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Centre for Ocular Research & Education

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
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Protocol

ADAPTATION TO AND SATISFACTION WITH MISIGHT CONTACT LENS WEAR IN MYOPIC YOUNG ADULT HABITUAL CONTACT LENS WEARERS (code name: MULBERRY)

Funding source & sponsor: CooperVision

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DOCUMENT CHANGE HISTORY

Version date	Author	Description of change(s)
21Dec2020	[redacted]	Original protocol
11mar2021	[redacted]	Section 6 (Risk section): Addition of risk details concerning COVID-19

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Disclaimer

This study will be conducted for research purposes only.

1 INTRODUCTION

Myopia is a significant public health problem, it has been predicted that by 2050, 50% of the word population will be myopic. (1) Myopia can be defined as an eye that is excessively long and with the increase in axial length comes an increased risk of developing ocular pathology. This increased risk is directly related to the amount of myopia, individuals with high myopia being as much as 40x more likely to have pathology that can result in loss of vision compared to individuals with low amounts of myopia.(2) There is very good evidence in the literature that there are interventions that can slow down the progression of myopia and hence reduce the risk of ocular pathology. One such intervention is the MiSight contact lens. In a three year study, the MiSight lens reduced the myopic progression of a group of subjects by 59% compared with their control group counterparts.(3) Subjects for the original MiSight study were aged 8-12 at recruitment, this being a typical age group when myopia is first seen. There is a cohort of patients who experience later onset of myopia and progression into early adult hood. The COMET study demonstrated that on average, myopia stabilizes by age 15 (48%), however, 90% of the cohort had stable myopia by age 21 and 96% by age 24.(4) Therefore it is clear that there is a proportion of the population whose myopic prescription continues to progress into early adulthood. To date there is no evidence in the literature that commencing a myopia control program in young adult myopes would have an impact on the progression of their myopia. The purpose of this study is to assess whether young adults can adapt to and achieve satisfaction with the MiSight lens. The results from this short term study may contribute towards the planning for longer term studies for the same population sample.

2 OBJECTIVES

The objectives of the study are:

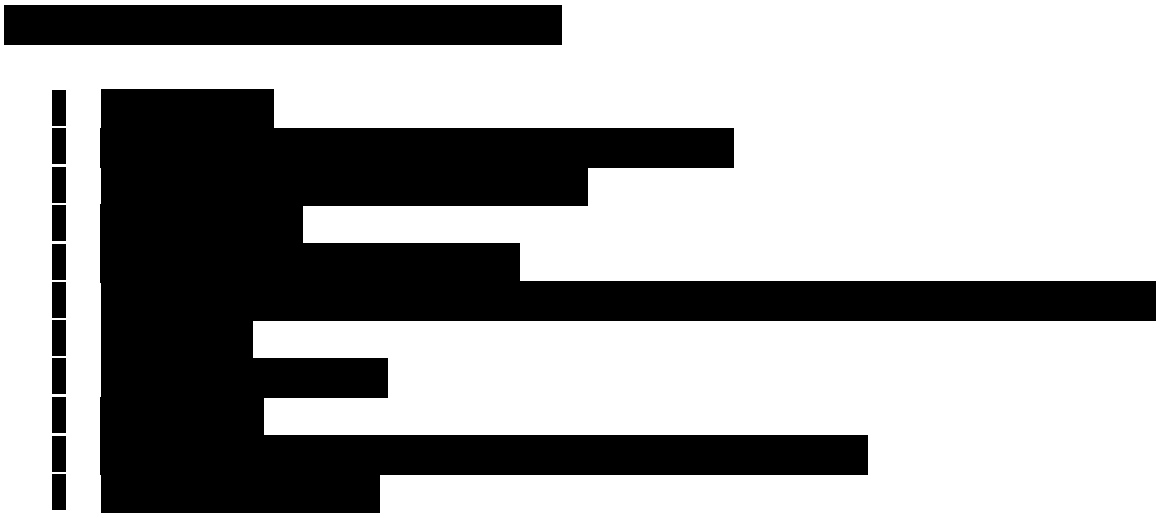
- To measure objective and subjective visual performance, patient satisfaction and to determine if these aspects change over time as myopic young adults adapt to MiSight soft contact lenses.

Primary outcome variable:

- Subjective quality of vision (QoV)

Secondary outcome variable:

- Contact lens Impact on Quality of Life (CLIQ)



3 HYPOTHESIS

Young adults will achieve good subjective quality of vision (QoV) scores with the MiSight lenses.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

4.1.1 OVERALL DESIGN

This is a prospective, single group, dispensing clinical trial to determine subjective and objective visual performance measures, patient satisfaction and adaptability to commercially available myopia control contact lenses (MiSight 1-day) in myopic young adults over 3 months of daily lens wear. There will be 4 scheduled in-office sessions and one remote/at home session spanning a total commitment time of 5.5 hours over the 3 months. The first session is anticipated to include the screening visit, visit 1 (V1) and, if eligible, visit 2 (V2) will be conducted in immediate succession. Visit 2 may be conducted on a separate day if necessary, but should be scheduled within 10 days of visit 1.

- **Visit 1 (V1):** Screening and Baseline (75 mins)
- **Visit 2 (V2):** Fitting/Dispensing of study lenses (15 mins if immediately following V1 on the same day)
  Note – V2 can take place on a separate day, if necessary, but should be scheduled within 10 days of V1. Entrance acuity and biomicroscopy will be required in this case, and time required would be increased to 30 minutes.
- **Visit 3 (V3):** Day 7, Follow-up (60 mins)

- **Visit 4 (V4):** 1 month, Follow-up (75 mins)
- **Visit 5 (V5):** 2 month, Remote at home questionnaires (15 mins)
- **Visit 6 (V6):** 3 month, Follow up and exit (90 mins)

4.1.2 MASKING

This is an open-label study that will not involve masking.

4.2 STUDY POPULATION

4.2.1 SAMPLE SIZE CALCULATION

Using a conservative estimate for repeated measure ANOVA paradigm, with 1 group, with 3 measurements (baseline, 1 month, 2 months) and f effect size of 0.25 (cumulative probability 75%), and 1-beta 0.95, the minimum sample size is n = 43. Using an attributed drop-out rate of 10-15%, the required sample size to be dispensed will be 50 participants.

4.2.2 NUMBER OF PARTICIPANTS

Participants will be recruited using CORE database and advertising approved by the UW Office of Research Ethics. Up to 50 participants who meet all eligibility criteria may be dispensed with MiSight study lenses and asked to wear these lenses for 3 months (± 7 days), with a target of 43 completing the study. Participants who were screened but did not meet all eligibility criteria are not included in the number of participants (n=50) to be dispensed. Informed consent will be obtained for all participants prior to their enrolment in the study and prior to collecting any study data (Appendix 1).

4.2.3 INCLUSION AND EXCLUSION CRITERIA

A person is eligible for inclusion in the study if he/she:

1. Is between 17 and 25 years of age (inclusive) and has full legal capacity to volunteer;
2. Has read and signed an information consent letter;
3. Is willing and able to follow instructions and maintain the appointment schedule;
4. Has a vertex corrected spherical equivalent distance refraction that ranges between -0.75D to -6.00D in each eye;
5. Has astigmatism ≤ -0.75 DC in either eye, by refraction;
6. Be correctable to better than 0.20 logMAR in each eye by refraction;
7. Has habitually worn spherical soft contact lenses to correct for distance vision (i.e. no multifocal or monovision) for the past 3 months;

8. Is willing to wear contact lenses for at least 10 hours a day, 6 days a week while in the study;
9. Demonstrates an acceptable fit with the study lenses;
10. Has ocular health findings considered to be “normal” and which would not prevent the participant from safely wearing contact lenses.

A person will be excluded from the study if he/she:

1. Is participating in any concurrent clinical or research study;
2. Has a history of amblyopia;
3. Has TNO Stereoacuity worse than 120” arc / or Titmus worse than 100” arc;
4. Has any known active* ocular disease and/or infection;
5. Has a systemic condition that in the opinion of the investigator may affect a study outcome variable;
6. Is using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable;
7. Has known sensitivity to the diagnostic pharmaceutical (sodium fluorescein) to be used in the study;
8. Is pregnant, lactating or planning a pregnancy at the time of enrolment (verbal confirmation at the screening visit);
9. Is pseudophakic;
10. Has undergone refractive error surgery;
11. Has one of following experiences with MiSight lenses:
    - Is currently wearing MiSight lenses or
    - Has worn MiSight lenses for more than one week at any given time or
    - Has worn MiSight lenses for any more than 30 minutes in the past 30 days;
12. Has had orthokeratology treatment within the last 3 months.

* For the purposes of this study, active ocular disease is defined as infection or inflammation, which requires therapeutic treatment. Mild (i.e. not considered clinically relevant) lid abnormalities (blepharitis, meibomian gland dysfunction, papillae), corneal and conjunctival staining and dry eye are not considered active ocular disease. Neovascularization and corneal scars are the result of previous hypoxia, infection or inflammation and are therefore not active.

Pregnant and lactating women are not being excluded from the study due to safety concerns but due to changes in physiology that occur secondary to systemic hormonal changes which may impact refractive error and visual acuity.

4.2.4 REPEATED SCREENINGS

In some circumstances a repeated screening may need to be scheduled (Visit 1-R). Examples include, but are not limited to:

1. Incomplete information available at time of screening to determine eligibility (e.g. current lens brands worn, history from current eye care practitioner etc.)
2. Study procedures unable to be completed in time scheduled for visit;
3. Study products not available at the time of the screening visit;
4. A transient health condition which may affect the eye(s) (e.g. a common cold, active allergies, fatigue etc;)
5. The short term use of medications (e.g. antibiotics, antihistamines etc.)
6. Reassessment of baseline ocular conditions (e.g. corneal and/or conjunctival staining, scars etc.)

The maximum total number of screenings permitted will be 3, i.e. 2 re-screen visits are permitted.

4.3 STUDY MATERIALS

4.3.1 LENSES

The study lenses are approved by Health Canada. They will be worn bilaterally, and on a daily disposable basis as per the approved indication, therefore no lens care solution is required.

Table 1: lens characteristics

Lens	MiSight
Material	Omafilcon A
HC licence #	83469
Medical device class	2
Dk/t (barrer/cm)	28
Water content	59%
Sphere power (D)	-0.50 to -6.00 (0.25 steps)
Base curve (mm)	8.7
Diameter	14.2
Replacement schedule	Daily disposable

4.3.2 ORDERING CONSUMABLES

MiSight study lenses will be supplied by CooperVision for the use in this study.

4.3.3 DISPOSING OF CONSUMABLES

Worn lenses removed during study visits will be discarded as per University of Waterloo regulations. Unworn lenses will be returned or disposed of, as advised by the sponsor, and according to University of Waterloo regulations.

4.3.4 PRODUCT ACCOUNTABILITY

Accountability logs will be kept to include the number of lenses received, dispensed, unused and, if required, returned to sponsor. All products dispensed to participants will be recorded in individual participant logs in the study binder.

4.4 SCHEDULED AND UNSCHEDULED VISITS

There will be four in-office study sessions, including a screening visit. Participants will attend the clinical site for a total of 5.25 hours and will also be asked to complete at home ratings after 2 months, to assess their experience with the study contact lenses.

4.4.1 STUDY VISITS

A summary of study visits is shown in Table 2.

Table 2: Summary of visits

	Visit #	Day/s	Visits	Duration (hours)
In-office session 1	Visit 1	0	Screening and fitting	1.25
	Visit 2	0	Baseline & Dispense.	0.25
In-office session 2	Visit 3	14 ± 4	2 week follow up	1.0
In-office session 3	Visit 4	28 ± 7	1 month follow up	1.25
At-home session 1	Visit 5 – Virtual visit	56 ±7	2 month at-home questionnaires	0.25
In-office session 4	Visit 6 & Exit	84 ±7	3 month follow up and exit	1.5

Visits that fall outside of the specified visit windows will be designated as minor protocol deviations and at the end of the study, the data collected during protocol deviations will be assessed for their suitability to be included in the analysis population.

4.4.2 VISIT 1, SCREENING

A documented informed consent process will be conducted with all participants prior to their enrolment in the study and prior to any data collection or measurements.

Participants will be assigned a study ID number after they sign the consent documentation process i.e. before their eligibility for the study has been confirmed. The investigator will determine participant eligibility using the inclusion and exclusion criteria. Ineligible participants will be discontinued from the study. The procedures to be performed are outlined below:

1. Informed consent
2. Participant demographics and medical history:
    - *Age, Sex*
    - *Medical history/medications, Allergies*
3. CL wear history
    - *Habitual contact lens wear (CL type, cleaning solution (if applicable), wear time)*
4. Subjective questionnaires (QoV and CLIQ) with habitual lenses within the last month of lens wear experience
5. Presenting visual acuity
6. Auto refraction/auto keratometry
7. Sphero-cylindrical refraction, monocular & binocular logMAR distance HIHC VA

[redacted]

13. Slit lamp biomicroscopy
14. MiSight study lens fitting
    a. The contact lens power will be chosen based on the vertex best sphere refraction.
    b. The participant will insert the lenses.

c. Acceptability of lens fit (centration, movement, limbal coverage, overall; YES/NO) will be confirmed.

d. Monocular over-refraction will be performed to determine if a different power is needed. If any changes are made, the above procedures will be repeated.

e. The final lens powers for OD and OS and monocular & binocular logMAR distance HIHC VA will be recorded.

15. Confirm eligibility.

4.4.3 VISIT 2, BASELINE & DISPENSE (DAY 0)

Participants who successfully met all eligibility criteria in Visit 1 will directly transition to Visit 2, while continuing to wear the pair of study lenses that has just been fitted.

1. Lens dispense: Participants will be provided with a supply of MiSight CLs to last them for the period of the study.
2. Participant instructions. The participants will be asked to:
    - *Wear the lenses at least 6 days per week and 10 hours per day throughout the study;*
    - *Attend V3 after 2 hours or more of MiSight study lens wear on that day;*

4.4.4 VISIT 3, 2 WEEK FOLLOW-UP

Participant to attend visit after 2 hours or more of MiSight study lens wear.

1. Changes in medical history/medications;
2. Compliance with # of CL wear days/hours per day
3. Presenting VA

[redacted]

5. Spherical over-refraction
6. Slit lamp biomicroscopy
7. Questionnaires (CLIQ, QoV)
8. Lens removal

9. Biomicroscopy examination

4.4.5 VISIT 4, 1 MONTH FOLLOW-UP

Participant to attend visit after 2 hours or more of MiSight study lens wear.

1. Changes in medical history/medications;
2. Compliance with # of CL wear days/hours per day
3. Presenting VA

[redacted]

[redacted]

6. Slit lamp biomicroscopy
7. Questionnaires (CLIQ, QoV)
8. Lens removal
9. Biomicroscopy examination
10. Instructions on completing QoV and CLIQ surveys within the V5 time window

4.4.6 VISIT 5, 2 MONTH FOLLOW-UP

This visit will be conducted remotely to reduce the number of study visits.

Participants will be sent a link to an electronic questionnaire which will include version questions to confirm their contact lens wearing time (i.e. typical hours per day and days per week) plus the QoV and CLIQ surveys. If electronic access is not available or fails then the questions can be emailed or provided in paper form.

4.4.7 VISIT 6, 3 MONTH FOLLOW UP VISIT AND EXIT

Participant to attend visit after 2 hours or more of MiSight study lens wear.

1. Collect unused study CLs;
2. Changes in medical history/medications;
3. Compliance with # of CL wear days/hours per day

4. Presenting VA

[redacted]

8. Spherical over-refraction
9. Slit lamp biomicroscopy
10. Questionnaires (CLIQ, QoV)
11. Lens removal
12. Biomicroscopy examination

[redacted]

14. Exit visual acuity with habitual correction

4.4.8 STUDY EXIT

The study exit form will be completed when a participant exits the study. This form will be completed either at study completion, or if the participant is discontinued from the study at another time. A study exit form must be completed for all participants who have taken a study ID number. If in the opinion of the investigator post-study follow-up visits are required, the exit form will be completed after the last follow-up visit.

Exit monocular and binocular distance vision will be recorded with either the participant's spectacles, refraction or habitual contact lenses. An exit biomicroscopy assessment will be conducted if not already completed on the same day for a concurrent study visit.

After the exit assessments have been completed, the participant and investigator will complete the study completion and remuneration forms. At this time the participant will be considered as having exited the study.

4.4.9 UNSCHEDULED VISITS

An unscheduled visit is defined as an interim visit requested by the participant or investigator due to an unanticipated problem. Data recorded at these visits will be entered into the database.

Only relevant and applicable unscheduled visit information will be included in the final report as deemed necessary by the lead investigator.

4.5 STUDY PROCEDURES

Table 3 summarizes the procedures at each visit. The order of procedures is described in sections 4.4.2 to 4.4.7.

Table 3: Summary of procedures to be conducted at scheduled visits

Procedures / Data	Screen & BL/Dispensing (75/90mins)	DV++ (30min)	2W (2W from DV) (60mins)	1M (1M from LD) (75mins)	2M (2M from DV) (15mins)	3M (3M from DV)(90mins) Final Visit	Unscheduled/ Adverse Events
Visit window	N/A	≤10 days from BL	± 4 days	+ 5 days - 5 days	+ 7 days -7days	+ 7 days - 7 days	N/A
Informed consent	✓	-	-	-	-	-	-
Meet inclusion / exclusion criteria	✓	✓	-	-	-	-	-
Demographics	✓	-	-	-	-	-	-
Presenting VA	✓	✓	✓	✓	-	✓	✓
History at baseline	✓	-	-	-	-	-	-
History since last visit, including updated medical problems / previous events / treatment	-	✓	✓	✓	-	✓	✓
Auto-refraction + keratometry	✓	-	-	-	-	-	-
Subjective refraction + VA	✓	-	-	-	-	✓	*
[redacted]		✓				✓	
[redacted]	✓	-	✓	✓	-	✓	-
[redacted]	✓	-	-	-	-	✓	-
[redacted]	✓	-	-	✓	-	✓	-

[redacted]	✓	-	-	✓	-	✓	-
Spherical Over-refraction + VA	-	-	✓	-	-	✓	-
Wear time review	-	-	✓	✓	✓	✓	*
Compliance assessment / Lens and solution returns	-	-	✓	✓	-	✓	*
Slit-lamp biomicroscopy: Assessment of lenses worn at visit and ocular assessment	✓	✓	✓	✓	-	✓	✓
Questionnaires (including QOL/OOV questionnaires)	***	+	✓	✓	✓	✓	-
Photos / video	*	*	*	*	-	*	*
Adverse event assessment	✓	✓	✓	✓	-	✓	✓
Visit summary	✓	✓	✓	✓	-	✓	✓

*	At investigators' discretion
**	If visual acuity (VA) is decreased by 2 lines or more from BL or LD
***	With habitual lenses
+	If lenses dispensed

4.5.1 CASE HISTORY

Demographics:

Demographic information from the participant will be obtained, including age and sex.

Medical History:

At screening, information will be obtained from participants about the current medication, allergies, and any medical conditions. At visits 2 (if applicable),3, 4 and 6 participants will be asked about changes in their medication or health.

Contact Lens History:

Information will be obtained from the participant about the current contact lens type (lens name, brand), lens power and use of artificial tears. Participants will be asked their typical lens wear time (hours/day and days/week).

4.5.2 QUALITY OF LIFE (CLIQ) AND QUALITY OF VISION QUESTIONNAIRES (QOV):

Participants will be asked to complete questionnaires based on the time period of contact lens wear specified in the questionnaire.

4.5.3 VISUAL ACUITY

Visual acuity for distance will be measured using high contrast computer-generated acuity charts in high illumination. Participants will be asked to read letters that progressively decrease in size on a computer screen located at a distance of 6 meters.

4.5.4 AUTOREFRACTION

Participants will be asked to focus on a target while seated at an instrument that measures their approximate spectacle prescription and corneal shape.

4.5.5 SUBJECTIVE REFRACTION

Participants will be asked to read a letter chart from a distance through lenses placed in front of their eyes. They will also be asked to compare clarity of their vision between different lenses placed in front of their eyes. This procedure aids to determine their spectacle and/or contact lens prescription.

4.5.6 SLIT LAMP BIOMICROSCOPY

The participant will be seated behind a slit lamp and the following may be assessed at any visit:

External adnexa anomalies:

Any observations of the anterior eye (e.g. pterygium, pinguecula, etc) will be recorded.

Cornea:

Any corneal observations (such as infiltrates, old scars, etc) will be documented.

Conjunctival redness:

Ocular redness will be assessed for the bulbar and limbal conjunctiva using the EFRON grading scale (0 to 4, 0 = normal; 0.1 increments).

Corneal and conjunctival staining with fluorescein:

Corneal staining will be assessed for 5 zones, by grading type (0-4, 0.5 steps), extent (0-4, 0.5 steps) and depth (0-4, integer steps);

Lens edge related conjunctival staining and conjunctival indentation will be assessed for 4 zones (0-4, 0.5 steps).

Palpebral conjunctival hyperemia and roughness:

The redness and roughness of the upper and lower eyelids (tarsal plate zone 2) will be assessed using the Efron grading scale (0 to 4, 0 = normal/ uniform satin appearance; 0.25 steps).

4.5.7 CONTACT LENS FIT

Contact lens fit:

Lens fit will be assessed to ensure acceptable lens fit with study lenses at the screening visit.

At V2 and V3, lens centration and movement will be assessed as follows

- *Lens centration (scale: optimal, slight decentration, moderate decentration but not encroaching limbus, excessive & occasionally encroaching limbus);*
- *Lens movement for primary gaze (-2 = Unacceptably tight; -1 = Slightly tight but acceptable; 0 = Optimal; +1 = Slightly loose but acceptable; +2 = Unacceptably loose); lens tightness on push-up test (0-100 scale, with 50 being optimal; 5-point steps).*

[redacted]

[redacted]

5 MONITORING PROTOCOL ADHERENCE

All personnel involved in this study will be listed on a delegation log and their training will be documented. Consent documentation will be reviewed by personnel not involved in the consent process. Visit windows will be reviewed when determining the analysis cohort. All protocol deviations will be reviewed by the Lead Investigator. Suspected major protocol deviations will be reviewed by the Principal Investigator and reported to the sponsor and the University of Waterloo's Office of Research Ethics (ORE) within 7 days of becoming aware of them (as per ORE's guidelines).

6 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

This is a minimal risk study because of the use of marketed products and standard optometric assessments.

Contact lenses in this study will be worn on a daily wear (and daily disposable) basis. Adverse events and/ or complications in daily wear of soft contact lenses can occur (e.g. inflammation and infection). Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The

incidence of infection due to daily-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. Thirty five million Americans who currently wear contact lenses assume this risk.

When contact lenses are worn on a daily wear basis there is a small risk of an adverse event compared to not wearing contact lenses. When contact lenses are worn on an extended wear basis, there is a significantly increased risk of an adverse reaction compared with wearing contact lenses on a daily wear basis.

A dye (fluorescein) normally used for eye exams is being used in this study. Although rare, it is possible that participants may have an allergic reaction to the dye. This could cause discomfort to their eye.

Participants are advised to inform the investigator of any sensitivities to the study products.

Parts or all of this study will be conducted during the COVID-19 pandemic. Therefore, risks exists with the infection with COVID-19. The risks of infection with COVID-19 arise due to possible exposure during commute to and from the study visit as well as during the study visit, particularly due to the closeness of the investigator and participant (within 2m for some assessments). The potential effects of COVID-19 are not yet fully known and may include long-term health consequences. In a small percentage, infection with COVID-19 can lead to serious illness, hospitalization, and in rare cases to complications leading to death. Individuals aged 60 and above and those with underlying medical conditions are considered at a greater risk for severe illness from the COVID-19 virus.

In consideration of risks associated with COVID-19, CORE has implemented a series of on-site safety procedures which have been reviewed and approved by the University of Waterloo. These include, but are not limited to, self-screening of investigators and participants prior to entering the building, maintaining physical distancing as much as possible, frequent handwashing, wearing of face masks by the investigator and participant, and frequent room and equipment hygiene and decontamination.

Participants will not benefit directly from taking part in this study.

Information from this study may help researchers come up with new soft contact lens designs to help others in the future. This study may help the study sponsor to better understand the performance of the products being used in this study in a different age cohort from that previously studied.

7 ADVERSE EVENTS

See CORE SOP012 for a description of all adverse events, including management and reporting.

Any observations taking place prior to determining that a subject meets all inclusion/ exclusion criteria for the study and which are not related to the performed study procedures are not considered an AE. An AE can be any unfavourable and unintended sign, symptom, or disease temporarily associated with a study procedure, whether there is a causal relationship or not.

Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' as defined below, Table 4.

A number of conditions may result in temporary suspension until resolution. These include corneal infiltrates, corneal staining, limbal injection, bulbar injection or tarsal conjunctival abnormalities.

Table 4: Classification of types of adverse event

Classification	Definition
Serious Adverse Event	Those events that are life-threatening, or result in permanent impairment of a body function, or permanent damage to a body structure or necessitate medical (therapeutic) or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
Significant Adverse Event	Those non-serious adverse events that occur with contact lens usage that are not sight-threatening but are usually symptomatic and may warrant therapeutic management and /or temporary or permanent discontinuation of contact lens wear.
Non-Significant Adverse Events	Those less severe non-serious adverse events that occur with contact lens usage that are not sight-threatening, may or may not be symptomatic and may warrant palliative management, such as ocular lubricants or temporary interruption of contact lens wear.
Unanticipated Adverse Device Effect	Adverse events in a study that were not previously identified in the protocol in terms of nature, severity, or degree of incidence. An Unanticipated Serious Adverse Device Effect is an unanticipated adverse event that is serious in nature and caused by or associated with the device and is considered reportable.

AE classification, coding (for reporting to the sponsor) and reporting details, plus examples, are provided in Table 5.

Table 5: Contact lens adverse event classification, coding and reporting guide

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	For all serious AEs: Notify sponsor as soon as possible, **within 24 hours;** ORE reporting will be **within 24 hours** as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		
11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	
17	Any sign and/or symptom for which participant is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	
10	Other significant event	
Non-significant Adverse Events		
21	Conjunctivitis (bacterial, viral or allergic)	Notify sponsor as soon as possible, **within 5 working days**; ORE
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	

23	Asymptomatic corneal infiltrative events	reporting as per requirements
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	

7.1 NORMAL OR ADAPTIVE SYMPTOMS

Transient symptoms such as end-of-day dryness, lens awareness, itching or burning or other discomfort may occur with contact lens wear and may occasionally reduce wearing time. These are not reported as adverse events unless in the investigator's opinion they are unexpected in nature, severe or have a high rate of occurrence.

7.2 PROCEDURES FOR ADVERSE EVENTS

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the participant may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the test device or a result of other factors. An adverse event form will be completed for each adverse event. Whenever possible, the adverse event will be photo-documented.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The participant must be followed until resolution or no further change is anticipated and/or referred for further care with the appropriate health care professional and/or recorded as being under appropriate health care as per investigator's discretion. A written report will be completed indicating the subsequent treatment and resolution of the condition.

7.3 REPORTING ADVERSE EVENTS

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to participant's participation will be reported to the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Investigator will report the event to the University of Waterloo's Office of Research Ethics (ORE) within 24 hours of becoming aware, as

per their requirements (by fax, mail/delivery, phone, or email). All fatal or life threatening events will be reported immediately to the ORE.

Significant and Non-Significant Adverse Events will be reported to the sponsor as soon as possible, but no later than 5 working days after the occurrence. The Investigator will report the event to the ORE as per ORE requirements (by fax, mail/delivery, phone, or email).

[redacted]

Details of all adverse events will be included in the study report.

8 DISCONTINUATION FROM THE STUDY

Participants may be discontinued at the discretion of the investigator or sponsor in consideration of participant safety or protocol compliance, or at discretion of the participant. Participants discontinued from a study will be reimbursed $20 per hour for their active involvement in the study (including the initial screening visit). Upon discontinuing, a participant will be offered the option of their data being withdrawn from future statistical analysis. The following is a list of possible reasons for discontinuation from the study:

- Screening failure: Participants will be discontinued if they do not meet the inclusion and exclusion criteria outlined in section 4.2.2.
- Unacceptable performance with products to be used in study: Participants may be discontinued if they are unable to achieve acceptable comfort and /or vision with the study products.
- Positive slit lamp finding: Participants may be permanently discontinued from the study depending on the severity of the condition and on the judgement of the investigator.

- Adverse event: If a participant experiences an adverse event during the study they may be discontinued based on the clinical judgement of the investigator.
- Symptoms: If the participant has persistent symptoms they may be discontinued based on the clinical judgement of the investigator.
- Disinterest, relocation or illness: The participant may choose to discontinue due to reasons within or beyond their control.
- Violation of protocol or non-compliance: The participant will be discontinued if they are unable or unwilling to follow the protocol specified visit schedules and/or study procedures.
- Instillation of topical ocular medication: The participant will be discontinued if they elect to use a topical ocular medication during the study unless that topical ocular medication is prescribed for a limited duration (less than two weeks) to treat a transient condition; in this case the participant may remain an active participant (at the discretion of the investigator) after stopping topical ocular medication following resolution of the ocular condition).
- Lost to follow-up: The participant will be discontinued if they cannot be contacted and do not return for a final exit visit, and if the investigator has made a reasonable effort to contact the participant for a final study visit.
- Premature termination of the study by the sponsor, CORE or the Office of Research Ethics at the University of Waterloo.

A discontinuation form , stating the reason for discontinuation will be completed, which requires the signatures of both the participant and the investigator except where the participant is lost to follow-up in which case only the signature of the investigator is required.

All discontinuations including their reasons will be included in the final report.

9 STUDY COMPLETION AND REMUNERATION

At the last scheduled protocol visit a study completion form will be completed, which requires the signatures of both the participant and the investigator.

Once their involvement in the study is complete, participants will be informed about receiving feedback following study completion in the Letter of Appreciation.

[redacted]

10 STATISTICAL ANALYSIS AND DATA MANAGEMENT

10.1 STATISTICAL ANALYSIS

All data will be analyzed by CORE at the University of Waterloo. Data analysis will be conducted using Statistica, SPSS, or other appropriate software.

Descriptive statistics will be provided for all primary outcome variables as well as information regarding baseline variables (e.g. age, sex).

QoV and CLIQ ratings will be compared between visits using either Paired t-tests or Wilcoxon matched pairs, or using ANOVA, as applicable; statistical significance will be set at 5%. The appropriate tests will be selected based on tests of normality - non-parametric tests will be used for data not showing a normal distribution. For assessments conducted for each eye separately, the right eye will be used for analysis if there is no difference between eyes.

Additional analysis may be conducted.

10.2 DATA MANAGEMENT

All study data will be recorded on paper CRFs. Data from this study will be entered in an electronic database and retained by CORE for a minimum of 25 years on a password-protected server. After 25 years, data will be disposed of in accordance with the guidelines laid out by the University of Waterloo.

At the completion of the study CORE may provide a copy of the study data to the funding company. Data will typically be sent using a secure file share system operated by the University of Waterloo called Sendit which uses 128bit (or 256bit) SSL encryption. This system provides a secure way to transfer files when email is not appropriate, whether because of file size, file type or concerns over security. Sendit includes features such as password protection, a restricted time period for download, IP logging and email notification of download. Files may be encrypted prior to transmission. Using this method means that data files are only stored on University of Waterloo servers during the transfer.

10.3 COMMENTS ON SOURCE DOCUMENTS

Data analysis will not be conducted on comments which have been recorded in the source documents. Only relevant and applicable comments will be included in the final report as deemed necessary by the lead investigator.

11 PROTOCOL TRAINING

All study personnel will be required to complete training prior to their involvement in the study. Records of training will be kept at CORE.

12 STUDY MONITORING

Study monitoring will be conducted throughout the study. In addition study records may be inspected at CORE by the Office of Research Ethics at the University of Waterloo, and by regulatory authorities in Canada and the United States, namely Health Canada and the United States Food and Drug Administration (FDA); however, no records containing identifiable/personal information will be permitted to leave the custody of CORE.

Study monitoring will include, but may not be limited to:

- The number of participants screened, enrolled, and randomized (i.e. assigned a study ID number), discontinued and completed;
- Consent documentation;
- Details of adverse events and protocol deviations;
- Reports of unintended events.

13 STUDY MANAGEMENT

13.1 STATEMENT OF COMPLIANCE

This clinical study is designed to be in compliance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for Good Clinical Practice (GCP), with the University of Waterloo's Guidelines for Research with Human Participants and with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, 2nd Edition.

- Declaration of Helsinki
- ICH E6 - International Conference on Harmonisation; Good Clinical Practice
- http://iris.uwaterloo.ca/ethics/human/guidelines/index.htm
- http://iris.uwaterloo.ca/ethics/human/ethicsReview/UWStatement.htm
- http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

13.2 ETHICS REVIEW

This protocol will be submitted to and reviewed through the Office of Research Ethics (ORE) at the University of Waterloo. Notification of ethics clearance of the application is required prior to the commencement of the study.

13.3 CLINICAL TRIAL REGISTRATION

The sponsor will register this study with clinicaltrials.gov.

13.4 PROTOCOL DEVIATIONS

Protocol deviations are unanticipated or unintentional changes to a study after it has received prior sponsor approval and ethics clearance. Protocol deviations can be major or minor.

13.4.1 MAJOR PROTOCOL DEVIATIONS

Major protocol deviations may impact the research protocol, information consent document or other study materials, usually cannot be anticipated ahead of time and are often necessary to ensure the safety and welfare of the participants.

The following are examples of protocol deviations that must be reported to the ORE:

- Changes in procedures initiated to eliminate immediate risks/hazards to participants;
- Enrollment of participants outside the protocol inclusion/exclusion criteria whether agreed to or not by the sponsor;
- Medication / device / intervention errors (i.e. incorrect drug or dosage of drug / incorrect contact lens(es) dispensed / incorrect care system dispensed);
- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design;
- Information consent documentation violations: no documentation of informed consent; incorrect version of, or incomplete, informed consent documentation used.

13.4.2 MINOR PROTOCOL DEVIATIONS

Protocol deviations caused by or which originate with research participants are considered minor, and normally are not reported to the ORE unless these result in increased risk to the participant(s). The following are examples of protocol deviations that are considered minor and do not require reporting to the ORE:

- Logistical or administrative aspects of the study (e.g., study participant missed appointment, change in appointment date);

- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would not impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

13.4.3 REPORTING AND DOCUMENTING PROTCOL DEVIATIONS

Major protocol deviations must be reported to the ORE and the sponsor within 7 days of the deviation occurring (or its discovery) using the Protocol Deviation Report Form 107 (PDRF). Information from the PDRF is provided to the Clinical Research Ethics Committee (CREC) at the next monthly meeting.

All protocol deviations (major and minor) occurring during the study will be documented and included in the final report.

13.5 PREMATURE TERMINATION OF THE STUDY

The sponsor, CORE or the Office of Research Ethics at the University of Waterloo may terminate the study at any time for any reason.

13.6 STUDY PARTICIPANT RECORDS

Study participant records will be completed to comply with GCP guidelines. Records will contain:

- Unique study acronym and/or code;
- Participant ID;
- Date enrolled;
- Confirmation by investigator that participant met eligibility criteria;
- Confirmation that participant received a signed and dated copy of informed consent;
- Exit date;
- Investigator's signature confirming study exit.

13.7 RETENTION OF STUDY RECORDS AND DATA

Records and data from this study will be retained for a minimum of 25 years. Details regarding storage procedures are given in CORE SOP014_v02 Clinical data management.

14 REPORT

A draft report will be provided according to the timeline specified in the contract.

15 REFERENCES

1. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-42.

2. Flitcroft DI. The complex interactions of retinal, optical and environmental factors in myopia aetiology. Prog Retin Eye Res. 2012;31(6):622-60.

3. Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D, Young G. A 3-year Randomized Clinical Trial of MiSight Lenses for Myopia Control. Optom Vis Sci. 2019;96(8):556-67.

4. Myopia stabilization and associated factors among participants in the Correction of Myopia Evaluation Trial (COMET). Invest Ophthalmol Vis Sci. 2013;54(13):7871-84.