RESEACH STUDY PROTOCOL

PROTOCOL TITLE:
A pilot evaluation of progression of refractive error in a pre-myopic population in Singapore with no treatment versus myopia control spectacles

PROTOCOL NUMBER:

VERSION NUMBER: **5**

VERSION DATE: **04 May 2026**

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PROTOCOL SIGNATURE PAGE

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Declaration of Investigator

I confirm that I have read the above-mentioned protocol and its attachments. I agree to conduct the described study in compliance with all stipulations of the protocol, regulations and ICH E6 Guideline for Good Clinical Practice (GCP).

Foo Li Lian

Name of Principal Investigator:

X

Foo Li Lian
Dr

Signature of Principal Investigator:

04/05/26

Date:

SNEC Myopia Centre

Name of Study Site:

Note:
- This page should be signed with wet-ink signature or digital signature. Do not paste digital image of a wet-ink signature.

- Signed copies of this signature page should be stored in the study file and in the respective study site's investigator file.

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1. BACKGROUND AND RATIONALE

Myopia is a 'global epidemic' owing to its rapid rise in prevalence across the world. Half of the world's population is expected to be myopic by the year 2050 (Holden et al. 2016). Myopia significantly affects the quality of life of an individual and is an economic burden to both the individual and the society on account of the costs involved in living with myopia (Sankaridurg et al. 2021). In addition, high myopia increases the risk of ocular morbidity such as retinal detachment, cataract, glaucoma which could lead to blindness. Several optical and pharmaceutical strategies developed over the recent years have been shown to control or slow the progression of myopia (Wildsoet, 2019; Sankaridurg, 2023; Bullimore et al., 2025).

However, there remains a critical knowledge gap in our understanding of refractive error progression during the pre-myopic phase, a period that precedes the onset of clinically manifest myopia and may represent a key window for early intervention. As such, increasing attention has been directed towards identifying children at risk of developing myopia and implementing preventive strategies before myopia onset, including those summarized in the IMI interventions for controlling myopia onset (Bullimore et al., 2025). Although it has been reported that interventions in the pre-myopic phase can be successful in slowing refractive error shift, much work remains to understand ocular development during this phase, and particularly the needs and motivation of pre-myopic children and their carers. For example, since the eye is not yet myopic, this group may demonstrate lower compliance with any prescribed modality. Furthermore, given the young age of this cohort (commonly 4 to 6 years in East Asia), there may be specific requirements that need to be better understood. In particular, the potential role of myopia control spectacle lenses, as highlighted in the IMI recommendations, in influencing refractive development in pre-myopic children remains inadequately explored. Understanding whether such optical interventions can modify refractive trajectories in this at-risk population may have important implications for early myopia prevention strategies.

2. HYPOTHESIS AND OBJECTIVES

We hypothesise that pre-myopic children randomised to ZEISS MyoActive lenses will demonstrate a reduced rate of progression to clinical myopia, defined by cycloplegic spherical equivalent ≤ –0.50 D, compared with children wearing single-vision spectacle lenses over the study duration.

Primary Objectives

To evaluate the change in cycloplegic objective spherical equivalent refractive error with ZEISS MyoActive spectacle lenses compared to plano single vision (SV) spectacles over 12 months of wear.

Secondary Objectives

- To determine motivation to use of interventions to slow refractive error shift in carers of children with pre-myopia.

• To evaluate the change in axial length with ZEISS MyoActive spectacle lenses compared to the SV control group over 12 months of lens wear.

- To determine compliance to use of optical intervention to slow refractive error shift in children with pre-myopia.

• To assess differences in choroidal thickness between children wearing ZEISS MyoActive lenses and those wearing SV.
• To assess the safety, tolerability (quality of life (QoL)), and adherence to ZEISS MyoActive lens wear compared to SV in premyopic children.

3. EXPECTED RISKS AND BENEFITS

There were no reported adverse events associated with the wear of myopia control spectacles and plano single vision spectacles. Myopia control spectacle lenses are available in the marketplace and successfully worn by children.

Cycloplegic refractions do require eyedrops which cause pupil dilation or blur. This is temporary are part of routine eye examination.

Children may benefit from early intervention to delay the onset of myopia.

4. STUDY POPULATION

4.1. List the number and nature of subjects to be enrolled.

50-124 children aged 6 to 12 years, both male and female will be enrolled. Only children with no systemic or ocular anomalies will be recruited.

4.2. Criteria for Recruitment and Recruitment Process

Participants will be screened for general suitability by way of general eye health and visual acuity. Those who fit the inclusion criteria below will be approached by the investigator for their interest in joining the study and informed consent performed. Assent and Informed consent will be obtained once only prior to any study related procedures. The participant's involvement remains voluntary, and they are permitted to withdraw from the study at any time.

4.3. Inclusion Criteria

Participants enrolled in the trial must:

a. be accompanied by a parent or guardian who is able to read and comprehend English and sign a record of informed consent/assent;
b. be able to understand and participate in the Assent process;
c. at baseline, be within the age range of 6 to 12 years old inclusive;
d. No prior spectacle correction
e. Cycloplegic spherical equivalent (SE) 0.00 to + 2.00 D
f. Astigmatism of less than -1.50D
g. Anisometropia of not more than 1.50D
h. At least 1 parent or more with myopia

4.4. Exclusion Criteria

Participants enrolled in the trial must NOT have:

- Any pre-existing systemic or ocular condition, including infection or disease that is likely to affect visual acuity and refractive error;
- Any systemic disease that adversely affects ocular health e.g. diabetes, Graves disease, and auto-immune diseases such as ankylosing spondylitis, multiple sclerosis, Sjögrens syndrome and systemic lupus erythematosus.
- Use of or a need for any systemic medication or topical medications which may alter normal ocular findings / are known to affect a participant's ocular health / physiology in an adverse or beneficial manner at enrolment and/or during the study. NB: Systemic antihistamines are allowed on an "as needed basis", provided they are not used prophylactically during the trial and at least 24 hours before the study product is used.
- History of eye trauma
- Amblyopia
- Strabismus
- History of any form of optical correction
- Any concomitant myopia control treatment including atropine eyedrops, contact lenses or other myopia control glasses.

The Investigator may, at their discretion, exclude anyone who they believe may not be able to fulfil the study requirements or it is believed to be in the participant's best interests.

5. STUDY DESIGN AND PROCEDURES/METHODOLOGY

Primary endpoint
Twelve-month change in cycloplegic objective spherical equivalent refractive error from baseline and between test and control groups.

Secondary endpoint

- **Percent of carers of pre-myopic children interested in interventions to slow refractive error shift.**
- Twelve-month change in axial length from baseline and between test and control groups.
- Twelve-month change in choroidal thickness from baseline and between test and control groups.
- Subjective responses and compliance to study spectacle lens wear.

A randomisation list will be generated by the biostatistician and applied through the REDCap randomisation module hosted at the Singapore Eye Research Institute (SERI) Clinic Data Management system.

The randomisation code will be applied by a Clinical Research Coordinator (CRC) prior to the baseline visit, and clearly documented. The Investigator(s) will not have access to this randomisation code until the trial is completed and final study data locked and analysis performed. At baseline visit, participants will be randomised to either the test or the control group.

Study Visits and Procedures

Prior to the initial assessment visit, participants will be given the opportunity to read the Participant Information/Informed Consent Form and contemplate participation undisturbed. An opportunity will be provided to answer any question a study participant may have relating to the study. The participant will then be randomized to either the study group or the control group.

All clinical study visits will allow up to 60 - 90 minutes. The study will consist of an initial baseline visit, a visit after 1-2 weeks for dispensing, 4 weeks after dispensing (phone call only), 6 months, 6 months dispensing (if change of prescription is required), and 12 months. For all study groups, the visits are as outlined in the flow chart (Figure 1) and the clinical procedures to be performed are listed in Table 3.

At the 6-month visit, lenses may be replaced if there is a change of refraction by -0.75D or more. Pupillary distance will be measured should glasses require replacing, and dispensing visit will be scheduled.

Study Visit Schedule and Procedures

1. Baseline Visit (Pre-intervention)
At the baseline visit, participant eligibility will be confirmed according to the study inclusion and exclusion criteria. The following assessments and procedures will be conducted:

- Collection of brief medical and ocular history.
- Measurement of distance and near visual acuity.
- Measurement of pupil size and interpupillary distance (non-dilated).
- Comprehensive ocular examination following administration of cycloplegic eye drops to temporarily paralyse accommodation and dilate the pupils.
- Cycloplegic autorefraction and cycloplegic subjective refraction for accurate determination of refractive error.
- Axial length measurement using a non-contact optical biometry device.
- Choroidal thickness measurement using optical imaging.
- Administration of a short questionnaire to assess motivation for intervention, visual function, and lifestyle factors.
- If deemed eligible, the participant will select a study spectacle frame.

No study spectacles will be dispensed at this visit.

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2. Dispensing Visit (Day 1)
Participants will return to collect the allocated study spectacles (either ZEISS MyoActive or single-vision lenses). Distance visual acuity and fitting will be assessed to ensure appropriate clarity, comfort, and lens positioning.

3. 4-Week Follow-up (Telephone Call)
A brief telephone follow-up will be conducted to assess:

- Comfort with spectacle wear
- Compliance and daily wear time
- Any adverse events, concerns, or difficulties

No in-clinic assessment is required at this time point.

4. 6-Month Follow-up Visit (Day 180 ± 60 days)
Participants will attend an in-person follow-up visit, during which the following procedures will be performed:

- Measurement of distance and near visual acuity
- Administration of cycloplegic eye drops and cycloplegic refraction
- Axial length measurement
- Choroidal thickness measurement
- Completion of the study questionnaire
- Review of spectacle compliance and wear time

If a change in refractive prescription is indicated, updated study spectacles will be prescribed and dispensed at a separate dispensing visit.

5. Dispensing Visit (If Prescription Changes)
For participants requiring a change in refractive correction at the 6-month visit, new study spectacles will be dispensed. Visual acuity and spectacle fitting will be assessed.

6. 12-Month Final Visit (Day 360 ± 120 days)
At the final study visit, the following assessments will be repeated:

- Measurement of distance and near visual acuity
- Administration of cycloplegic eye drops and cycloplegic refraction
- Axial length measurement
- Choroidal thickness measurement
- Completion of the study questionnaire
- Review of spectacle compliance and wear time

Table 1: Assessment of variables and window period for each visit

Procedures / Data	Baseline visit	Dispensing (Day 1)	4-week visit (phone call only)	6-month visit (Day 180 ± 60 days)	Dispensing (if change of prescription)	12-month visit (Day 360 ± 120 days)
Assent/Informed consent form	✓	-	-	-	-	-
Meet inclusion / exclusion criteria	✓	-	-	-	-	-
History/interview	✓	-	-	-	-	-
Visual acuity (VA) at distance and near (habitual and BCVA)	✓	✓	-	✓	✓	✓
Non-cyclo pupil size	✓	-	-	-	-	-
Non-cyclo pupil distance	✓	-	-	-	-	
Cycloplegia	✓	-	-	✓	-	✓
Cycloplegic autorefraction	✓	-	-	✓	-	✓
Axial length measurement	✓	-	-	✓	-	✓
Choroidal thickness	✓	-	-	✓	-	✓
Cycloplegic subjective refraction	✓	-	-	✓	-	✓
Study frame selection	✓	-	-	-	-	-
Study spectacles dispensing	-	✓	-	-	✓	-
Questionnaire	✓	-	✓	✓	-	✓
Compliance	✓	-	✓	✓	-	✓

6. SAFETY MEASUREMENTS

6.1. Definitions

Serious adverse event (SAE) in relation to human biomedical research, means any untoward medical occurrence as a result of any human biomedical research which:

- results in or contributes to death
- is life-threatening
- requires in-patient hospitalisation or prolongation of existing hospitalisation
- results in or contributes to persistent or significant disability/incapacity or
- results in or contributes to a congenital anomaly/birth defect
- results in such other events as may be prescribed

Adverse event (AE) in relation to human biomedical research means any untoward medical occurrence as a result of any human biomedical research which is NOT serious. Adverse event can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease possibly/ probably/ definitely associated with the participant in the human biomedical research.

6.2. Collecting, Recording and Reporting of Serious Adverse Events (SAEs) to CIRB

The reporting requirements will be in accordance to the reporting requirements published on CIRB website at the time when the event took place.

Only related SAEs (definitely/ probably/ possibly) will be reported to CIRB. Related means there is a reasonable possibility that the event may have been caused by participation in the research.

The investigator is responsible for informing CIRB after first knowledge that the case qualifies for reporting. Follow-up information will be actively sought and submitted as it becomes available.

Related AEs will not be reported to CIRB. However, the investigator is responsible to keep record of such AEs cases at the Study Site File.

6.3. Safety Monitoring Plan

Patients are given follow up appointments to monitor their condition. They are also given contact numbers to allow for self-reporting of major issues or clarification purposes.

6.4. Complaint Handling

Subjects and their parents/guardians will be informed of their ability to contact the study coordinators for any complaints during the study period. They will be provided with contact information. Investigators will review the complaints for appropriate follow up actions.

7. DATA ANALYSIS

7.1. Data Quality Assurance

Myopia Centre will permit study-related monitoring audits, MCRC and/or EC review and regulatory inspection(s), providing direct access to source data/documents.

7.2. Data Entry and Storage

Data will be stored in a private database at Myopia Centre at Bedok. Data can be accessed by principal investigators and co-investigators. The data will also be coded and participants de-identified. The master list will be locked in a separate file, with password.

8. SAMPLE SIZE AND STATISTICAL METHODS

8.1. Determination of Sample Size

As this is a pilot study, we are aiming for 50-124 participants to join the study.

8.2. Statistical and Analytical Plans

Statistical analyses will be conducted using standard statistical software (SPSS, STATA). Progression in myopia (Spherical Equivalent as well as axial elongation) will be evaluated.

9. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator(s)/institution(s) will permit study-related monitoring, audits and/or IRB review and regulatory inspection(s), providing direct access to source data/document.

10. QUALITY CONTROL AND QUALITY ASSURANCE

N/A

11. ETHICAL CONSIDERATIONS

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the Good Clinical Practice and the applicable regulatory requirements.

This final Study Protocol, including the final version of the Participant Information and Consent Form, must be approved in writing by the Centralised Institutional Review Board (CIRB), prior to enrolment of any patient into the study.

The principal investigator is responsible for informing the CIRB of any amendments to the protocol or other study-related documents, as per local requirement.

11.1. Informed Consent

Consent will be taken by study team members after explaining the study protocol and obtaining voluntary consent from participants and their parents/guardians. Study team members would also explain the visit schedule and alternatives. Patient's or parent's decision not to participate in the study will not influence or affect their clinical care.

11.2. Confidentiality of Data and Patient Records

Research data will be stored in a password protected database, only accessible by delegated study team members. Hard copies of data will be stored in a locked cabinet at Myopia Centre.

12. PUBLICATIONS

Please refer to SERI publication policy.

13. RETENTION OF STUDY DOCUMENTS

Research data will be stored for at least 15 years before being destroyed.

14. FUNDING AND INSURANCE

NA

List of Attachments

Appendix 1 – References

Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016 May;123(5):1036-42.

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Wildsoet CF, Chia A, Cho P, Guggenheim JA, Polling JR, Read S, Sankaridurg P, Saw SM, Trier K, Walline JJ, Wu PC, Wolffsohn JS. IMI - Interventions Myopia Institute: Interventions for Controlling Myopia Onset and Progression Report Invest Ophthalmol Vis Sci. 2019 Apr 1;60(5):1768.

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