Cover page for ClinicalTrials.gov

Document: Statistical Analysis Plan (SAP)

Official Study Title: Defocus Incorporated Multiple Segment (DIMS) Spectacle Lenses versus Orthokeratology lenses (OKL) for slowing myopia progression in children aged 6-12 years. A non-inferiority randomized clinical trial. The NISDO Study.

NCT registration number: ClinicalTrials.gov: NCT05134935

Document date: 24 November 2025

Statistical analysis plan (SAP)

Section 1: Administrative information

1.1	**Title and trial registration number**	**Defocus Incorporated Multiple Segment (DIMS) Spectacle Lenses versus Orthokeratology lenses (OKL) for slowing myopia progression in children aged 6-12 years. A non-inferiority randomized clinical trial. The NISDO Study.** **ClinicalTrials.gov: NCT05134935** The title has been clarified further to enhance transparency
1.2	Names, affiliations and roles of SAP contributors	Lou-Ann C. Andersen, MD, PhD-student Research Unit for the Department of Ophthalmology, University Hospital of Southern Denmark, Lillebaelt Hospital, Vejle, Denmark; University of Southern Denmark, Odense, Denmark Trine M. Jakobsen, MD, PhD, Post.doc Research Unit for the Department of Ophthalmology, University Hospital of Southern Denmark, Lillebaelt Hospital, Vejle, Denmark; University of Southern Denmark, Odense, Denmark Flemming Møller, MD, Consultant, PhD, DMsc, Assoc. Prof. Research Unit for the Department of Ophthalmology, University Hospital of Southern Denmark, Lillebaelt Hospital, Vejle, Denmark; University of Southern Denmark, Odense, Denmark
1.3	Principal investigator/project lead	Lou-Ann C. Andersen, MD, PhD-student Department of Ophthalmology, Vejle Hospital, Lillebaelt Hospital, Department of Regional Health Research, University of Southern Denmark
1.4	Statistician/data analyst	Lou-Ann C. Andersen, MD, PhD-student Department of Ophthalmology, Vejle Hospital, Lillebaelt Hospital, Department of Regional Health Research, University of Southern Denmark (prepares analysis methods and act as a blinded interpreter of analysis results) Anna Mejldal, Biostatistician, MSc PhD Research unit of OPEN - Open Patient data Explorative Network (Odense), Department of Clinical Research, University of Southern Denmark (advisor on analysis preparation and presents the analysis result for blinded interpretation)
1.5	Reference to protocol version being used	2A Protocol 116050 Version 6 27.03.25 Approved by the Regional Committees on Health Research Ethics of Southern Denmark
1.6	SAP version and revision history	Version 2, 24-11-25: Corrected typographical errors, adjustment of Table 2 and 5.4, and added cover page.
1.7	**Date for approval of final SAP version**	**24.11.2025 (24 November 2025)**
1.8	Timeframe for conducting the proposed analysis	Dec25

Section 2: Introduction

2.1	Describe briefly background, research questions and rationale behind the study	Orthokeratology lenses (OKL) slow the progression of near-sightedness (myopia) by slowing the longitudinal growth of the eye in childhood. The new Defocus Incorporated Multiple Segments (DIMS) spectacle lens design shows similar results. However, it has yet to be resolved whether the DIMS spectacle lens treatment is as good as the OKL treatment. If the DIMS spectacle lens is non-inferior to the OKL, then the DIMS spectacle lens would be a suitable treatment modality for children who cannot or do not wish to use OKL. *Our purpose* is to determine whether the DIMS spectacle lens is noninferior to OKL lenses in slowing the progression of myopia in children.
2.2	Describe briefly objectives and/or hypotheses	In this non-inferiority randomised clinical trial, *our primary goal* is to compare the myopia control treatment efficacy of the new Defocus Incorporated Multiple Segments (DIMS) spectacle lenses to Orthokeratology lenses (OKL) after 18 months of therapy in myopic children. Secondly, we investigate the effect of choroidal thickness and pupil size on the treatment efficacy, as well as the difference in vision-related quality of life in the two groups prior to and after treatment initiation. **Primary outcome** 1. Axial length growth after 18 months of therapy. **Key secondary outcome ("secondary" in clinicaltrial.org)** 1. Overall eye length growth after 18 months of therapy. **Secondary outcome ("other" in clinicaltrial.org)** 1. To examine the effect of short-term changes in choroidal thickness on the treatment efficacy 2. To examine the influence of treatment on Pupil size after 6 months of therapy with OKL or DIMS spectacle lenses. 3. To examine the effect of pupil size on the treatment efficacy. 4. To evaluate the vision related quality of life using the questionnaire PREP2 prior to and 9 months after treatment initiation of OKL and DIMS spectacle lenses. Axial length is defined as a primary outcome in myopia progression clinical trials, and recommended to be reported as an absolute value (Sankaridurg et al. 2023).

Section 3: Study methods

3.1	<u>Study design</u> Describe type of study (i.e. experimental/observational, parallel group/cross over, singlecenter/multicenter ect.) and describe briefly interventions	Single-centre non-inferiority randomized clinical trial. The participants are included at baseline before randomization. Interventional study type with parallel groups. Active Comparator (reference treatment): OKL Experimental (new treatment): DIMS spectacle lens The DIMS spectacle lenses comprise a central optical zone for correction of distance vision surrounded by a myopic defocus

		zone with a relative power of +3.50 dioptres (D) comprised of about 400 defocus segments. The OKL are custom-fit, form-stable, four-zone reverse geometry contact lenses with a 6 mm back optic zone diameter and 0.75 D compression factor. The lenses are used during sleep and temporary flatten the central cornea reducing central corneal power and steepening the paracentral cornea with relatively more corneal power.
3.2	Randomization details (if applicable) Describe randomization i.e. allocation ratio, potential factors randomization will be stratified for and describe how and when randomization will be performed	Allocation ratio: 1:1 Number of possible assignments in the allocation table: 104 Block sizes: 4, 6 and 8. The allocation sequence was generated by the data manager at OPEN, Open Patient Data Explorative Network, and concealed from research staff and participants using REDCap electronic data capture tools, a secure, web-based platform designed to support data capture for research studies. No stratification. Randomization is performed after inclusion at the end of the baseline visit by research staff using REDCap. Open label: No blinding of participants or personnel from knowledge of which intervention a participant received.
3.3	Sample size Describe calculation of sample size or reference to sample size calculation in study protocol	Primary outcome: Based on the randomised clinical study of myopic children using DIMS spectacle lenses (Lam et al. 2020) standard error of mean was 0.02 mm and n = 79 in the DIMS group, hence the standard deviation (Smith et al. 2010) was calculated to be $SE = \frac{SD}{\sqrt{n}}$ given a SD of 0.178 mm. Based on the CONTROL-study (Jakobsen & Møller 2021) the SD of the treatment effect after 18 months was 0.18 mm in the OKL group. A sample size calculation for a non-inferiority study between the two groups given a significance level of 0.025 (one-sided test) and a power of 80% with a mean difference between treatment groups of 0.13 mm and a SD of 0.18 mm the sample size for each group should be 32 children. With an expected drop out of 30% a total of 42 children will be needed in each group. A difference of 0.13 mm was chosen with reference to the correlation between change in cycloplegic spherical equivalent refractive error and axial length equivalent to 0.25D for female subjects aged 6 to 12 years in a Danish population (Jakobsen, Gehr & Moller 2020). 0.25D is the minimum measurement increment of refraction itself. Thus, to conclude non-inferiority, the difference between the two treatments (DIMS and OKL) need to be equal to, or less than, 0.25 D after 18 months of treatment. The dropout rate evaluation one month after the inclusion of the last participant showed a dropout rate of 20%. Consequently, after clinical and statistical considerations, we increased the

		total number of participants from 84 to 90, which corresponds to a 40% dropout rate. This was to ensure the sufficient power of the study. Sample size: 90 children Non inferiority margin: Minimal clinically important difference: 0.13 mm (= 0.25D), SD 0.18
3.4	Hypotheses framework Describe hypotheses framework i.e. superiority, equivalence or noninferiority hypothesis testing and which group comparisons will be analysed	Noninferiority hypothesis: H_0: DIMS is inferior to OKL, i.e. the difference in axial length change (DIMS – OKL) is > 0.13 mm. H_1: DIMS is non-inferior to OKL, i.e. the difference in axial length change (DIMS – OKL) is ≤ 0.13 mm. That is, we test whether the DIMS spectacle lens (new treatment) is not worse than the OKL (reference treatment) by more than 0.13 mm after 18 months. The non-inferiority test is only applied to the primary outcome. All other outcomes are tested using standard superiority hypotheses.
3.5	Statistical interim analyses and stopping guidelines (if applicable) Describe how and when interim analyses will be performed, and potential planned adjustment of significance level due to interim analyses. Describe guidelines for stopping the trial early.	No stopping guidelines. No planned interim analyses.
3.6	Timing of outcome assessments and follow-up Describe time points at which outcomes/covariates will be measured (consider a figure to visualize the time windows of measurements – see appendix)	Primary and key secondary outcome: The primary outcome (axial length) and the key secondary outcome (overall eye length) is measured at baseline and every 6 months for 18 months on both eyes. If T0 (handout) exceeded 5 weeks from the baseline visit, a new measurement is conducted to replace the baseline measurement. An additional visit was conducted at 1 month for both groups and additional visits for lens fitting and ocular health evaluation were conducted in the OKL group. Covariates: - Age at baseline - Cycloplegic spherical equivalent refractive error at baseline - Axial length at baseline - Number of myopic parents (spherical equivalent refractive error ≤ -0.50D) at baseline Time-varying post-randomisation variables: - Adherence: Non-wear (patient-reported as the participants total amount of days without OKL or hours without DIMS). No-wear since last visit is recorded at every visit during the study.

3.7	Timing of final analysis i.e. all outcomes analysed collectively or analyses performed according to planned follow-ups	The primary outcome and the key secondary outcome are analysed collectively.

Section 4: Statistical principles and protocol deviations

4.1	Confidence intervals and P-values Specification of level of statistical significance and confidence intervals to be reported. Describe, if relevant, rationale for adjustment for multiple testing and how type 1 error will be controlled for	For the primary outcome, a one-sided test at α = 0.025 will be used. Non-inferiority will be concluded if the upper bound of the 95% confidence interval is equal to or below the margin of 0.13 mm. Secondary outcomes will be tested two-sided at α = 0.05, with corresponding 95% confidence intervals. No adjustment for multiple testing will be made; secondary results are considered exploratory.
4.2	Adherence/compliance and protocol deviations Define adherence/compliance and how this is assessed in the study. Define protocol deviations and which protocol deviations will be summarized and presented	Main challenges: - Treatment adherence: Degree of adherence is assessed by patient-reported days without OKL or hours without DIMS between visits as “No-wear”. “No-wear” is included in the mixed effects model as a time-varying post-randomisation variable (see 6.2) and in a sensitivity analysis (see 6.3). Missing measurements is assumed to be best case = 0 days/hours without OKL/DIMS. Day time hours is assumed to be 16 hours. Following defines the binary definitions of adherence: -- Low adherence (in the 6-month period between visits) • OKL: > or = 75% of days without OKL • DIMS: > or = 75% of hours without DIMS -- Moderate Adherence (in a 6-month period) • OKL: 25-75% of days without OKL • DIMS: 25-75% of daytime hours without DIMS -- High Adherence (in a 6-month period) • OKL: < or = 25% of days without OKL • DIMS: < or = 25% of daytime hours without DIMS OKL: Each eye contributes with 50% of adherence; E.g. The right eye has 25% of days without OKL and the left eye has 75% of days without OKL, which gives a total % days without OKL of: (0.25/2) + (0.75/2) = 50%, corresponding to moderate adherence. - Technical error in the reading of the autorefractor apparatus output at baseline resulting in four children included without correct cycloplegic refraction, assuming random error. The true output was available for analysis. No children were excluded by this error. This is handled by making a sensitivity analysis (see 6.3) - Drop out at treatment allocation/follow-up, will be handled by offering the participant a follow-up examination corresponding to the 18-month visit (noting use of types of treatments used and days using treatment) and used in a sensitivity analysis (see 6.3).

		- Ocular magnification correction algorithm of the choroid thickness for the key secondary outcome: -- Missing corneal radius is handled as 0 (= no correction for corneal radius). It is noted in which participants and visits this occur, to report how many measurements this will concern. -- Missing refractive error is handled as 0 (= no correction for refractive error). It is noted in which participants and visits this occur, to report how many measurements this will concern. -- Algorithm non-functioning in participants with a refractive error = 0 (e.g. the OKL group) and an axial length exceeding maximum to be handled in the algorithm. It is handled by calculating the theoretical refractive error for the relevant visit using the AL increase since baseline: -0.25D is added to the baseline cycloplegic refractive error for every 0.15 mm longer AL for males and every 0.13 mm longer AL for females (Jakobsen, Gehr & Moller 2020). It is noted in which participants and visits this occur, to report how many measurements this will concern.
4.3	Analysis populations Define analysis population i.e. intention-to-treat, per-protocol, complete case, safety population	As adherence challenges are expected (see 4.2) both Intention to treat and a per-protocol approach will be performed. The primary analysis will follow the intention-to-treat (ITT) principle, including all randomized participants regardless of adherence or protocol deviations. A per-protocol (PP) analysis will be conducted as a sensitivity analysis, including participants with high or moderate adherence and no major protocol violations described in (4.2) Missing data will be handled using mixed effects models under the missing at random (MAR) assumption (6.4). Additional sensitivity analyses will be performed to assess the impact of deviations

Section 5: Study population

5.1	Screening (if applicable) Describe screening data to determine eligibility (i.e. scoring and scales)	Potential participants were preliminary referred from private ophthalmic practices to the Department of Ophthalmology, University Hospital of Southern Denmark, Lillebaelt Hospital, Vejle, Denmark, based on cycloplegic refractive error in relation to age. After screening, potential eligible participants and their guardians were invited to an information meeting.
5.1	Eligibility Summarize in- and exclusion criteria	Inclusion criteria: - Myopic children aged 6 to 12 years: Myopia of the 6 to 8-year-olds (inclusive): -1.00 to -4.75 D spherical component and up to -2.50 D of regular astigmatism (both eyes). Myopia of the 9 to 12-year-olds (inclusive): -2.00 to -4.75 D spherical component and up to -2.50 D of regular astigmatism (both eyes). - Anisometropia ≤ 1.50 D cycloplegic spherical equivalent refractive error. - Best corrected visual acuity at age 6 to 12 years (inclusive): 0.8 Snellen (equivalent to ≥ 3/5 letter on the 0.8 line = 78 ETDRS letters) Exclusion criteria:

		- Manifest or intermittent squint. - Contraindications to the use of OKL comprising (not exhaustive): keratoconus, chronic allergic conjunctivitis and keratoconjunctivitis sicca. - Previous eye surgery. - Chronic eye disease demanding daily use of eye drops. - Non-compliance to eye examinations (unstable fixation or anxiety towards contact lenses). - Previous myopia control treatment. After trial commencement, project staff confused criteria of best corrected visual acuity in the 9 to-12 years group with the criteria of the 6 to 8-years group resulting in four children of 9 years old included using the 6 to 8-years old criteria for best corrected visual acuity. No children were excluded by this mistake. Preliminary referral or screening was not based on the visual acuity criteria. The visual acuity criterium was chosen to screen for abnormal vision. After clinical considerations, the visual acuity inclusion criteria in the 9–12-year group was too strict, as some of the younger children may not have fully matured visual development as 9-year-olds. Hence the inclusion criteria was adjusted to age 6 to 12 years (inclusive): 0.8 Snellen (equivalent to ≥ 3/5 letter on the 0.8 line = 78 ETDRS letters), which reflects the visual acuity criteria used in the CONTROL-study (Jakobsen & Møller 2021)
5.2	Recruitment and flow chart Specification of steps in the recruitment process i.e. enrolment, screening allocation for use in flow chart (see appendix)	Potential participants were preliminary referred from private ophthalmic practices to the Department of Ophthalmology, University Hospital of Southern Denmark, Lillebaelt Hospital, Vejle, Denmark, based on cycloplegic refractive error in relation to age. After screening, potential eligible participants and their gradian(s) receive a written participation information including an invitation to an information meeting and an informed consent form. Exclusion will be recorded in the following categories: At screening: - Not meeting inclusion criteria (give reasons) - Meet exclusion criteria (give reasons) - Declined to participate (gives reason if possible) - Other reasons At information meeting: - Not meeting inclusion criteria (give reasons) - Meet exclusion criteria (give reasons) - Declined to participate (gives reason if possible) - Other reasons At baseline before inclusion: - Not meeting inclusion criteria (give reasons) - Meet exclusion criteria (give reasons) - Declined to participate (gives reason if possible) - Other reasons
5.3	Withdrawal/loss to follow-up Specification on how reason and timing of withdrawal or loss to follow-up will be	Will be recorded in the following categories: - Did not receive allocated intervention (give reasons) - Loss to follow-up - Discontinued intervention (give reasons)

	recorded and presented (i.e. in the flow chart – see appendix)	- Excluded from analysis (give reasons)
5.4	Baseline patient characteristics List of baseline characteristics and how these data will be descriptively summarized in a "Table 1" (see appendix)	Normal distribution: Mean, SD Not at normal distribution: Median, Range (As determined by a normal quantile-quantile plot) -Age at enrolment -Sex -Cycloplegic spherical equivalent refractive error -Best corrected visual acuity -Axial length -Subfoveal Choroidal thickness -Season (monthly quarter in which baseline was conducted) -Number of myopic parents (spherical equivalent refractive error ≤ -0.50D) Descriptive data will be reported tables and descriptive figures: - Non-wear (patient-reported as days without OKL or hours without DIMS) as a binary variable (see also 4.2, 6.2 and 6.3). - Efron score (Efron Grading Scale for Contact Lens Complications) as a mixed model (see 6.5) - SS-OCT measurement quality assessment: time of day (Figure 1), image quality, measurements needing manual correction of automated segmentation errors, number of scans manually corrected for automated segmentation errors in a measurement. - Visit scheduling assessment: date range

Section 6: Analysis

6.1	Exposure and outcome definitions Describe details on exposure i.e. assessment, definitions, units and thresholds or the intervention/treatment under study. List and describe details on primary and secondary outcomes i.e. definition of outcome and timing, specific clinical measurements and units (i.e. mmol/mol) or any calculation or transformation of data to derive the outcome (i.e. sum score, change from baseline,	Primary Outcome Measure: Axial length growth of the eye. Length is measured in mm [Time frame: 18 months of therapy] Orthokeratology lenses induce flattening of the cornea, which reduces Axial length (AL). AL in the OKL group is adjusted for the decrease in central corneal thickness (CCT): adjusted $AL_{follow\text{-}up}$ = $AL_{follow\text{-}up}$ + (CCT_{BL} - $CCT_{follow\text{-}up}$). The IOLMaster 700 version 1.90 (Carl Zeiss Meditech AG, Jena, Germany) measure the axial length, and is highly repeatable in healthy and myopic children (Garcia Ardoy et al. 2023, Huang et al. 2020) with a smallest detectable change (test-retest repeatability) of myopic children of 0.025 mm for spectacle users and 0.041 mm for OKL users (Garcia Ardoy et al. 2023). Key Secondary Outcome Measure: Overall Eye length growth. Length is measured in mm [Time frame: 18 months of therapy] Overall Eye length is defined as: AL + Subfoveal choroidal thickness (SFCT).

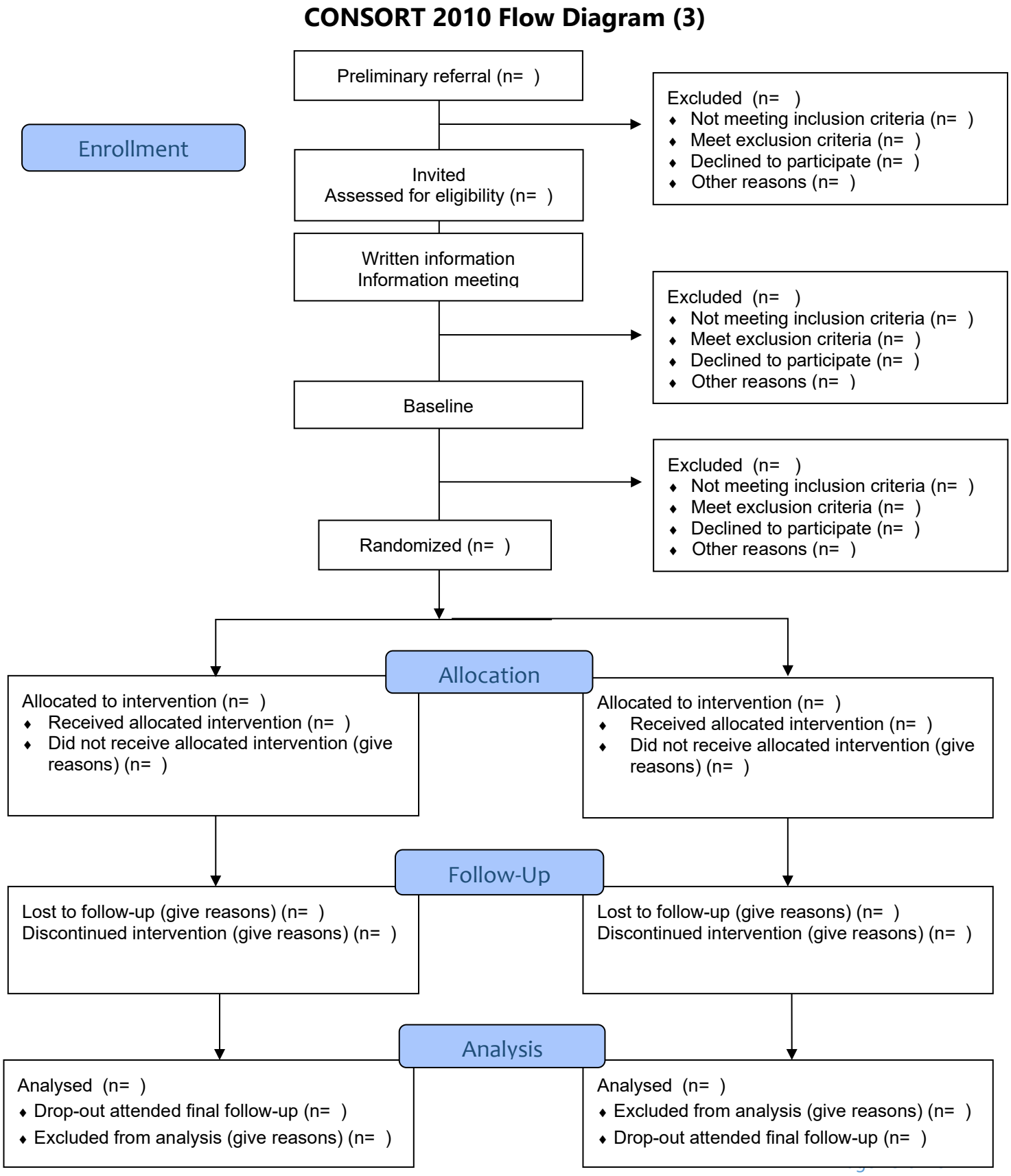
	logarithm, quality-of-life scoring algorithm)	The choroidal thickness is corrected for ocular magnification using the axial length, mean corneal radius, and refractive error entered in an algorithm. Open label: Outcome assessment was not blinded from knowledge of which intervention a participant received.
6.2	<u>Primary analysis methods</u> Describe in details which statistical methods will be used (i.e. regression), how treatment effects will be presented (i.e. which effect measure - OR, HR etc.) and if estimates will be adjusted for covariates (see appendix). If analyses will be adjusted for covariates, describe how the sufficient adjustment set will be defined (i.e. using DAGs) Describe methods used to check assumptions (i.e. normality, proportional hazards) behind the statistical models, and alternative methods if assumptions about distribution do not hold.	<u>Primary outcome</u> Blinded interpretation of primary analysis: Study groups labelled as A & B is presented to the authors. We will compare the two treatment groups with one linear mixed effects regression model with the participant as random intercept using axial length as the dependent variable and visit as the (categorical) independent variable, with baseline as reference point. Both eyes are used in the analysis. Both an Intention to treat and a per-protocol approach will be performed. The regression models will be reported as unadjusted, and as adjusted for the following covariates for a more precise result: - Age at baseline - Cycloplegic spherical equivalent refractive error at baseline - Axial length at baseline - Number of myopic parents (spherical equivalent refractive error ≤ -0.50D) at baseline The adjusted model will also be adjusted for time-varying post-randomisation variable to explain the performance bias in the "effect" of adherence: - Non-wear (patient-reported as the participants total amount of days without OKL or hours without DIMS) The non-inferiority margin is 0.13 mm. Non-inferiority will be concluded if the upper bound of the 95% confidence interval for the estimated treatment difference (DIMS – OKL) after 18 months is equal to or below 0.13 mm, in both ITT and PP analyses. Results will be presented as estimated coefficients with standard errors (SE), p-values (p) and 95% confidence intervals (CI): 1) Mean axial elongation at each 6-month interval over 18 months by treatment group 2) Between-group differences in axial elongation at each time point. Model assumptions will be assessed using Q-Q plots for normality of residuals and random effects, and residual vs. fitted plots to check for homoscedasticity. If assumptions are violated (e.g. non-normality or heteroscedasticity), robust standard errors or non-parametric bootstrapping will be applied. <u>Key secondary outcome</u>: A similar approach will be made for the key secondary outcome.
6.3	<u>Additional analysis methods</u>	In case of non-inferiority, superiority is tested in the same population at 0.05 without a statistical penalty because of the

	Describe any planned sensitivity and subgroup analysis including how subgroups will be defined (see appendix).	closed testing principle. Superiority is declared if the upper 95%CI bound is below zero (Figure 3). In case of inferiority, a subgroup analysis of participants in the DIMS group with axial elongation exceeding emmetropic progression rate will be conducted as a hypothesis generating post hoc analysis. <u>Adherence:</u> Sensitivity analysis of binary adherence "No-wear", is repeated in groups of "high adherence", "moderate adherence" and "low adherence" (see 4.2). <u>Protocol deviations</u>: -Sensitivity analysis with and without the four children mistakenly included by technical error in the autorefractor apparatus result reading at baseline (see 4.2). Analysis is either provided in supplementary or by request. -Sensitivity analysis of dropouts. <u>Additionally, post hoc analysis:</u> - axial elongation after 18 months in relation to age at enrolment. - axial elongation after 18 months in relation cycloplegic spherical equivalent refractive error at baseline.
6.4	<u>Missing data</u> Describe how missing data will be explored and which assumptions and methods will be used to handle missing data (i.e. multiple imputation)	Missing data assumed to be missing at random (MAR) and will be handled by the mixed effects regression model.
6.5	<u>Harms (only applicable in experimental studies)</u> Describe the collection of safety data i.e. data on severity, expectedness, causality. Describe grouping and analyses planned i.e. incidence analyses on grade 3-4 events only.	The DIMS spectacle lens treatment is considered safe, with no treatment-related adverse events reported in a randomized controlled trial (Lam et al. 2020). Regarding the OKL treatment, safety data was collected using the Efron score (Efron Grading Scale for Contact Lens Complications) for both eyes. Adverse event was defined as; Any vision threatening or treatment-requiring conditions related to contact lens usage AND corneal staining Efron score Grade 2 or more. Reporting zero events if no harms were observed. Efron score is used in both treatment groups. The Efron score of the OKL group is compared to the DIMS group using a mixed model.
6.6	<u>Statistical software</u> Specify statistical packages to be used for the analyses	Stata

Garcia Ardoy E, Mateos N, Roda L, Torrado Sierra O, Baptista AM & Serra PM (2023): Repeatability and agreement of swept-source optical coherence tomography and partial coherence interferometry biometers in myopes. Clin Exp Optom **106**: 783–792.
Huang J, Zhao Y, Savini G, Yu G, Yu J, Chen Z, Tu R & Zhao Y (2020): Reliability of a New Swept-Source Optical Coherence Tomography Biometer in Healthy Children, Adults, and Cataract Patients. J Ophthalmol **2020**: 1–9.
Jakobsen T, Gehr N & Moller F (2020): Correlation between change in cycloplegic spherical equivalent refractive error and change in axial length in Danish children aged 6 to 12 year. Acta Ophthalmol.
Jakobsen TM & Møller F (2021): Control of myopia using orthokeratology lenses in Scandinavian children aged 6 to 12 years. Eighteen-month data from the Danish Randomized Study: Clinical study Of Near-sightedness; TReatment with Orthokeratology Lenses (CONTROL study). Acta Ophthalmol (Copenh) aos.14911.
Lam CSY, Tang WC, Tse DY, et al. (2020): Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol **104**: 363–368.
Piaggio G, Elbourne DR, Pocock SJ, Evans SJW & Altman DG (2010): Reporting of Noninferiority and Equivalence Randomized Trials.
Sankaridurg P, Berntsen DA, Bullimore MA, et al. (2023): IMI 2023 Digest. Investig Opthalmology Vis Sci **64**: 7.
Smith EL, Hung L-F, Huang J, Blasdel TL, Humbird TL & Bockhorst KH (2010): Effects of Optical Defocus on Refractive Development in Monkeys: Evidence for Local, Regionally Selective Mechanisms. Investig Opthalmology Vis Sci **51**: 3864.

Appendix: Figure and table templates

5.2-3 Flow chart template for randomized trials



5.4 Baseline table ("Table 1") template

Table 1: Baseline characteristics of the study population

	DIMS (N = xx)	OKL (N = xx)	All (N = xx)	Missing
Age at enrolment, year ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Males, N (%) ( )	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
SER, D ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
BCVA, ETDRS ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
AL, mm ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
SFCT, µm ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Season, quarter ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Myopic parents, N ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)

N = number; DIMS = Defocus Incorporated Multiple Segment; OKL = Orthokeratology lenses; SD = standard deviation; D = dioptre; SER = cycloplegic spherical equivalent refractive error; BCVA = Best corrected visual acuity; ETDRS = standard scale to test visual acuity; AL = Axial length at baseline or at T0 (Handout) if T0 exceeds 5 weeks from baseline; mm = millimetre; SFCT = subfoveal choroidal thickness; µm = micrometre; Season = Monthly quarter in which baseline was conducted; Myopic parents = number of myopic parents (0 – 2) with a spherical equivalent refractive error ≤ -0.50D

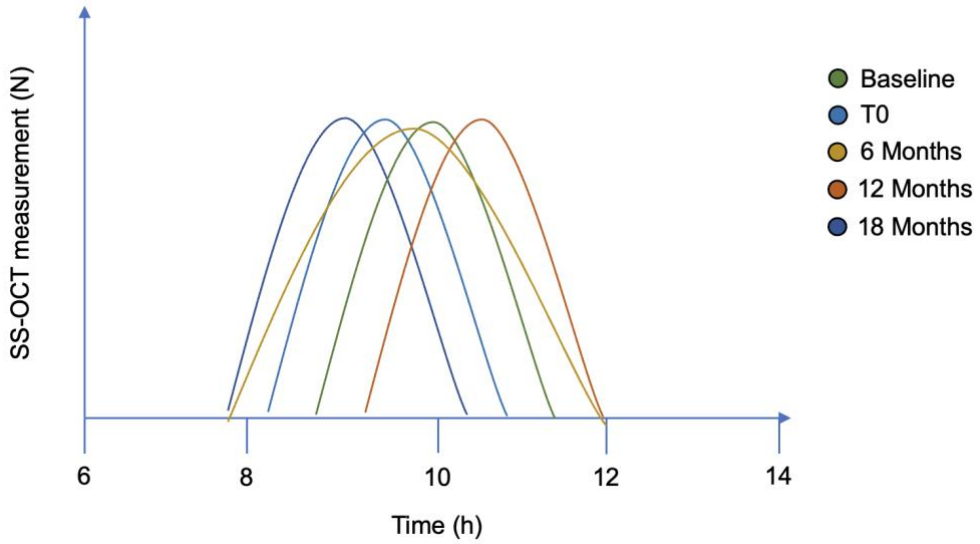
Table 2: Descriptives of the study population

	DIMS (N = xx)	OKL (N = xx)	All (N = xx)	Missing
Non-wear ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
6 Months				
High adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Moderate adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Low adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
12 Months				
High adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Moderate adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Low adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
18 Months				
High adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Moderate adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Low adherence	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
SS-OCT measurement Quality assessment				
Image quality ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
SS-OCT measurements needing manual correction of automated segmentation errors, N ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)

Number of scans manually corrected for automated segmentation errors within a SS-OCT measurement ( )	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
Visiting schedule assessment: Date range from T0 ( )				
6 Months	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
12 Months	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)
18 Months	xx (xx)	xx (xx)	xx (xx%)	xx (xx%)

N = number; DIMS = Defocus Incorporated Multiple Segment Spectacle lenses; OKL = Orthokeratology lenses; SD = standard deviation; Non-wear = patient-reported as days without OKL or hours without DIMS; High adherence = x; Moderate adherence = x; Low adherence = x; SS-OCT = Swept-Source Optical Coherence Tomography; T0 = Handout of DIMS or OKL

Figure 1: SS-OCT measurement time assessment



SS-OCT = Swept-Source Optical Coherence Tomography; T0 = Handout of Defocus Incorporated Multiple Segment Spectacle lenses (DIMS) or Orthokeratology lenses (OKL)

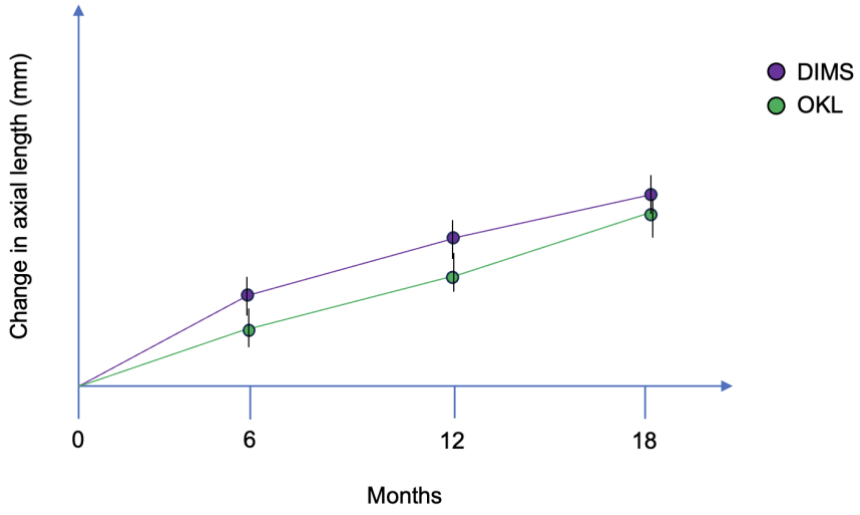
6.2 Primary analyses table template

Table 3: Linear mixed-effects models of axial length for the x participants

Visit	The DIMS group Difference from baseline mm (95% CI) SE, p	The OKL group Difference from baseline mm (95% CI) SE, p	The Difference between DIMS and OKL (DIMS – OKL) mm (95% CI) SE, p	Missing
Unadjusted				
Baseline	(Reference)	(Reference)	(Reference)	xx (xx%)
6 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
12 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
18 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
Adjusted				
Baseline	(Reference)	(Reference)	(Reference)	xx (xx%)
6 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
12 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
18 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)

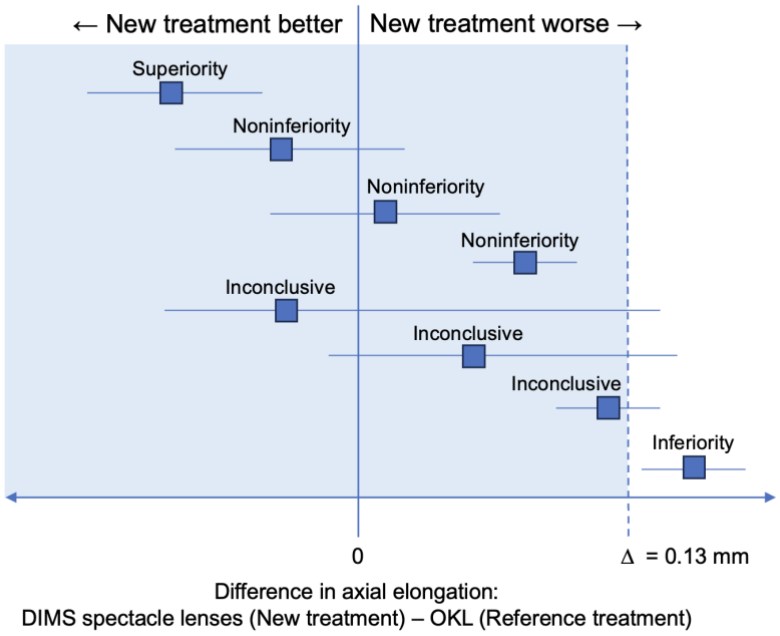
Linear mixed-effects model with the participant as a random intercept, axial length as the dependent variable, visit as the independent variable, and baseline as the reference visit. DIMS = Defocus Incorporated Multiple Segment spectacle lenses; OKL = Orthokeratology lenses; mm = millimetre; 95%CI = confidence interval; SE = standard error; p = p-value

Figure 2: Model-adjusted mean and 95% Confidence interval of axial length from baseline to 18 months



DIMS = Defocus Incorporated Multiple Segment spectacle lenses; OKL = Orthokeratology lenses; mm = millimetre

Figure 3: 2-sided 95% Confidence interval error bars and noninferiority margin for the difference in axial elongation between DIMS spectacle lenses and OKL after 18 months (Possible scenarios illustrated and adapted from (Piaggio et al. 2010)). The graphic will show the results of the Intention to Treat and the per-protocol model, both with and without adjustments.



DIMS = Defocus Incorporated Multiple Segment spectacle lenses; OKL = Orthokeratology lenses; Δ = noninferiority margin

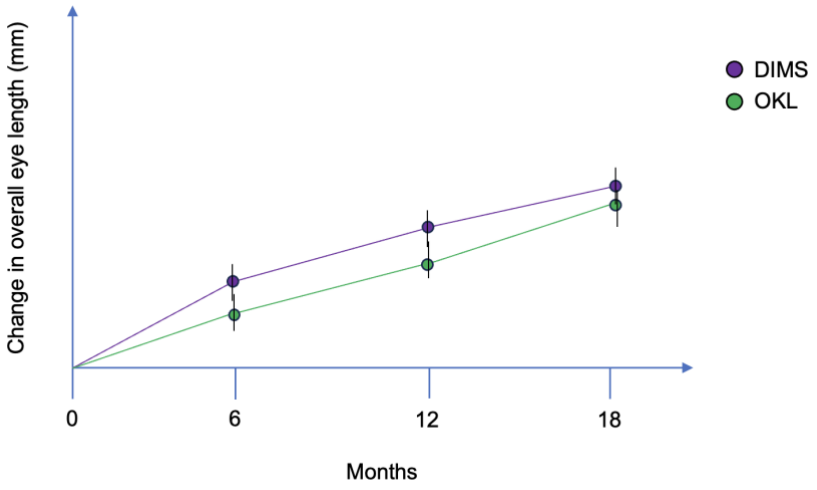
Key secondary outcome:

Table 5: Linear mixed-effects models of overall eye length for the x participants

Visit	The DIMS group Difference from baseline mm (95% CI) SE, p	The OKL group Difference from baseline mm (95% CI) SE, p	The Difference between DIMS and OKL (DIMS – OKL) mm (95% CI) SE, p	Missing
Unadjusted				
Baseline	(Reference)	(Reference)	(Reference)	xx (xx%)
6 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
12 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
18 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
Adjusted				
Baseline	(Reference)	(Reference)	(Reference)	xx (xx%)
6 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
12 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)
18 Months	–x (–x to x) x, x	–x (–x to x) x, x	–x (–x to x) x, x	xx (xx%)

Linear mixed-effects model with the participant as a random intercept, overall eye length as the dependent variable, visit as the independent variable, and baseline as the reference visit. Overall Eye length = Axial length + Subfoveal choroidal thickness; DIMS = Defocus Incorporated Multiple Segment spectacle lenses; OKL = Orthokeratology lenses; mm = millimetre; 95%CI = confidence interval; SE = standard error; p = p-value

Figure 4: Model-adjusted mean and 95% Confidence interval of overall eye length from baseline to 18 months



Overall Eye length = Axial length + Subfoveal choroidal thickness. DIMS = Defocus Incorporated Multiple Segment spectacle lenses; OKL = Orthokeratology lenses; mm = millimetre

References for further reading on SAP and reporting guidelines

1) Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Dore C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337-43. doi: 10.1001/jama.2017.18556.

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