and adolescents. Research by Holden BA et al. estimates that by 2050, the prevalence of myopia and high myopia will significantly increase worldwide, affecting nearly 5 billion and 1 billion people respectively, with particularly prominent impacts in East Asia. Data from the China CDC show that in 2022, the overall myopia rate among Chinese children and adolescents was 51.9% (elementary school students: 36.7%, junior high school students: 71.4%, senior high school students: 81.2%).

The continuous rise in myopia prevalence and the increasing incidence of complications associated with high myopia will have multifaceted socioeconomic impacts2. The elongation of the eye axis caused by high myopia elevates the risk of various ocular diseases, such as cataracts and glaucoma, not only exacerbating the healthcare burden but also increasing the incidence of ocular complications3. Therefore, preventing myopia onset and controlling axial length progression have become critically important4.

Orthokeratology lenses (Ortho-k) represent the only non-surgical method that does not require daytime optical correction and are currently regarded as a first-line intervention for myopia control5-7. These lenses induce temporary corneal surface remodeling and reduce daytime myopia by wearing specially designed, breathable contact lenses with reverse geometric patterns at night8-9. In children with mild to moderate myopia, they have demonstrated excellent visual correction efficacy ranging from 80% to 92%10-11. However, their efficacy in myopia control may be inferior to that in myopia correction. Compared to the control group, orthokeratology lenses show therapeutic effects of 43−63% in slowing axial length progression. Despite lens use, approximately 15% of children still exhibit annual axial length progression exceeding 0.36 mm12-13.

Currently, interventions for myopia control in children primarily include orthokeratology (OK), repeated low-level red-light therapy (RLRL), and low-dose atropine (AT). In recent years, researchers have begun exploring whether the combined use of these methods can produce synergistic effects to more effectively delay myopia progression.

Tang Wenting et al. reported that low-concentration atropine (0.01%) combined with orthokeratology lenses for myopia correction in adolescents resulted in significant improvements in parameters such as refractive error, corneal curvature, and CCT compared to orthokeratology lenses alone, with good safety profiles. The 0.01% atropine eye drops used in combination may exert an effect on controlling further progression of axial length (AL) by altering scleral morphology and thickening the nerve fiber layer. In other related studies, Zhu Xianfeng et al. reported that the combination of 0.01% atropine eye drops and orthokeratology lenses for treating high myopia in adolescents showed reduced AL progression compared to orthokeratology lenses alone. Kinoshita et al. conducted a study on children aged 8−12 years, demonstrating that the AOK group exhibited more effective AL growth retardation (0.09 mm−0.19 mm) compared to the 0K lens group. Additionally, Tan et al. investigated children aged 6−11 years with standard error of measurement (sE) ranging from −1.00 to −4.00 D, finding that AL growth in the AOK group was delayed by 0.09 mm in the first year of treatment compared to the 0K lens group, and by 0.17 mm after two years of treatment. Zhao et al. reported that AL growth in children aged 5−14 years treated with AOK or 0K lenses for one year was 0.14 mm and 0.29 mm, respectively. Another study involving children aged 8−12 years22 demonstrated that after a 1-year treatment course, the AOK group achieved a 17% delay in axial length (AL) progression (0.20 mm in the AOK group vs. 0.24 mm in the control group). However, the 2-year study results from Zhou et al.23 showed that compared to monotherapy with 0.1 $g \cdot L^{-1}$ atropine, the AOK group exhibited significantly better efficacy in delaying refractive progression. In terms of AL growth control, however, the two groups showed comparable outcomes, with values of (0.50±0.17) mm and (0.61±0.21) mm, respectively.

The posterior optical zone diameter (BOZD) of orthokeratology lenses is one of the most critical parameters in custom orthokeratology lens design. Studies have demonstrated that reducing BOZD can effectively decrease the treatment area while increasing the steepening area and degree in the central corneal region24-26. However, in 2013, Kang et al.24 first modified lens design parameters to attempt orthokeratology lenses with a smaller BOZD (5 mm) and steeper peripheral tangents, but failed to observe significant changes in peripheral refractive error or corneal topography morphology among subjects. Guo et al.272021 found during 6-month and 12-month follow-ups that patients wearing KATT orthokeratology lenses with a 5 mm BOZD exhibited significantly less axial length progression compared to those with a 6 mm BOZD group. Although the correlation between axial length progression and treatment area size was weak ($r^2$ = 0.15), the results indicated that orthokeratology lenses with a smaller 5 mm BOZD were more effective in controlling axial length growth. Li et al.282023 reported that at 12-month follow-up, patients in the 5 mm BOZD group showed significantly lower axial length progression than those with a 6.2 mm BOZD group, with axial length progression reduced by 53.6% in the smaller BOZD group.

The study by Xiong et al. demonstrated that for children who experienced at least 0.50 mm of axial length progression within one year of Ortho-k wear, combining RLRL therapy with Ortho-k significantly outperformed Ortho-k alone in slowing axial length growth. While the safety profile of this combined approach appears promising, further long-term research is required for comprehensive evaluation. Clinically, these findings hold significant implications, as they indicate that although Ortho-k treatment enables children to achieve clear daytime vision without glasses, incorporating RLRL therapy may yield greater efficacy in reducing axial length progression compared to Ortho-k monotherapy, thereby achieving satisfactory myopia control.

Current studies indicate that combination therapies involving orthokeratology lenses, low-intensity red light therapy, and low-concentration atropine exhibit a synergistic trend in enhancing myopia control effects.

# 2. purpose of research

Myopia prevention and control is not only a critical issue in ophthalmology but also an essential component of public health. With the rising prevalence of myopia, effective strategies to manage its progression, particularly slowing axial length growth, have become a focal point of current research. Although orthokeratology (OK) lenses demonstrate certain efficacy in myopia control, suboptimal outcomes have been observed in some pediatric patients, necessitating novel therapeutic approaches. Low-intensity red light therapy (LLRT), as an emerging treatment modality, has garnered significant attention in recent years; however, its application in combination therapies remains inadequately studied. Consequently, this study holds substantial theoretical and practical significance. The objective of this study was to conduct a comparative analysis of different prevention and control strategies for myopia management in 8-12-year-old children at Tianjin Medical University Eye Hospital who exhibited suboptimal axial length control (annual growth>0.3 mm) after one year of orthokeratology lens wear, aiming to provide real-world clinical data and scientific evidence for progressive myopia management protocols.

# 3. research design

## 3.1 Study Site and Study Population

This study aims to evaluate the efficacy of orthokeratology (OK) lenses used alone versus combined with other myopia control methods in children aged 8-12 years through systematic review and comparative analysis, with particular focus on axial length increase exceeding 0.3 mm after 1 year of OK lens wear. By comprehensively analyzing the advantages and limitations of different strategies, this study provides a scientific basis for developing personalized myopia control plans.

## 3.2 Method for Determining Required Sample Size in Research

This study screened children who had undergone follow-up for at least one year and exhibited annual axial length progression>0.3 mm from 3,890 individuals who visited the optometry clinic and myopia prevention clinic at the Ophthalmology Hospital of Tianjin Medical University between November 2019 and June 2023, and who were fitted with orthokeratology lenses. These participants were included in the study.

Inclusion criteria were:

1) Age 8 to 12 years;

2) Binocular SE range: 0 to-6.00 D;

3) Best corrected visual acuity in both eyes ≥1.0;

4) It ensures nightly wearing of orthokeratology lenses for 8 to 10 hours;

5) No history of ocular trauma or surgical intervention;

6) No history of acute or chronic ocular inflammation, such as keratoconjunctivitis or lacrimal dysfunction;

7) Care for the lenses as prescribed by the physician and undergo regular standardized follow-up examinations;

8) Standardize the use of 0.1 g·L-1 atropine, red light therapy, and other medications or interventions for myopia progression control;

9) Complete follow-up data.

Exclusion criteria:

1）After one year of wearing orthokeratology (OK) lenses, the axial length increase in both eyes was less than 0.30 mm.

2）Severe complications occurred during this period (such as recurrent corneal inflammation);

3）Cases with incomplete data or lost to follow-up;

4）The equivalent spherical refractive error (SE) of both eyes ranges below-6.00D, with astigmatism below-2.00D.

5）During the use of orthokeratology (OK) lenses, visual acuity was unstable, with multiple readings below 0.2 (LogMAR).

6）Change the brand of orthokeratology lenses.

## 3.3 Survey Content

1. Evaluate the overall myopia prevention and control outcomes for children aged 8-12 years wearing orthokeratology lenses at Tianjin Medical University from November 2019 to June 2023.

2. Evaluate children who experience an axial length increase exceeding 0.3 mm after one year of orthokeratology lens wear, selecting different prevention and control strategies. Monitor axial length growth at 3 months, 6 months, and 12 months, compare the control efficacy between groups after combined prevention and control measures, and conduct intergroup comparisons prior to implementing combined prevention and control strategies.

3. Analysis of parental myopia history (e.g., whether parents have myopia or high myopia), age of onset of myopia in children, and the impact of initial myopia degree on refractive error and axial length in children with myopia.

## 3.4 Data Management and Statistical Analysis Plan

1. Data Sources and Collection

This study was an observational clinical study, with all data derived from routine diagnostic and treatment records of participants, including ophthalmic examination data, medical history records, intervention measures documentation, and follow-up materials, without additional unnecessary examinations. All data were collected promptly, accurately, and comprehensively by investigators who underwent standardized training, following uniform criteria and standardized forms.

2. Data Recording and Entry

The study data were recorded using paper case report forms or electronic data systems to ensure legible handwriting and complete content. Data entry was performed by designated personnel, with critical data undergoing dual-entry verification to minimize errors. Logical and scope checks were implemented during the entry process, and any abnormal data were promptly cross-checked against original records for correction.

3. Data Traceability and Authenticity

All research data can be traced back to original medical records, examination reports,

imaging materials, and equipment logs. Any data modifications shall retain modification traces, specifying the modifier, modification date, and rationale, to ensure data authenticity and traceability, with no arbitrary deletion or alteration of data.

Statistical Analysis Section: Statistical analysis was performed using SPSS v.25 statistical software (SPSS Corporation, USA). Quantitative parameters were expressed as mean ± standard deviation. The normality of data distribution was assessed using the Shapiro-Wilk test. Qualitative parameters were presented as frequency and percentage. Differences in gender distribution between groups were compared using the chi-square test. Differences in baseline age, baseline equivalent spherical curvature, baseline axial length, baseline annual axial length growth rate, and axial length growth rates at 6 months and 12 months post-treatment were analyzed using one-way ANOVA. Post-hoc Bonferroni analysis was employed to compare pairwise differences. The proportion of patients with stable progression (AL growth ≤ 0.18 mm/year) was compared among OK group, OKA group, OKBC group, and OKRL group using the chi-square test. A P-value <0.05 was considered statistically significant.

## 3.5 Bias Control

This study is a retrospective observational study, with bias control primarily achieved through the following measures:

1. Selection bias: Cases were strictly screened according to predefined inclusion/exclusion criteria, with only pediatric patients who underwent complete ophthalmology follow-up of ≥12 months at our hospital from November 2019 to June 2023 being included to avoid baseline imbalance between groups caused by selective enrollment.

2. Confounding bias: Collect and balance baseline characteristics between groups (age, gender, baseline refractive error, corneal curvature, axial length, etc.). If significant differences exist between groups, propensity score matching (PSM) or multivariate regression analysis will be employed for correction. Standardize follow-up time windows and examination procedures to avoid measurement bias caused by variations in follow-up intervals or examination equipment.

3. Information bias: All clinical data were obtained from the hospital's medical record system and standardized examination database, with independent data extraction performed by two

investigators. Inconsistent data were reviewed by a third party to ensure accuracy. Examination equipment underwent regular calibration, and operators received standardized training to minimize measurement errors.

4. Loss-to-follow-up bias: Only cases with complete follow-up data were included. Cases with loss-to-follow-up were explicitly excluded from the eligibility criteria, and the reasons for loss-to-follow-up as well as potential impacts were explained in the discussion section.

## 3.6 Quality Management

1. Data Management: Establish standardized electronic data entry forms and implement logical validation rules for key parameters such as refractive power, axial length, intraocular pressure, and corneal topography to prevent input errors. Adopt a dual-entry system with cross-verification, and have senior physicians review critical data (e.g., axial length variation) for confirmation.

2. Process Standardization: Develop a unified Standard Operating Procedure (SOP) for Case Screening and Data Extraction, specifying inclusion/exclusion criteria, data extraction fields, and time nodes. Regularly conduct quality control meetings and perform random sampling of 10% cases for data traceability to ensure the study process is traceable.

3. Equipment and Personnel Quality Control: Devices such as optometers, axial length meters, and tonometers are calibrated regularly in accordance with national metrological requirements, with self-inspections conducted prior to each inspection. All researchers involved in data extraction and analysis undergo standardized training and are only permitted to participate in the study after passing the assessment to minimize operational variability.

## 3.7 Safety Evaluation

1. Definition of adverse events: The adverse events of interest in this study included corneal epithelial injury, conjunctivitis, dry eye, elevated intraocular pressure, rapid progression of myopia (axial length increase>0.3 mm/6 months), and other ocular abnormalities associated with orthokeratology lenses, low-concentration atropine, or low-intensity red light.

2. Adverse event collection: By reviewing electronic medical records, extract ocular discomfort, physical sign changes, and management measures recorded during each follow-up

visit, and classify them according to severity (mild/moderate/severe) and relevance (definitely relevant/likely relevant/may be relevant/irrelevant).

## 3.8 Ethical Review and Informed Consent

1. Subject Protection: This study is a retrospective observational study that exclusively utilizes de-identified clinical routine diagnostic and treatment data, without involving additional interventions or invasive examinations, in compliance with the ethical requirements of the Declaration of Helsinki and China's Measures for the Ethical Review of Biomedical Research Involving Human Subjects.

2. Ethics Committee Application: The research protocol, data acquisition statement, and informed consent exemption application have been submitted to the Ethics Committee of our institution, clearly outlining the research objectives, methods, scope of data usage, and confidentiality measures. The study may only commence after approval by the Ethics Committee.

3. Benefits and Risks:

Risks: There is only an extremely low risk of information leakage, which has been mitigated through data de-identification, encrypted storage, and access control management. Benefits: The research findings will provide real-world evidence for optimizing myopia control strategies in children, benefiting more pediatric patients and their families.

4. Confidentiality Measures: All cases are assigned unique study identifiers, with personal identifiers such as names, ID numbers, and contact information removed, retaining only clinically relevant data related to the study. The research data is stored on encrypted servers, accessible exclusively by the principal investigator and data administrator. After study completion, data must be retained for at least 5 years in accordance with regulations. When publishing papers, only aggregated data is utilized, with no disclosure of any personally identifiable information.

# 4. References


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# 5. appendix

Signature of the principal investigator: Meinan He

Date: 9 March 2026

Recommended reference materials: 1. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. http://www.equator-network.org/reporting-guidelines/strobe/

# Waiver of Informed Consent Application

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|---|---|---|---|
| project name | Effectiveness of Different Interventions for Progressive Myopia After Wearing Orthokeratology Lenses | | |
| Project source | IIT study | | |
| Solution version number | 1.0 | Version date of the solution | 9 March 2026 |
| Responsible Department | Optometry Center | Principal Investigator | He Meinan |

**1. Application for exemption from informed consent based on research utilizing medical records/biochemical specimens obtained from previous clinical diagnosis and treatment**

·This study is an observational study utilizing medical records/biological specimens obtained from previous clinical diagnosis and treatment: ☑ Yes, No

·The research purpose is significant: ☑Yes, or No

The study poses no greater risk to subjects than that encountered in daily life, routine physical examinations, or psychological testing: ☑Yes, No

·Exemption from informed consent will not adversely affect the rights and health of subjects: ☑Yes, No

·Subject privacy and personal identity information are protected: ☑ Yes, No

·If obtaining informed consent is stipulated, the study cannot proceed (patients have the right to be informed that their medical records/samples may be used for research; their refusal or disagreement to participate does not constitute evidence of study non-implementation or exemption from informed consent): Verbal consent

(Please specify:_____) , ☑ deny

·This study does not utilize medical records or specimens that the patient/subject has previously explicitly refused to provide: ☑ Yes, No

**II. Research on secondary utilization of medical records/biological specimens and application for exemption from informed consent**

· This study aims to explore the secondary utilization of medical records and biological specimens, specifically utilizing medical records or specimens collected through prior research projects with informed consent. Application for exemption from informed consent: yes, no

· Previous studies have obtained written consent from participants, permitting other research projects to utilize their medical records or specimens: yes, no

·This study complies with the original informed consent requirements: yes, no

·The privacy and confidentiality of subjects' identity information are guaranteed: yes or no

| | | | |
|---|---|---|---|
| Signature of the applicant | Meinan He | date | 9March 2026 |