HOW OFTEN ORTHOKERATOLOGY LENSES NEED TO BE REPLACED?

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SYNOPSIS

Protocol title: How often orthokeratology lenses need to be replaced?

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SUMMARY (Protocol version: 1)

Study title: How often orthokeratology lenses need to be replaced?

Introduction: Myopia or short-sightedness is described as difficulty seeing objects at a distance.[1] This condition emerged as a major public health issue, particularly among younger population, with projections indicating nearly half (4.76 billion people) of the world population will be myopic by the year 2050.[2,3] Over the years, multiple strategies have been developed to slowdown the myopia, including glasses, contact lenses, atropine, orthokeratology, and refractive surgery.[4] Among these, orthokeratology (OK) has been shown to be an effective option to control myopia progression.[5] In the therapy, a specialized OK lenses are worn overnight to reshape the cornea, a clear, front part of the eye. thus, clear vision is achieved during the day without need for spectacles or contact lenses.[5] Regular eye health checks and timely contact lens replacement are essential for safe lens wear. Over time, lenses can accumulate deposits that may harbour harmful microorganisms, increasing the risk of eye infections. As OK lenses are worn overnight—a key risk factor for infection—their replacement schedule is important but remains uncertain. Currently, replacement schedule of OK lens is largely determined by the eye care practitioner's discretion, relying on eye symptoms and signs, as well as observable spoilage on the lens surface.

Objective: This study aims to assess the levels of lens spoilage under standard wear and disinfection practices in order to determine the optimal lens replacement frequency of OK lens. Furthermore, this study will evaluate the health of anterior surface of the eye and lens comfort levels during one-year overnight use of OK lenses.

Study design: The proposed study uses a prospective, observational quasi-experimental research design where the contact lens spoilage from same participants will be observed over the time before and after contact lens wear. Individuals (between 18 to 40 years of age) with a refractive error between -1.00 and -4.00D of sphere and astigmatism ≤ 2.50D will be recruited in the study. The eligible participants will receive study OK lenses during the dispensing visit, following the screening visit. Participants will attend total eight visits, including a follow up visit 2 weeks after the lens cessation.

Planned sample size: We are planning a study with an ordinal data response variable from matched pairs of study participants. We estimate that the difference in the lens spoilage grading between matched pairs is normally distributed with a standard deviation 0.9. To detect a true mean difference of 1.90 between pairs, we will need 12 subjects to achieve 80% power, assuming a Type I error rate of 0.05. To account for a 20% dropout rate, a total of 16 participants will be recruited.

Study procedure: All 16 participants participant will receive suitable OK lenses following the teaching of insertion and removal lens methods and lens care regimen. Participants will be

reviewed at regular visits (*Screening visit, baseline visit, 1 day, 7 days, 21 days, 6 months, 12 months and 2weeks lens cessation visit*). At each visit, the anterior surface of the eye will be assessed using clinical microscope and lens comfort levels will be assessed using Ocular Surface Disease Index questionnaire (OSDI) and Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8). A photographic method will be used to qualitatively assess lens spoilage at each visit. Additionally, during the lens dispensing visit, the 6-month visit, and the 1-year visit, lens deposition will be quantitatively evaluated using established standard laboratory procedures.

Primary outcome: OK lens spoilage grading scores**.**

Secondary outcomes: Contact lens comfort Scores (OSDI, CLDEQ-8) and ocular surface changes.

Duration of the Study: The study is anticipated to commence in December 2024 and will run for 1 year.

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I. BACKGROUND

Overview

Myopia or short-sightedness is described as difficulty seeing objects at a distance.[1] This condition has emerged as a major public health issue, particularly among younger population, with projections indicating nearly half (4.76 billion people) of the world population will be myopic by the year 2050.[2,3] Over the years, multiple strategies have been developed to slowdown the myopia, including glasses, contact lenses, atropine, orthokeratology, and refractive surgery.[4] Among these, orthokeratology (OK) has been shown to be an effective option to control myopia progression.[5]

OK lens fitting is niche therapy representing about 1.2% of all contact lens fits worldwide and 2-3% across Australia.[6] This therapy involves wearing a rigid contact lenses with a specialized design overnight to reshape the cornea, a clear front part of the eye. As a result, clear vision is achieved during the day without need for any spectacles or day time contact lenses.[5]

The safety and success of contact lens wear depend heavily on regular assessment of eye health, close evaluation of the lens surface, and optimal lens replacement. A lens surface with adhered deposits can harbor harmful microorganisms that may infect the anterior surface of the eye, potentially leading to lens-related discomfort and, in severe cases, sight-threatening complications such as microbial keratitis. Overnight lens wear remains one of the key risk factors in developing microbial keratitis and it must be noted that OK is an overnight wearing lens modality. The overall estimated incidence of microbial keratitis with OK lens wear is 6.8 per 10,000 years of wear, lower to that of other overnight wear modalities of soft contact lenses.[7]

Rationale for preforming this study

Maintaining good lens hygiene and compliance in terms of regular replacement of contact lenses are critical in minimizing the risk of eye complications such as microbial keratitis.[8] *However, there is no established scientific consensus exploring the optimal replacement schedule or life span for OK lenses from the clinical standpoint. Currently, replacement schedule or life span of OK lens is largely determined by the eye care practitioner's discretion, relying on eye symptoms and signs, as well as observable spoilage on the lens surface*.

To address this gap, a well-designed research study is needed to evaluate the extent of lens spoilage, including surface scratches and deposition, over at least one year of lens wear, with assessments at frequent intervals. Furthermore, understanding the lens spoilage allows to consider a lens care regimen that aimed at reducing microbial load.

Therefore, this study aimed to understand the level of OK lens spoilage by fitting OK lenses on study participants, who are willing to wear lenses for a duration of one year. The lenses used in the study will be Menicon Z Night lenses (material: Tisilfocon A), registered with the Therapeutic Goods Administration (TGA) under ARTG entry 226883, and approved for overnight wear for myopia correction. Lens spoilage, including surface scratches and deposition, will be assessed at three time points: at lens dispensing, after 6 months of wear, and after 1 year of lens wear using established methods. In this study, we determine to explore the association between OK lens replacement schedules and keratitis risk. By tracking lens spoilage, patient symptoms, and clinical indicators of infection over 12 months, we intend to gather preliminary data on infection

risk. Given the difficulty of detecting keratitis with a small sample, we will use lens spoilage indicators as proxies for risk. We will also track all eye-related adverse events. while we may not establish a definitive keratitis rate, our approach will generate valuable insights on factors affecting OK lens-related health and guide future research on optimal replacement schedules to reduce keratitis risk.

Possible Risks

In this research, lens prescribing and fitting procedures, clinical assessments and follow-up care will be conducted as per the guidelines provided by the lens manufacture (Menicon Pty Ltd). Regarding the risks, studies have demonstrated OK lenses are safe to use when fitted correctly by an eye care professional following the manufacturer's instructions.[9]

During the study, lens wearers may experience possible temporary adherence of the contact lenses to the eye surface, mild irritation and discomfort due to lens edges rubbing against the eyelid margin or an allergic reaction to lens solution. The risk of these complications is minimal when the study is monitored by a registered optometrist. While there is an exceptionally rare but possible risk of developing corneal infection and this risk is significantly lower with rigid contact lens than a soft contact lens.

Hypothesis

We hypothesize that the OK lens spoilage, including scratches and surface deposits, as well as eye discomfort levels, will progressively worsen across the visits at baseline visit, 6 months and 12 months visit.

II. STUDY OBJECTIVES

Objective: This study aims to assess the levels of lens spoilage under standard wear and disinfection practices in order to determine the optimal lens replacement frequency of OK lens. Further, this study will evaluate the health of anterior surface of the eye and lens comfort levels during one-year overnight use of OK lenses.

III. STUDY DESIGN

The proposed study uses a *prospective, observational quasi-experimental research design* where the contact lens spoilage from same participants will be observed over the time before and after contact lens wear. This design is well-suited for monitoring real-world lens wear and eye health outcomes. The term "quasi-experimental" suggests that the non-randomized, single group study, which is appropriate for this type of longitudinal observations studies.

Individuals (between 18 to 40 years of age) with a refractive error between -1.00 and -4.00D of sphere and astigmatism ≤ 2.50D will be recruited in the study. The eligible participants will receive study OK lenses during the dispensing visit, following the screening visit. Participants will attend total eight visits, including a follow up visit 2 weeks after the lens cessation which will

allow to assess the recovery or stabilization of eye surface measurements. At each visit, the anterior surface of the eye and comfort levels will be assessed using clinical microscope and by administrating questionnaires. Further, lens fit assessment and care regimen compliance will be monitored closely. A photographic method will be used to qualitatively assess lens spoilage at each visit. Furthermore, during the lens dispensing visit, the 6-month visit, and the 1-year visit, lens deposition will be quantitatively evaluated using established standard laboratory procedures. This will allow us to investigate the long-term changes in the eye surface during the OK lens wear and to determine their association with eye discomfort. Additionally, the levels of lens spoilage at different time points and their association with eye discomfort will determine the optimal replacement schedule of OK lens.

Participants will be monitored for:

- Signs of eye surface changes (e.g., corneal staining, conjunctival health).
- Contact lens comfort measured using standardized surveys (e.g., OSDI, CLDEQ-8).
- Lens spoilage (e.g., surface scratches, protein deposition).

Outcomes:

- ***Primary outcome:***
    - OK lens spoilage grading scores.
- ***Secondary outcomes:***
    - Comfort (Ocular Surface Disease Index, OSDI and Contact Lens Dry Eye Questionnaire-8, CLDEQ-8) and ocular surface changes (corneal and conjunctival staining).

Detailed Study procedure

Interested individuals are required to attend a *screening visit* to determine their eligibility. Eligible participants will be enrolled and asked to return for a baseline visit to collect OK lenses. Participants will be then reviewed at regular aftercare-visits (*baseline visit, 1 day, 7 days, 21 days, 6 months, 12 months and 2weeks lens cessation visit*) and to minimize the potential effects of diurnal variation, all data collection visits will be scheduled at about the same time of the day as the baseline visit (within two hours).

1. ***Screening Visit (60 min):*** At the screening visit, the following assessments will be conducted:
    a. **Visual acuity:** Measured using computerized visual acuity charts (Test Chart 2000 Pro, UK). Participants will be asked to read out letters from a chart where the letters get increasingly smaller. The line of smallest letters correctly identified will be recorded.
    b. **Auto-refraction:** Conducted using Shin-Nippon NVision K-5001 autorefractor (Shin-Nippon, Japan), which measures the refractive power of the eye. The participant will be asked to rest their chin and head against the machine's chin and head rest and look at a target while the measurement is taken.

c. **Subjective refraction:** Refines the autorefraction results using standard optometric procedure where the participant will look through various lenses and be asked to give verbal responses to finalize the spectacle prescription.

d. **Anterior eye health check**: will be performed using slit-lamp biomicroscopy routinely used by optometrists as this allows examination of the health of the front part of the eye in magnified view, using standardised grading scales. The participant will be asked to rest their chin and forehead against the chin and head rest while the instrument shines a small beam of light on the eye. Corneal and conjunctival staining will be assessed with fluorescein and graded according using the Oxford grading scale.

e. **Corneal topography**: Captured with the Medmont corneal topographer (Medmont Pty Ltd, Melbourne), which captures the shape and curvature of the front surface of the eye. The participant will be asked to use an eye patch to cover the eye that is not being measured and rest their chin and forehead against the corresponding rests. The participant will look at a target while the measurements are taken.

f. **OK lens parameter selection**: Then corneal topography measures will be imported to a proprietary (Johnson and Johnson) software to determine the final OK lens parameters. Study OK lenses will be then ordered empirically, and the participant will be scheduled for the fitting and dispensing visit.

If the candidate does not meet the selection criteria, they will be informed verbally of the reasons for ineligibility, and all data obtained during the screening visit will be discarded.

2. ***Baseline visit (45-60 min):*** Upon the arrival of lenses, participants required to attend the lens fitting and dispensing visit. This involves:

   a. **Lens fitting assessment:** Participants will be fitted with OK lenses and the lens fitting will be assessed and monitored using slit lamp biomicroscope and fluoresceine by a registered optometrist. This assessment will be repeated in all the follow-up visits**.** The properties of the lenses used in this study are presented in **Table *1***.

Table 1. Parameters of the contact lenses

ACUVUE® Abiliti™ Overnight – Finished Lens Specifi cations	
Manufactured by	Menicon Z
Material	Tisilfocon A
Oxygen Permeability	$163x10^{-11}$ (cm^2 /sec) (mL O_2/(mL × mmHg))
Diameter	10.20 mm, 10.60 mm, 11.00 mm
Center Thickness	0.24 mm
Base Curve	7.20 to 10.0 mm (0.05 mm steps)
Tangential Angle	46 to 65° (1° steps)
Sagittal Depth	0.95 to1.55 mm (0.01 mm steps)
Vertex Power	0.00 to +2.00 D (0.25 D steps) (default: 0.00)
Fenestrations	3 holes in the reverse zone, diameter 0.25mm

b. **Baseline lens spoilage assessment:** The lens surface spoilage will be assessed both before and after the lenses are worn by participants, using established methods and will be served as a baseline measure. These methods are as follows:

   i. **Photographic technique (Qualitative, Off-eye):** Lenses will be placed on a specialized mount that can be attached slit-lamp biomicroscope. Once the lenses are dry, photographs of both the front and back surfaces will be taken using a Zeiss SL 120 equipped with a Cam Compact (Carl Zeiss Meditec AG, Jena).

   ii. **Qualitative assessment (On-eye):** After the lenses are worn by the participant, slit-lamp photographs will be captured to assess the lens surface quality (surface scratches and deposition) using the Zeiss SL 120 equipped with Cam Compact (Carl Zeiss Meditec AG, Jena).

   iii. **Wettability assessment (On-eye):**
   On-lens tear break-up time: In this test, participants will be asked to blink twice and hold the blink. Time from the last blink to the first random appearance of dry patch will be measured in seconds.
   Fastness of dryness: The examiner will assess the fastness from the random appearance of dry patch to expand to the rest of the lens surface. Subjective grading – slow, medium and fast.

   Grading of lens surface deposits and scratches:

   - Surface deposits on the contact lens will be graded on a scale of 0 (absent, no deposits) to 4 (severe, deposits covering >75% of surface).
   - Surface scratches
     - Extent: Front surface scratches (on eye) on the contact lens will be graded on a scale of 0 (absent, no scratches) to 4 (extensive, scratches covering >75% of surface).
     - Magnitude: Front surface scratches (on eye) on the contact lens were graded on a scale of 0 (absent, no scratches) to 4 (severe, very deep).

Contact lens comfort: Assessed by using Ocular Surface Disease Index (OSDI), the Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8). The data obtained from this visit will serve as a baseline measurement.

After the lens surface assessment, participants will be trained on safe insertion and removal of OK lenses by the investigator. Once proficient, lens care procedures, including disinfection and storage, will be explained. Participants will be provided with contact lens care solutions. The details of contact lens care solutions are presented in **Table *2***. Participants will receive handouts detailing insertion, removal, and cleaning

instructions, along with an "**O-K Wear Time Journal**" to log lens use, bedtime, and wake times. Participants will be instructed to wear the lenses overnight for at least 6 hours. For after-hours support, contact details for the NSW Health Emergency Department will be provided in case of any unusual symptoms or issues.

Since it takes approximately one week for vision to be optimal with the study OK lens wear, daily disposable soft contact lenses will be provided to participants, if participants are expected to drive to the research facility in all the follow-up visits. These soft contact lenses will correct any expected residual power. In this case, participatns will be taught the insertion and removal and hygiene practices required for safe soft contact lens use by the investigators.

Table 2. The details of contact lens care solutions

Solutions	Disinfection system	Active ingredients
Menicare Plus	Multipurpose solution	Polyhexamethylene biguanide 0.0005%, Poloxamer0.5%, Hypromellose 0.275%
Menicon Progent	Weekly protein remover, disinfectant and intensive cleaner	Liquid A: Sodium Hypochlorite 20.3mg, Liquid B: Potassium Bromide (KBr) 30.75mg

3. ***Follow-up visits*** **(1-day overnight visit: 7-days visit; 14-days visit ;1month; 6 months; 9 months ;12 month; 2-weeks lens cessation visit):** During each visit, visual acuity assessment, auto-refraction, subjective refraction, anterior eye health check and corneal topography will be repeated as outlined in the screening visit section. Contact lens comfort using questionnaires and qualitative assessment of lens spoilage will also be performed in each lens wear visit. Similarly, lens fitting assessment will be conducted using slit-lamp bio microscopy and fluoresceine except during the 2-weeks lens cessation visit. The **2-weeks lens cessation visit,** which occur approximately two weeks after the 12-month visit, during which participants will cease lens wear for two weeks. This cessation period allows for the evaluation of recovery and stabilization of eye surface parameters, providing baseline comparisons. It will also help detect any eye-related events requiring further evaluation.
   All visits will be scheduled for a duration of approximately 1 hour (45-60 min) in the morning within 2 hours after waking and at these visits, lens care regimen and hygiene will be emphasised, and “OK Wear Time Journal” will be reviewed.

4. ***Quantitative assessment of the lens surface protein deposition:*** The amount of protein and lipid deposited on the lens surface will be quantified using standardized lab procedures. This assessment will be performed on the right eye lens at the base line visit, 6-month visit and the left eye lens at the 12-month visit. At 6-month visit, a new lens with similar parameters will be dispensed for the right eye, as the original lens will be used for quantitative assessment.

IV. PARTICIPANT SELECTION

Number of participants

We are planning a study with an ordinal data response variable from matched pairs of study participants. We estimate that the difference in the lens spoilage grading between matched pairs is normally distributed with a standard deviation 0.9. To detect a true mean difference of 1.90 between pairs, we will need 12 subjects to achieve 80% power, assuming a Type I error rate of 0.05. To account for a 20% dropout rate, a total of 16 participants will be recruited. We will keep screening until we have met that target.

Inclusion Criteria

- Age between 18 to 40
- Have refractive error between -1.00 and -4.00D of Sphere, Astigmatism ≤ 2.50D.
- Good eye health with no history of eye trauma or surgery, no eye disease
- Soft contact lens wearers willing to discontinue lens wear for at least 24 hours before participation. Individuals with or without a history of wearing rigid lenses (including orthokeratology) for a short-term (≤3months) and have discontinued wearing them for one month.
- Good general health and no medications which may influence eye health.
- Willing and able to comply with the research procedures and follow-up schedule.

Exclusion Criteria

- Age less than 18 years-old and more than 40 years-old
- Refractive error between less than -1.00D and more than -4.00D, astigmatism >2.50

Recruitment

This research will be conducted at the School of Optometry and Vision Science (SOVS), University of New South Wales, Sydney. Potential participants will be contacted via student and staff emails, as well as via approved recruitment posters displayed on the notice boards (paper and/or digital displays) of the SOVS, Rupert Myer Building (North Wing), Kensington Campus, UNSW Sydney. The study posters will also be shared via student representative social media groups (including WhatsApp, Facebook, LinkedIn groups) by SOVS administrative staff. The study investigators will not directly share the recruitment materials with the potential study participants. The recruitment posters will have brief details of what the research study is about and the eligibility criteria. Interested participants will contact the study investigators using the contact methods provided in the recruitment email or poster. In the absence of a response to the initial contact, a reminder/follow-up contact will be sent using the same recruitment methods.

Screening

Individuals who are interested to participate in the study will contact the study investigators using the contact methods provided in the recruitment email or poster. Before scheduling the screening visit, candidates will be reminded to consider the eligibility requirements outlined on

the recruitment email/poster. A digital copy of the Participant Information Statement and Consent Form (PISCF) will also be sent to candidates for them to review prior to attending the screening visit. After the participant has provided written consent, the investigators will proceed with the screening visit. The tests outlined in the study design will be conducted by the investigators as screening assessment. If the candidate is eligible for the study, the investigators will use screening visit data to determine appropriate OK lens parameters through proprietary (Johnson and Johnson) software. Study OK lenses will be ordered empirically, and the participant will be scheduled for the fitting and dispensing visit. If the candidate does not meet the selection criteria, they will be informed verbally of the reasons for ineligibility, and all data obtained during the screening visit will be discarded.

Informed Consent

Potential participants will be provided with Participant Information Sheets and Consent form (PISCF) to read, outlining the potential risks and benefits. There will be an opportunity to clarify details regarding the research study before participating. Interested participants, who contacted the investigators will be provided with PISCF through emails. All participants will be above the age of 18 years and will have adequate English language to be able to sign their consent for the study. The informed consent information sheet is attached.

Participants will be given at least 24 hours to review the PISCF before the screening visit. If they have any questions, they can contact the researchers. Written consent will be obtained at the screening visit, where participants will return the signed PISCF to the investigators. Only after consent is provided will the screening visit proceed.

Enrolment Procedure

The participant will only be considered enrolled into the study after the informed consent process has been completed and the participant has met all inclusion criteria and none of the exclusion ones. The participant will receive a study enrolment number, and this will be documented on all study documents.

V. STUDY OUTLINE

Table 3. Study outline and visit details.

Procedures/ Data (Y/N)	Screening visit (60 min)	Baseline visit (45-60 min)	1-day visit (45-60 min)	7-days visit (45-60 min)	21-days visit (45-60 min)	6-months visit (45-60 min)	12-month visit (45-60 min)	2-wk lens cessation visit (45-60 min)
Visit Window	*N/A*	*N/A*	*N/A*	± 2 days	± 2 days	± 7 days	± 7 days	± 2 days
Informed Consent	Y	N	N	N	N	N	N	N
Meet Inclusion / Exclusion Criteria	Y	N	N	N	N	N	N	N
Questionnaires	N	Y	Y	Y	Y	Y	Y	Y
Visual Acuity	Y	Y	Y	Y	Y	Y	Y	Y
Refraction	Y	Y	Y	Y	Y	Y	Y	Y
Anterior Eye Health Check	Y	Y	Y	Y	Y	Y	Y	Y

Procedures/ Data (Y/N)	Screening visit (60 min)	Baseline visit (45-60 min)	1-day visit (45-60 min)	7-days visit (45-60 min)	21-days visit (45-60 min)	6-months visit (45-60 min)	12-month visit (45-60 min)	2-wk lens cessation visit (45-60 min)
Visit Window	*N/A*	*N/A*	*N/A*	± 2 days	± 2 days	± 7 days	± 7 days	± 2 days
Corneal Topography	Y	Y	Y	Y	Y	Y	Y	Y
OK Lens Parameter Selection	N	Y	N	N	N	N	N	N
Lens Fitting Assessment	*N/A*	Y	Y	Y	Y	Y	Y	N
Lens Spoilage Assessment (qualitative)	*N/A*	Y	Y	Y	Y	Y	Y	N
Lens Spoilage Assessment (quantitative – protein assay)	*N/A*	Y	N	N	N	Y	Y	N
Lens compliance using "O-K Wear Time Journal"	*N/A*	Y	Y	Y	Y	Y	Y	Y

VI. SAFETY

1. Study Procedure Risks:

During the study, participants are required to wear OK lenses overnight and may experience possible temporary adherence of the contact lenses to the eye surface, mild irritation and discomfort due to lens edges rubbing against the eyelid margin, epithelial disruption or an allergic reaction to lens solution, mild discomfort, and a rare risk of corneal inflammation or infection.

Lens adherence is rare in open-eye rigid contact lens wear and is observed transiently on eye opening at a prevalence of about 80% after closed-eye rigid contact lens wear, where it may cause temporary localised corneal distortion and epithelial disruption. Previous research has demonstrated that these transient after-effects are rarely of clinical concern.

Epithelial disruption is a very common minor effect of wearing any contact lens, whether in research or clinical practice. The incidence of disruption varies considerably with wearing modality and lens type and is also patient-specific (for example, where there is underlying compromise of tear film or epithelial integrity prior to lens wear). Any such subjects will not be recruited for this research.

The risk of corneal inflammation and infection in short term soft and rigid contact lens wear are very low. Corneal infection is a rare disease in rigid contact lens wear and significantly lower than the risk posed by soft contact lens use. This slight risk is further reduced in this study because of the close clinical monitoring for warning signs and patient compliance, and the use of oxygen-permeable rigid lens materials appropriate for closed eye lens wear.

2. **Likelihood and severity of complications:**

The likelihood of developing corneal infections, including microbial keratitis, with orthokeratology (OK) lenses is relatively low, with an estimated incidence of 6.8 cases per 10,000 years of wear. This rate is lower than that associated with other overnight wear modalities of soft contact lenses. While the risk is rare, it cannot be classified as 'minimal' due to the potential for serious eye complications if an infection does occur. The severity of microbial keratitis can vary but may lead to significant discomfort, vision impairment, and, in severe cases, sight-threatening complications. This study aims to evaluate whether adjusting the lens replacement schedule can further mitigate this risk, enhancing the safety of OK lens wear for user.

3. **Steps to minimise or prevent complications:**

Participants will be closely monitored by a registered optometrist throughout the study to detect any early signs of discomfort or adverse effects. Proper lens hygiene practices, including disinfection procedures, will be thoroughly explained to participants, and reinforced at each visit. These practices are critical for reducing the risk of infections and other complications associated with lens wear. Additionally, participants will be provided with clear instructions on when to seek help or contact investigators in case of any discomfort, irritation, or unusual symptoms, ensuring timely intervention if needed.

4. **Informing potential harms and providing appropriate follow-up care:**

Managing distressed participants

Risks associated with the study is clearly outlined in the Participant Information Statement and Consent Form (PISCF), allowing the participants with ample time to review them before consenting. During the lens fitting visit when participants are taught safe wear and maintenance of OK lenses, they will be informed again of potential risks related to the study how to recognise symptoms and signs of any adverse event related to ortho-k lens wear and to contact the chief investigator on a 24-hour emergency contact number. The Chief Investigator is an Australian registered optometrist who will be able to triage the patient to appropriate care based on signs and symptoms. Despite our anticipation that there will be no clinically significant adverse effects in these studies from rigid contact lens wear, in the unlikely event of any clinically significant adverse response, a careful ocular examination will be carried out and lens wear will be discontinued. If required, the participant will be referred to an appropriate health care practitioner and will be closely monitored thereafter by the investigators. If the Chief Investigator is unable to examine the patient, they will be referred to the Red Eye Clinic at the UNSW Optometry Clinic during business hours and to the Sydney Eye Hospital during out of hours (8 Macquarie St, Sydney, NSW, 2000). Participants will have the opportunity to reassess their willingness to continue participating in the study at every study visit. If the participants wish to withdraw, they may do so by signing the study revocation form.

Overview

The investigators are mindful of the need to actively reflect upon the balance between benefits and risks of a project while it is being conducted and the degree to which continuation of the study is justified should an adverse event be reported. Thus, any adverse event will be reported and handled in accordance with HREC Adverse Event Reporting Guidelines.

5. **Benefits of the research outweigh the risk of harm or discomfort**:

Eye infections associated with orthokeratology (OK) lenses is generally considered a low-incidence risk, particularly with proper lens care and adherence to recommended replacement schedules. While investigators cannot guarantee the direct benefits from this research, the potential benefits may include clear vision without needing to wear glasses or contact lenses during the day. The benefit of participating in this research study will contribute to the development of strategies that are aimed to minimise severe form of eye disease associated with long-term use of spoiled OK lenses.

Early Termination

The techniques proposed have been applied by the same and different investigators previously in multiple clinical studies and have not ever resulted in termination of any of these studies due to adverse events, so this is very unlikely. However, consideration for early termination of the study would occur if a serious adverse event is reported or if all collected data were of insufficient quality for analysis after repeated attempts at improving recording techniques and methods.

VII. STATISTICAL CONSIDERATIONS.

Sample size calculations

We are planning a study with an ordinal data response variable from matched pairs of study participants. We estimate that the difference in the lens spoilage grading between matched pairs is normally distributed with a standard deviation 0.9. To detect a true mean difference of 1.90 between pairs, we will need 12 subjects to achieve 80% power, assuming a Type I error rate of 0.05. To account for a 20% dropout rate, a total of 16 participants will be recruited. We will keep screening until we have met that target. However, since this sample size was not determined using the exact methodology relevant to the current study, we will collect pilot data as part of the research. Based on the pilot data results, we will recalculate the final sample size to ensure the statistical power is appropriately adjusted for the use of orthokeratology (OK) lenses.

Statistical Analysis

The study hypothesises that OK lens spoilage, including scratches and surface deposits, as well as eye discomfort levels, will progressively worsen across the visits at baseline visit, 6 months and 12 months visit. All the statistical methods will be aimed to address the given hypothesis.

Once all data are collected, different tests will be conducted to establish whether they follow normal distributions. This step will ensure us to choose the appropriate statistical test based on the data distribution. Continuous variables will be expressed as means ± standard deviations, while categorical variable will be reported as medians and interquartile ranges (IQR). The time

effect (baseline, 6month and 12 month) and between-group differences in lens deposition levels, lens wettability scores, eye discomfort data from questionnaires, and eye surface changes will be tested with repeated measures ANOVAs (post-hoc tests) or Friedman test, with Bonferroni correction, where appropriate. This method will assess whether there are significant differences in spoilage across the three time points. If significant, post-hoc tests will help confirm if the worsening follows a progressive pattern from baseline visit to 12 months.

This study will use Spearman's correlation test to evaluate the correlations between the questionnaires scores (eye discomfort levels) and clinical test results (deposition and scratches). This correlation analysis will determine how these subjective and objective measures relate, further supporting the study hypothesis if a correlation is found. A value of $P < 0.05$ will be considered as significant. Furthermore, we determine to explore the association between OK lens replacement schedules and keratitis risk. By tracking lens spoilage, patient symptoms, and clinical indicators of infection over 12 months, we intend to gather preliminary data on infection risk. Given the difficulty of detecting keratitis with a small sample, we will use lens spoilage indicators as proxies for risk. We will also track all eye-related adverse events. while we may not establish a definitive keratitis rate, our approach will generate valuable insights on factors affecting OK lens-related health and guide future research on optimal replacement schedules to reduce keratitis risk.

VIII. STORAGE AND ARCHIVING OF STUDY DOCUMENTS.

Data format and storage location

The data collected in paper format will be stored in Rm 2.006A, Rupert Myers Building, North Wing, School of Optometry and Vision Science, UNSW Sydney. Data collected in an electronic format will be stored on a UNSW password protected OneDrive only accessible to the approved research investigators.

Data disposal

Once the study is completed the temporary data will be destroyed using safe data practices. This includes physical shredding of DVD's and any paper files and low-level formatting and overwriting of hard-drive data. De-identified data from the study stored at the UNSW Data Storage facility will be kept for 5 years and destroyed after the conclusion of this period in accordance with NHMRC guidelines.

Publishing and Dissemination of Research Results

The research team aiming to publish the study outcomes in Q1 journals, and where possible, presented at international and domestic conferences, either virtually, or face-to-face. All information will be published in a way that will not identify participants. If participants would like to receive a copy of the results, they can let the research team know by adding their email or mailing address in the consent form. We will only use those details to send participants the results of the research.

IX. Conflict of interest statement

Johnson & Johnson shall have the right to review each publication and presentation (including, but not limited to, full papers, abstracts, poster presentations, and oral presentations) of results of the Study prior to its submission to anyone not affiliated with Johnson & Johnson or Institution. No identifiable participant data will be disclosed to Johnson & Johnson. A copy of each proposed publication and presentation shall be submitted to Johnson & Johnson (by email, one draft per email in .doc and .pdf formats to Johnson & Johnson medical affairs team for review at least 45 business days (or 15 business days in the case of abstracts and full papers, posters presentations and oral presentations not exceeding 2 double spaced pages in length) prior to such submission. Such right is for the purpose of enabling Johnson & Johnson to provide peer input regarding the scientific content of such publications, to check the technical accuracy of information regarding products, to provide the Principal Investigator with information which may not have been previously provided, to verify that Johnson & Johnson as the source of funding or support for the research has been fully and adequately disclosed, to protect Johnson & Johnson patents, and to verify that none of Johnson & Johnson's information will be disclosed or inappropriately used contrary to the terms of this Agreement. In no case will Johnson & Johnson use the review for the purpose of influencing or amending the reported outcomes.

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