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REVIEW ARTICLE

Efficacy of interventions for myopia control in children: A systematic review with network meta-analyses

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Abstract

To determine the effectiveness of various interventions in reducing myopia progression in children. Literature databases were searched on December 2, 2023: PubMed, Embase, the Cochrane Central, Web of Science Core Collection, BIOSIS Previews, Current Contents Connect, Data Citation Index, Derwent Innovations Index, KCI-Korean Journal Database, Preprint Citation Index, ProQuest™ Dissertations and Theses Citation Index and SciELO Citation Index. PRISMA guidelines and the Cochrane Handbook recommendations were followed. All unique interventions were analyzed individually in order to generate clinically applicable results. The main outcome was axial length progression. Secondary outcomes were incident corneal infiltrates, photophobia, development of an allergic response towards the intervention, visual acuity at near and distance and drop-out from allocated intervention/control. We identified 74 RCTs involving 12 154 participants aged 6–18 years. Network meta-analysis compared axial length after 1 year between 45 interventions and placebo or single-vision spectacles. The most effective interventions reported in weighted mean difference and 95% confidence interval were low-level red-light (−0.33 mm (−0.40, −0.25)), ortho-K with 5 mm treatment zone (−0.32 mm (−0.41, −0.24)), ortho-K with aspheric base curve (−0.29 mm (−0.37, −0.22)), atropine 1.0% (−0.28 mm (−0.30, −0.26)), combined atropine 0.01% and ortho-K (−0.24 mm (−0.37, −0.11)), spectacles with highly aspherical lenslets (−0.23 mm (−0.26, −0.19)), ortho-K with increased compression factor (−0.23 mm (−0.28, −0.17), atropine 0.05% (−0.21 mm (−0.30, −0.13)) and defocus incorporated multiple segments spectacles (−0.21 mm (−0.27, −0.15)). Photophobia and reduced near-visual acuity were reported for atropine, and lower adherence to treatment was found for atropine at 1.0%. There was no significant association between any interventions and corneal infiltrates or allergic reactions. Over 70% of the studies were conducted in Asian populations. This systematic review and network meta-analysis highlights the efficacy of various interventions, including orthokeratology lenses, atropine, highly aspherical lenslets and defocus incorporated multiple segments spectacles in slowing axial elongation in children. Low-level red-light therapy also slowed axial length progression, but further research is needed to assess the potential side effects. Future studies should include diverse populations and standardized methodologies to enhance the applicability and comparability of results.

KEYWORDS
axial length, efficacy comparison, myopia control, network meta-analysis

1 | INTRODUCTION

Myopia affects approximately a quarter of the global population, and by 2050, nearly half of the world's population is expected to be myopic, with 10% having high myopia (defined as a refraction of −5 dioptres) (Holden et al., 2016). Development and progression of myopia in children have been associated with factors such as intensity and duration of education, near work, less time spent outdoors and parental myopia (Jones-Jordan et al., 2011; Pärssinen & Kauppinen, 2022; Saw et al., 2001). Race and ethnicity also appear to influence prevalence and progression, indicating that myopia arises from genetic and environmental factors (Pan et al., 2012).

Myopia poses an increased risk of developing several complications, such as cataracts, glaucoma, retinal detachment and myopic maculopathy, possibly leading to irreversible vision loss or blindness (Ikuno, 2017). Younger age at diagnosis is related to the development of high myopia leading to an increased risk of sight-threatening complications, emphasizing the need for effective interventions delaying myopia progression (Braun et al., 1996).

Various interventions have been suggested to prevent the development or progression of myopia in children, such as pharmaceutical treatments with atropine, optical treatments with spectacles or contact lenses (CL), behavioural therapy and low-level red-light treatment. However, determining the most effective intervention remains a challenge.

In this systematic review and network meta-analysis of randomized controlled trials, we aimed to determine the most effective interventions for preventing the progression of myopia in children aged 6–18 years. Unlike conventional meta-analyses that estimate the efficacy of one intervention, network meta-analyses enable the comparison and ranking of multiple interventions, providing an evaluation of the current treatment options.

2 | METHODS

2.1 | Study design

This systematic review and network meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009) and methodological aspects were planned using the recommendations outlined in the Cochrane Handbook (Higgins et al., 2021; Sterne et al., 2019). Our protocol was registered in the PROSPERO database (no. CRD42024518280).

2.2 | Eligibility criteria and outcome measures

2.2.1 | Population

Myopic children. Children were defined as individuals (regardless of gender) in the age range of 6–18 years. In studies with populations that extended beyond this age range, we included studies where at least 90% of the population was within the defined age range of eligibility. Myopia was defined as a cycloplegic refraction of at least one eye with a spherical equivalent of −0.5 diopters (D) or more (i.e., more myopic) at the baseline of the intervention. We did not enforce further restrictions on the definition of cycloplegia. We did not enforce further restrictions on the measurement of refraction.

2.2.2 | Intervention and comparison

Any intervention is defined as a means to achieve myopia control. We are neither restricted bythe approach nor the means of action. We restricted eligibility to studies with an intervention period of at least 1-year follow-up. For practical reasons, 1-year follow-up was defined as any follow-up within 10–14 months. Comparison group(s) were defined as any other intervention to achieve myopia control or observation/placebo. Studies without any data on a comparison group were not considered eligible. All unique interventions were analyzed individually. This was chosen with the aim of generating clinically relevant results. Atropine eye drops were grouped according to concentration. Ortho-k lenses were grouped in four different categories: ortho-K with ≤5 mm treatment zone, ortho-K with increased compression factor, ortho-K with aspheric base curve and all other ortho-K types. Unique optical principles incorporated in daily wear CL or in spectacle lenses were analyzed individually.

2.2.3 | Outcomes

The primary outcome of interest was a change in axial length from baseline of the intervention to follow-up. We restricted eligibility to studies that measured axial length using light-based methods. The secondary outcomes of interest were incident corneal infiltrates, photophobia, development of an allergic response towards the intervention, visual acuity at near and distance and drop-out from allocated intervention/control. Our analyses were targeted at outcomes at 1 year (±2 months), 2 years (±2 months) and 3 years (±2 months).

2.2.4 | Study type

We only considered randomized controlled trials. We did not enforce any restrictions based on blinding strategy, randomization or any other methodological characteristics. We only considered peer-reviewed full-text studies reported in the English language. We did not restrict eligibility based on geography or journal. We did not consider conference abstracts or non-peer-reviewed studies.

2.3 | Information source and literature search strategy

One trained author (Y.S.) searched the literature databases *PubMed*, *Embase*, *the Cochrane Central*, *Web*

of Science Core Collection, *BIOSIS Previews*, *Current Contents Connect*, *Data Citation Index*, *Derwent Innovations Index*, *KCI-Korean Journal Database*, *Preprint Citation Index*, *ProQuest™ Dissertations & Theses Citation Index and SciELO Citation Index* on December 2, 2023, with search phrases tailored to the individual databases. Details of these searches are outlined in File S1.

2.4 | Study selection, data items and collection and risk of bias within studies

References were exported from databases and imported to EndNote X9.3.1. for Mac (Clarivate Analytics, Philadelphia, PA, USA) for reference management and sorting. Titles and abstracts were screened by one author (Y.S.) for duplicates and obviously irrelevant reports. All remaining records were retrieved in full text and examined for eligibility in an independent fashion by at least two authors (D.C.S., A.H., N.J., T.M.J., P.M.L., K.K.L., F.M., A.S., L.K.). Reference lists from full-text records were screened for potentially eligible studies. Study eligibility results were compared and discussed with a separate author (Y.S.) who made the final decision when a consensus could not be reached.

We extracted data from eligible studies on design, characteristics, methods and outcomes of interest. The risk of bias within studies was assessed using the Cochrane Risk of Bias Tool version 2, based on the assignment to intervention (i.e., the intention-to-treat effect). Evaluations were conducted across separate domains dealing with the randomization process, deviations from the intended interventions, missing outcome data, measurement of outcome and selection of the reported results (Sterne et al., 2019). Data extraction and risk of bias assessment were made independently by at least two authors (D.C.S., A.H., N.J., T.M.J., P.M.L., K.K.L., F.M., A.S., L.K.). Results were compared and discussed with a separate author (Y.S.) who made the final decision when a consensus could not be reached.

2.5 | Data synthesis and risk of bias across studies

Data was synthesized qualitatively in text and tables, and quantitatively by network meta-analyses since we anticipated a range of different treatment modalities. For comparability, all axial length measurements were transformed to mm for analyses. For network meta-analyses, we constructed network plots to confirm the existence of a complete network and to provide an overview of existing direct comparisons. We used the generalized pairwise modelling approach, which is a method based on the repeated application of adjusted indirect comparisons (Doi & Barendregt, 2018) and a method known to deliver robust results comparable to the Bayesian and multivariate modelling approaches (Doi & Barendregt, 2018).

The statistical software MetaXL version 5.3 (EpiGear International, Sunrise Beach, QLD, Australia) for Microsoft Excel version 2401 (Microsoft, Redmont, WA, USA) was used for the quantitative analyses of this study. MetaXL applies the generalized pairwise modelling framework for meta-analysis. To account for potential heterogeneity across studies, the random-effects model was used. Meta-analyses were planned on our primary outcome of interest (change in axial length, continuous outcome) and our secondary outcomes (corneal infiltrates, categorical outcome; photophobia, categorical outcome; development of an allergic response towards the intervention, categorical outcome; visual acuity at near, continuous outcome; visual acuity at distance, continuous outcome; drop-out from allocated intervention/control, categorical outcome). However, a complete network and a meaningful meta-analysis were not present for all outcomes; thus, meta-analyses were only made for outcomes in which relevant data were present.

Heterogeneity statistics of prevalence meta-analyses were made using C and Cochran's Q. For network meta-analyses, evaluation of consistency is a more appropriate statistical approach. Heterogeneity and consistency are terms that describe disagreement between direct estimates of the same comparison across the studies, while inconsistency applies to a similar disagreement but coming from various pooled sources within the same comparison (including indirect comparisons). Thus, inconsistency can be considered an extension of heterogeneity across different forms of pooled studies of the network comparison. To evaluate consistency in each network meta-analysis, Consistency H was calculated. The minimum possible H value is 1. An H value of <3 indicates minimal inconsistency in treatment effects, 3–6 indicates moderate network inconsistency and >6 indicates large network inconsistency.

Several studies did not report the standard deviation (SD). In such cases, SDs were estimated using the standard error of the mean or otherwise using averaged data from other studies using similar methods. In some studies, data were available from baseline and follow-up examinations, but not on the change between examinations. In such cases, we calculated the mean change by subtraction of the means and the SD of the change (File S2). Summary estimates were reported as weighted mean difference (WMD) for continuous data and odds ratio (OR) for categorical data. For all estimates, 95% confidence intervals (95% CI) were provided and p-values <0.05 were interpreted as statistically significant.

For the categorical secondary outcomes 1-year incidence of corneal infiltrates, 1-year incidence of photophobia, 1-year incidence of allergic response towards the intervention and 1-year adherence to allocation, we also conducted prevalence meta-analyses to understand the overall rates of such outcomes across the plethora of interventions/studies. With prevalence meta-analyses, caution must be taken when reaching extremes (i.e., 0% or 100%) as such rates can result in variance instability and erroneous weighting of studies (Barendregt et al., 2013).

To accommodate this issue, all rates were transformed for analysis using the double arcsine method and then transformed back for dissemination (Barendregt et al., 2013).

3 | RESULTS

3.1 | Study selection

We identified 2224 records through the literature search. Duplicates ($n=934$) and obviously irrelevant records ($n=1110$) were discarded. The remaining 180 records were read in full text for evaluation of eligibility. One additional record fulfilling our eligibility criteria was identified by a detailed review of all reference lists of studies read in full text. Finally, 74 studies were found eligible for the qualitative and the quantitative review (Figure 1). Some of the excluded papers reported follow-up results at a later time points of the same study, i.e., these were secondary publications of studies already included once. However, these follow-up results were important for our analyses of long-term efficacy, and thus results from these studies were included in our review where appropriate, but each study only contributed once at each follow-up time point.

3.2 | Study characteristics and results of individual studies

The 74 studies eligible for review summarized data from a total of 12 154 patients. Studies were conducted in China ($n=43$), Japan ($n=6$), USA ($n=5$), Denmark ($n=3$), Spain ($n=3$), Australia ($n=2$), Singapore ($n=2$), Greece ($n=1$), India ($n=1$), Ireland ($n=1$), Israel ($n=1$), New Zealand ($n=1$), Taiwan ($n=1$), Vietnam ($n=1$) and three other studies were conducted in a multinational setting. The minimum age of participants across studies ranged from 4 to 11 years. The maximum age of participants across studies ranged from 10 to 18 years. The proportion of participants with female sex across studies ranged from 39% to 81%. Study characteristics and details of the study population are summarized in Table 1.

Interventions included treatment with atropine versus single-vision spectacles ($n=6$), ortho-K ($n=14$), other atropine concentrations (0.0025%, 0.005%, 0.01%, 0.02%,

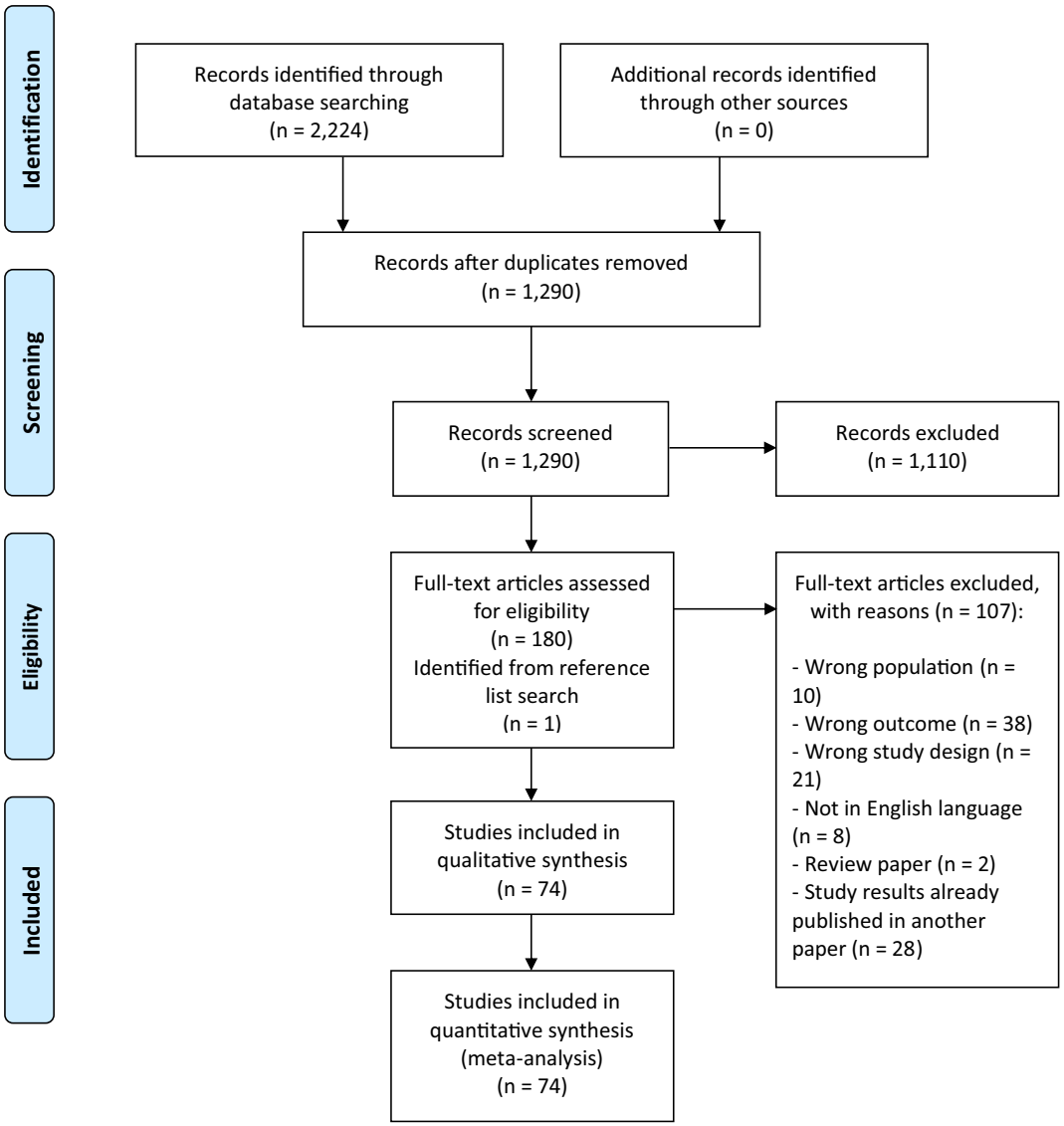

FIGURE 1 PRISMA flow diagram of study selection.

TABLE 1 Characteristics of studies in the review.

Reference	Country	*N*	Age range, years	Biological sex, females	Study population
Aller et al. (2016)	Australia	86	6–18	70%	−0.50 D or more myopia in least myopic meridian, −6.00 D or less in most myopic meridian, ≤2.00 D anisometropia, ≤1.00 D astigmatism. BCVA ≥20/20 Snellen in each eye. Myopia progression ≥0.50 D since the last examination. Eso fixation disparities at near
Anstice & Phillips (2011)	New Zealand	40	11–14	N/A	SER between −1.25 and −4.50 D in the least myopic eye as determined by non-cycloplegic subjective refraction; myopia progression ≥0.50 D in the previous 12 months; BCVA ≥6/6 Snellen in each eye; prepared to wear contact lenses for ≥8 h/day during the study
Bao, Huang, et al. (2022)	China	170	8–13	74%	SER between −0.75 D and −4.75 D, astigmatism of ≤1.50 D cylinder, anisometropia of ≤1.00 D and BCVA of ≤0.05 logMAR in each eye
Berntsen et al. (2012)	USA	84	6–11	52%	Between −0.75 and −4.50 D of myopia in each meridian of each eye, ≤2.00 D astigmatism, ≤2.00 D anisometropia as measured by cycloplegic autorefraction. BCVA ≥20/30 Snellen in each eye. A lag of accommodation of at least 1.30 D to a 4 D Badal letter stimulus (before correction for lens effectivity). If the participant's eye SER was more myopic than −2.25 D, the participant had to be esophoric at near while wearing full correction
Chamberlain et al. (2019)	International	144	8–12	48%	SER between −0.75 and −4.00 D, astigmatism ≤ −0.75 D, anisometropia <1.00 D and BCVA ≤0.10 logMAR in each eye
Chan et al. (2022)	China	71	7–10	49%	SER between −0.50 D and −5.00 D, ≤1.00 D astigmatism, ≤0.00 LogMAR, normal colour vision
Charm and Cho (2013)	China	52	8–11	N/A	Cycloplegic SER −5.75 D or more myopic, with the spherical component −5.00 D or more myopic. BCVA ≥6/7.5 Snellen
Chen et al. (2022)	China	62	7–15	50%	Myopia greater than −1.0 D and cycloplegic SER ≤−1.00 D, astigmatism ≤2.50 D, anisometropia ≤1.50 D and BCVA of ≥20/20 Snellen in both eyes
Chen et al. (2023)	China	102	6–13	42%	Cycloplegic SER between −0.75 and −6.00 D, astigmatism ≤1.50 D in both eyes, anisometropia ≤1.50 D, BCVA of ≤0.00 logMAR in both eyes and IOP between 10 and 21 mmHg
Cheng et al. (2016)	USA	127	8–11	54%	Cycloplegic SER between −0.75 and −4.00 D, astigmatism ≤1.00 D in each eye, ≤1.00 D difference in SER between the two eyes and BCVA ≥20/25 Snellen
Chia et al. (2012)	Singapore	400	6–12	47%	Spherical refractive error of −2.0 D or more myopic in both eyes, astigmatism ≤1.50 D and documented myopic progression of at least 0.50 D in the past year
Chia et al. (2023)	Singapore	100	6–11	52%	SER between −1.00 and −6.00 D in both eyes; myopia progression of at least −0.50 D in both eyes over the last 12 months; astigmatism ≤−1.50 D in both eyes; CDVA ≤0.2 logMAR in both eyes.
Cho and Cheung (2012)	China	102	6–10	51%	SER between −0.50 and −4.00 D in at least one eye, SER between −0.50 and −4.50 D in both eyes, astigmatism <1.50 D, with-the-rule astigmatism ≤1.25 D and astigmatism of other axes ≤0.50 D in both eyes, anisometropia ≤1.50 D, BCVA ≤0.10 logMAR in both eyes, symmetrical corneal topography with corneal toricity <2.00 D in either eye
Choi et al. (2023)	China	91	6–12	N/A	Spherical refractive error between −1.00 and −4.00 D in each eye, astigmatism ≤half the spherical error in each eye, BCVA ≤0.10 logMAR in both eyes
Fang et al. (2022)	China	81	7–15	41%	Cycloplegic refraction between −1.00 D and −8.00 D, astigmatism ≤1.00 D, myopia progression of ≥0.75 D in the last year or ≥0.50 D in the last 6 months
Fu et al. (2021)	China	328	6–14	48%	Cycloplegic autorefraction SER between −1.25 and −6.00 D, astigmatism ≤2.00 D, anisometropia ≤1.00 D and monocular BCVA ≥16/20 Snellen

(Continues)

TABLE 1 (Continued)

Reference	Country	*N*	Age range, years	Biological sex, females	Study population
Fujikado et al. (2014)	Japan	24	10–16	71%	SER between −0.75 and −3.50 D, astigmatism <1.00 D, BCVA ≥20/20 Snellen in both eyes with spherical lenses and anisometropia <1.00 D
Garcia-Del Valle et al. (2021)	Spain	70	7–15	64%	Cycloplegic spherical refractive error between −0.50 to −8.75 D and spherical component and astigmatism allowing CDVA 1.0 Snellen
Guo et al. (2021)	China	82	6–11	62%	Spherical refractive error between −0.75 and −4.00 D; astigmatism with axes 180 ± 30: ≥−2.50 D, other axes: ≥ − 0.50 D; ≤1.00 D difference in SER between the two eyes, BCVA ≤0.10 logMAR in both eyes, symmetrical corneal topography with corneal toricity <2.00 D in either eye
Hansen et al. (2023)	Denmark	97	6–12	57%	Spherical refractive error −1.00 D or more myopic in at least one eye (children aged 6–9 years), −2.00 D or more myopic in at least one eye (children aged 9–12 years). Astigmatism ≤1.50 D
Hao and Zhao (2021)	China	67	8–12	49%	Cycloplegic SER at least −1.00 D and spherical error within −1.00 to −6.00 D in both eyes, myopic astigmatism of −1.00 D cylinder and ≤half the spherical refractive error and anisometropia ≤1.50 D
Hasebe et al. (2008)	Japan	92	6–12	49%	SER between −1.25 and −6.00 D in both eyes, astigmatism ≤1.50 D in both eyes, anisometropia ≤1.50 D and BCVA ≥1.0 Snellen in each eye
Hasebe et al. (2014)	International	197	6–12	44%	Cycloplegic SER between −0.50 and −4.50 D, in both eyes, astigmatism ≤1.50 D in both eyes, anisometropia ≤1.50 D in spherical and cylindrical error and BCVA of ≥6/9 Snellen in each eye
Hieda et al. (2021)	Japan	171	6–12	55%	Cycloplegic SER between −1.00 to −6.00 D in both eyes, astigmatism ≤1.50 D and myopia progression in the past year according to the findings of a standard school health examination
Hua et al. (2015)	China	161	6–14	N/A	SER of −0.50 D or more myopic
Huang et al. (2023)	China	170	8–13	53%	SER between −0.75 and −4.75 D, astigmatism ≤1.50 D and anisometropia ≤1.00 D
Jakobsen and Møller (2022)	Denmark	60	6–12	57%	Cycloplegic spherical refraction between −0.5 and −4.75 D in both eyes, astigmatism ≤2.5 D in both eyes and BCVA ≥78 ETDRS letters in both eyes
Jiang et al. (2022)	China	264	8–13	51%	Cycloplegic SER of −1.00 to −5.00 D, astigmatism of ≤2.50 D, anisometropia of ≤1.50 D and BCVA of ≤0.00 logMAR in either eye
Kanda et al. (2018)	Japan	207	6–12	57%	Bilateral myopia with SER between −1.50 and −4.50 D and astigmatism ≤1.50 D
Kinoshita et al. (2018)	Japan	41	8–12	53%	Bilateral cycloplegic SER between −1.00 and −6.00 D, astigmatism ≤1.50 D, anisometropia ≤1.50 D and BCVA ≤0.00 logMAR
Lam et al. (2014)	China	221	8–13	62%	SER between −1.00 and −5.00 D, astigmatism ≤1.00 D, anisometropia ≤1.25 D, monocular spectacle CDVA ≤0.00 logMAR, monocular contact lens CDVA ≤0.10 logMAR
Lam et al. (2020)	China	183	8–13	43%	SER between −1.00 and −5.00 D, astigmatism ≤1.50 D, anisometropia ≤1.50 D, monocular spectacle CDVA ≤0.00 logMAR
Lee et al. (2022)	Australia	153	6–16	58%	SER −1.50 D or more myopic, astigmatism ≤1.50 D and documented myopia progression of at least 0.50 D/year
Liang et al. (2023)	China	220	6–12	49%	Cycloplegic SER between −1.00 and −6.00 D in both eyes, astigmatism <1.50 D, anisometropia <1.00 D and BCVA ≤0.20 logMAR in both eyes
Lin et al. (2024)	China	102	8–14	52%	Cycloplegic SER between −0.75 and − 5.00 D, anisometropia ≤1.00 D, with-the-rule astigmatism of <1.50 D, myopia in both eyes and BCVA ≥20/20 Snellen

TABLE 1 (Continued)

Reference	Country	*N*	Age range, years	Biological sex, females	Study population
Liu, Chen, et al. (2023)	China	70	8–12	44%	Myopia between −0.75 and −4.00 D, astigmatism ≤1.00 D, anisometropia ≤1.00 D, corneal astigmatism ≤1.50 D with axis 180° ± 30° and monocular distance BCVA ≤0.10 logMAR
Liu, Wang, et al. (2023)	China	118	8–12	50%	Cycloplegic SER between −1.00 and −4.00 D, astigmatism <1.50 D, anisometropia <1.00 D based on SER, BCVA of ≤0.10 logMAR in each eye and binocular BCVA ≤0.00 logMAR
Loughman et al. (2024)	Ireland	250	6–16	62%	SER of −1.00 D or more myopic, myopic progression over the preceding year, astigmatism <2.50 D and the least myopic meridian must be more myopic or equal to −0.50 D, BCVA ≤0.29 logMAR in both eyes
Lyu et al. (2020)	China	102	8–15	N/A	SER between −6.00 and −8.75 D, astigmatism <1.50 D and BCVA ≤0.00 logMAR
Mori et al. (2021)	Japan	113	6–12	62%	Cycloplegic refection between −1.50 and 4.50 D in each eye and anisometropia ≤1.50 D
Moriche-Carretero et al. (2021)	Spain	339	5–11	52%	Cycloplegic SER between −0.50 and −4.50 D in each eye, astigmatism ≤1.50 D in both eyes; anisometropia ≤1.00 D and BCVA ≥20/30 Snellen
Peng and Jiang (2023)	China	36	7–12	81%	Cycloplegic SER between −1.00 and −5.00 D, astigmatism ≤1.00 D, anisometropia ≤1.00 D and CDVA ≥20/20 Snellen
Prousali et al. (2022)	Greece	30	4–16	40%	Cycloplegic SER between −0.50 and −6.00 D in each eye, astigmatism ≤1.50 D in each eye, anisometropia ≤1.50 D and BCVA ≤0.10 logMAR in each eye
Rappon et al. (2023)	USA	256	6–10	58%	SER between −0.75 and −4.50 D BCVA ≤0.10 logMAR in each eye and anisometropia ≤1.50 D
Repka et al. (2023)	USA	187	5–12	54%	SER between −1.00 and −6.00 D, astigmatism ≤1.50 D in both eyes and anisometropia <1.00 D
Ruiz-Pomeda et al. (2018)	Spain	89	8–12	46%	Spherical refractive error between −0.75 and 4.00 D, astigmatism <1.00 D and BCVA ≤0.10 logMAR in each eye
Sankaridurg et al. (2011)	China	210	6–16	48%	Spherical refractive error between −0.75 and −3.50 D, astigmatism ≤1.50 D, anisometropia ≤1.00 D and BCVA ≥6/9.5 Snellen in each eye
Sankaridurg et al. (2019)	China	508	8–13	51%	Cycloplegic SER between −0.75 to −3.50 D, astigmatism ≤0.75 D and BCVA ≥6/9.5 Snellen.
Sankaridurg et al. (2023)	Vietnam	119	7–13	45%	SER between −0.75 and −4.75 D, astigmatism ≤1.50 D, anisometropia ≤1.00 D and BCVA ≤0.05 logMAR
Saxena et al. (2021)	India	100	6–14	N/A	Cycloplegic spherical refractive error between −0.50 and −6.00 D, myopia progression of >0.50 D in the preceding year, astigmatism ≤1.50 D, anisometropia ≤1.00 D and BCVA ≥20/40 Snellen
Shen et al. (2022)	Taiwan	72	9–14	44%	SER between −1.00 D and −8.00 D, astigmatism ≤1.75 D, myopia progression of ≥0.75 D within the past 12 months and BCVA ≤0.10 logMAR
Tan et al. (2020)	China	68	6–11	61%	Spherical refractive error between −1.00 and 4.00 D in both eyes, astigmatism ≤2.50 D and anisometropia <1.00 D.
Tang et al. (2023)	China	131	8–16	N/A	Spherical refractive error between −1.00 and −5.00 D, astigmatism ≤1.50 D, anisometropia ≤1.00 D and BCVA ≤0.00 logMAR
Tong et al. (2024)	China	400	8–10	48%	SER between −0.50 and −6.00 D, astigmatism <1.50 D, anisometropia <1.00 D and BCVA ≤0.10 logMAR or better in each eye
Trier et al. (2008)	Denmark	68	8–13	N/A	Cycloplegic spherical refractive error of −0.75 D or more myopic
Walline et al. (2020)	USA	294	7–11	60%	Cycloplegic spherical refractive error between −0.75 and −5.00 D, astigmatism <1.00 D, BCVA ≥20/25 in each eye, binocular visual acuity of ≥20/25 with +2.50 D addition power soft multifocal contact lens and a clinically acceptable fit with study contact lenses at baseline

(Continues)

TABLE 1 (Continued)

Reference	Country	*N*	Age range, years	Biological sex, females	Study population
Wei et al. (2020)	China	220	6–12	47%	SER between −1.00 and −6.00 D in both eyes, astigmatism ≤1.50 D and BCVA ≤0.20 logMAR
Xia et al. (2023)	China	164	6–16	47%	Binocular myopia and CDVA 1.00 Snellen
Xu et al. (2023)	China	164	8–12	54%	SER between −1.00 and −6.00 D in both eyes, astigmatism ≤1.50 D, anisometropia ≤1.50 D and BCVA ≥20/25 Snellen in both eyes
Yam et al. (2019)	China	438	4–12	43%	Spherical refractive error of −1.0 D or more myopic in both eyes and astigmatism <2.50 D
Yang et al. (2021)	China	80	8–15	64%	Cycloplegic spherical refractive error between −0.75 and −6.00 D, astigmatism ≤1.50 D and CDVA ≥20/20 Snellen
Ye et al. (2022)	China	207	6–12	53%	Spherical refractive error of −0.5 D or more myopic in both eyes and astigmatism <2.00 D
Yu et al. (2022)	China	60	8–12	53%	Cycloplegic SER between −1.00 to −4.00 D, astigmatism <1.50 D, anisometropia <1.00 D and monocular BCVA ≥20/20
Yuval et al. (2024)	Israel	126	6–13	52%	Cycloplegic SER between −0.50 and −6.00 D in at least one eye, astigmatism ≤1.50 D, CDVA ≥20/25 Snellen
Zadnik et al. (2023)	International	576	6–10	54%	SER between −0.50 and −6.00 D in each eye, astigmatism ≤1.50 D and anisometropia ≤1.50 D
Zhang, Sun, et al. (2023)	China	60	8–14	77%	Spherical refractive error between −0.75 and −5.00 D in both eyes, astigmatism ≤1.50 D, anisometropia ≥1.00 D and BCVA ≤0.10 logMAR visual acuity in both eyes
Zhang, Yang, et al. (2024)	China	424	6–12	45%	SER between −1.00 and −6.00 D and astigmatism ≤1.50 D.
Zhao and Hao (Int Oph 2021a)	China	80	5–14	50%	Cycloplegic SER of −1.00 D or more myopic, spherical error between −1.00 and −6.00 D, astigmatism ≤1.00 D and astigmatism must be ≤half the spherical refractive error
Zhao and Hao (Oph Epi 2021b)	China	120	8–14	N/A	Cycloplegic SER of −1.00 D or more myopic, astigmatism ≤1.00 D and astigmatism must be ≤ half the spherical refractive error.
Zhou et al. (2023)	China	50	8–12	39%	Cycloplegic SER between −0.50 and −8.00 D, astigmatism ≤2.50 D and CDVA ≤0.00 logMAR
Zhu et al. (2020)	China	660	6–12	50%	SER between −2.00 and −8.00 D, astigmatism ≤1.00 D and spherical error progression rate ≥1.00 D/year.
Zhu et al. (2022)	China	93	7–14	55%	Cycloplegic SER between −0.75 and −4.00 D, astigmatism ≤1.50 D, anisometropia ≤1.00 D, BCVA ≥6/6 Snellen and near phoria (Δ) ≥2Δ
Zhu, Tang, et al. (2023)	China	142	7–12	50%	SER between −1.00 and −6.00 D and myopia progression of ≥0.75 D/year
Zhu, Yin, et al. (2023)	China	308	8–12	51%	Cycloplegic spherical refractive error between −1.00 to −5.00 D, conforming corneal astigmatism <1.50 D, inverse corneal astigmatism <0.75 D, corneal topography with minimum curvature of the cornea minus the expected reduction >36 D, corneal diameter of 10.9–12.5 mm and BCVA ≥0.00 logMAR

Abbreviations: BCVA, best-corrected visual acuity; CDVA, corrected distance visual acuity; D, diopter; ETDRS, Early Treatment of Diabetic Retinopathy Study; logMAR, logarithm of the Minimum Angle of Resolution; SER, spherical equivalent refraction.

0.025%, 0.05%, 0.1%, 0.5%, 1%) ($n=9$), placebo ($n=16$) or no treatment ($n=1$). Some of these studies assessed multiple comparison groups with a combination of different interventions.

Other interventions included various spectacle lens designs versus single-vision spectacles ($n=15$) or special CL such as multifocal CL ($n=10$), bifocal CL ($n=1$), EDOF CL ($n=3$), MiSight CL ($n=2$), positive spherical aberration CL ($n=1$) or ortho-K ($n=27$). Additionally, studies examined the effect of low-level red-light therapy (LLRL) ($n=3$), elevated light ($n=1$), oral 7-methylxanthine ($n=1$) and daily singing of a 'myopia ballad' ($n=1$). Study durations ranged from 1 to 4 years. Some studies had several publications for different times of follow-up (e.g., 1-year follow-up, 2-year follow-up, etc.). In such cases with multiple publications per actual study, only one data set was extracted for tables and quantitative analyses. The results from the individual studies are described in Table 2.

3.3 | Risk of bias within studies

We observed low risk of bias in 77% of studies for the randomization process, 97% of studies for deviations

TABLE 2 Overview and summary of results for individual studies within each treatment group.

Treatment category	Intervention	Comparator	Study duration	Overall conclusions for controlling axial length elongation	Reference
Atropine	Atropine 0.01%	Placebo	1.5 year	Atropine = placebo	Chan et al. (2022)
Atropine	Atropine 0.5% vs. 0.1%	Atropine 0.01%	2 years	Atropine 0.5% = 0.1% > 0.01%	Chia et al. (2012)
Atropine	Atropine 0.01% vs. 0.005% vs. 0.0025%	Placebo	1 year	Atropine 0.01% = 0.005% > 0.0025% = placebo	Chia et al. (2023)
Atropine	Atropine 0.02% vs. Atropine 0.01%	SVS	1 year	Atropine 0.02% > 0.01% > placebo	Fu et al. (2021)
Atropine	Atropine 0.1% for 6 months → 0.01% vs. 0.01%	Placebo	1 year	Atropine 0.1% → 0.01% = 0.01% = placebo	Hansen et al. (2023)
Atropine	Atropine 0.01% vs. 0.01% + ortho-k	Ortho-k	1 year	Atropine+ortho-k > atropine > ortho-k	Hao and Zhao (2021)
Atropine	Atropine 0.01%	Placebo	2 years	Atropine > placebo	Hieda et al. (2021)
Atropine	Atropine 0.01% + ortho-k	Ortho-k	1 year	Atropine+ortho-k > ortho-k	Kinoshita et al. (2018)
Atropine	Atropine 0.01%	Placebo	2 years	Atropine > placebo	Lee et al. (2022)
Atropine	Atropine 0.01%	Placebo	1 year	Atropine > placebo	Liang et al. (2023)
Atropine	Atropine 0.01%	Placebo	2 years	Atropine > placebo	Loughman et al. (2024)
Atropine	Atropine 0.01%	No treatment	2 years	Atropine > placebo	Moriche-Carretero et al. (2021)
Atropine	Atropine 0.01%	Placebo	2 years	Atropine = placebo	Repka et al. (2023)
Atropine	Atropine 0.01%	Placebo	1 year	Atropine = placebo	Saxena et al. (2021)
Atropine	Atropine 0.01% + ortho-k	Ortho-k	2 years	Atropine+ortho-k > ortho-k	Tan et al. (2020)
Atropine	Atropine 0.01%	Placebo	2 years	Atropine > placebo	Wei et al. (2020)
Atropine	Atropine 0.01%	SVS	1 year	Atropine > placebo	Xia et al. (2023)
Atropine	Atropine 0.01% vs. 0.01% + ortho-k vs. ortho-k	SVS	2 years	Atropine+ortho-k > atropine = ortho-k > SVS	Xu et al. (2023)
Atropine	Atropine 0.05% vs. 0.025% vs. 0.01%	Placebo	3 years	Atropine 0.05% > 0.025% > 0.01 > placebo	Yam et al. (2019)
Atropine	Atropine 1% for 6 months	Atropine 0.01%	1 year	Atropine 1% → 0.01% > 0.01%	Ye et al. (2022)
Atropine	Atropine 0.01% + ortho-k	Placebo + ortho-k	1 year	Atropine + ortho-k > ortho-k	Yu et al. (2022)
Atropine	Atropine 0.02% vs. 0.01%	Placebo	3 years	Atropine 0.02% = 0.01% > placebo	Zadnik et al. (2023)
Atropine	Atropine 0.05%	Placebo	2 years	Atropine > placebo	Zhang, Yang, et al. (2024)
Atropine	Atropine 0.01% vs. 0.01% + ortho-k vs. ortho-k	SVS	1 year	Atropine+ortho-k > atropine = ortho-k > spectacles	Zhao and Hao (Int Oph 2021a)
Atropine	Atropine 0.01%	Ortho-k	1 year	Atropine = ortho-k	Zhao and Hao (Oph Epi 2021b)
Atropine	Atropine 1.0%	Placebo	4 years	Atropine > placebo	Zhu et al. (2020)
Atropine	Atropine 0.05%	Placebo	3 years	Atropine > placebo	Zhu, Tang, et al. (2023)
Spectacle based	Spectacles with HAL vs. SAL	SVS	2 years	1 year: HAL > SAL > SVS 2 years: HAL > SAL = SVS	Bao, Huang, et al. (2022)
Spectacle based	Spectacles with PAL	SVS	2 years	PAL > SVS	Berntsen et al. (2012)
Spectacle based	Spectacles with PAL	SVS	3 years	PAL > SVS	Hasebe et al. (2008)
Spectacle based	Spectacles with PA-PAL +1.00 D vs. +1.50 D	SVS	2 years	PA-PALS + 1.50 D > PA-PAL + 1.0 D = SVS	Hasebe et al. (2014)
Spectacle based	Spectacles with HAL vs. SAL	SVS	2 years	HAL > SAL > SVS	Huang et al. (2023)
Spectacle based	Spectales with MyoVision lenses	SVS	2 years	MyoVision = SVS	Kanda et al. (2018)

(Continues)

TABLE 2 (Continued)

Treatment category	Intervention	Comparator	Study duration	Overall conclusions for controlling axial length elongation	Reference
Spectacle based	Spectacles with DIMS	SVS	2 years	DIMS>SVS	Lam et al. (2020)
Spectacle based	Spectacles with CARE	SVS	1 year	CARE>SVS	Liu, Wang, et al. (2023)
Spectacle based	Spectacles with VL	SVS	2 years	VL=SVS	Mori et al. (2021)
Spectacle based	SVS part-time	SVS	1 year	SVS part-time=SVS	Prousali et al. (2022)
Spectacle based	Spectacles with DOT with spacing 0.365 vs. 0.240	SVS	3 years	DOT 0.365>DOT 0.240>SVS	Rappon et al. (2023)
Spectacle based	Type I design with aperture of 20 mm vs. type II design with aperture of 14 mm vs. type III design with aperture to either side	SVS	1 year	Type I=type II=type III=SVS	Sankaridurg et al. (2011)
Spectacle based	Spectacles with HAL	SVS	1.5 year	HAL>SVS	Sankaridurg et al. (2023)
Spectacle based	Spectacles with SMC	SVS	1 year	SMC>SVS	Yuval et al. (2024)
Spectacle based	Spectacles with PAL	SVS	2 years	PAL>SVS	Zhu et al. (2022)
CL based	Bifocal CL (add range+0.25 to +3.75 D)	SVCL	1 year	Bifocal CL>SVCL	Aller et al. (2016)
CL based	Multifocal CL add +2.00 D	SVCL	10 months x 2	Multifocal CL add +2.00 D>SVCL	Anstice & Phillips (2011)
CL based	MiSight CL	SVCL	3 years	MiSight CL>SVCL	Chamberlain et al. (2019)
CL based	Ortho-k partial reduction + and SVS for residual	SVS	2 years	Ortho-k+SVS>SVS	Charm and Cho (2013)
CL based	CL with positive spherical aberration (+SA)	SVCL	2 years	CL with +SA>SVCL	Cheng et al. (2016)
CL based	Ortho-k	SVS	2 years	Ortho-k>SVS	Cho and Cheung (2012)
CL based	Ortho-k	SVS	2 years	Ortho-k>SVS	Choi et al. (2023)
CL based	Ortho-k vs. multifocal CL add +2.00 D	SVS	1 year	Ortho-k=multifocal CL add +2.00 D>SVS	Fang et al. (2022)
CL based	Multifocal CL add +0.50 D	SVCL	2 years	Multifocal CL add +0.50 D>SVCL	Fujikado et al. (2014)
CL based	Multifocal CL add +2.00 D	SVCL	1 year	Multifocal CL add +2.00 D>SVCL	Garcia-Del Valle et al. (2021)
CL based	Ortho-k	Ortho-k (5 mm)	2 years	Ortho-k=Ortho-k (5 mm)	Guo et al. (2021)
CL based	Atropine 0.01% vs. 0.01%+ortho-k	Ortho-k	1 year	Atropine+ortho-k>atropine>ortho-k	Hao and Zhao (2021)
CL based	Ortho-k	SVS	18 months	Ortho-k>SVS	Jakobsen and Møller (2022)
CL based	Atropine 0.01%+ortho-k	Ortho-k	1 year	Atropine+ortho-k>ortho-k	Kinoshita et al. (2018)
CL based	Multifocal CL add +2.50 D	SVCL	2 years	Multifocal CL add +2.50 D>SVCL	Lam et al. (2014)
CL based	Ortho-k	SVS	1 year	Ortho-k>SVS	Lin et al. (2024)
CL based	Ortho-k with aspheric base curve	Ortho-k	1 year	Ortho-k with aspheric base curve>Ortho-k	Liu, Chen, et al. (2023)
CL based	Ortho-k target reduction of 6 D vs. ortho-k target reduction of 4 D	SVS	1 year	Ortho-k 6 D=ortho-k 4 D>SVS	Lyu et al. (2020)
CL based	Multifocal CL add +3.00 D	SVCL	1 year	Multifocal CL add +3.00 D>SVCL	Peng and Jiang (2023)
CL based	MiSight CL	SVCL	2 years	MiSight CL>SVCL	Ruiz-Pomeda et al. (2018)
CL based	Multifocal CL add +2.50 D vs. multifocal add +1.50 D vs. EDOF +1.75 D CL vs. EDOF +1.25 D CL	SVCL	2 years	Multifocal CL add +2.50 D=multifocal add +1.50 D=EDOF +2.50 D CL=EDOF +1.75 D CL > SVCL	Sankaridurg et al. (2019)

TABLE 2 (Continued)

Treatment category	Intervention	Comparator	Study duration	Overall conclusions for controlling axial length elongation	Reference
CL based	EDOF CL	SVCL	1 year	EDOF CL > SVCL	Shen et al. (2022)
CL based	Atropine 0.01% + ortho-k	Ortho-k	2 years	Atropine+ortho-k > ortho-k	Tan et al. (2020)
CL based	Ortho-k with increased compression factor	Ortho-k	2 years	Ortho-k with increased compression factor > Ortho-k	Tang et al. (2023)
CL based	Multifocal CL add +2.50 D vs. add +1.50 D	SVCL	3 years	Multifocal CL add +2.50 D > add +1.50 D = SVCL	Walline et al. (2020)
CL based	Atropine 0.01% vs. 0.01% + ortho-k vs. ortho-k	SVS	2 years	Atropine+ortho-k > atropine = ortho-k > SVS	Xu et al. (2023)
CL based	Ortho-k with aspheric base curve	Ortho-k	1 year	Ortho-k with aspheric base curve>Ortho-k	Yang et al. (2021)
CL based	Atropine 0.01% + ortho-k	Placebo + ortho-k	1 year	Atropine+ortho-k > ortho-k	Yu et al. (2022)
CL based	Atropine 0.01% vs. 0.01% + ortho-k vs. ortho-k	SVS	1 year	Atropine+ortho-k > atropine = ortho-k > spectacles	Zhao and Hao (Int Oph 2021a)
CL based	Atropine 0.01%	Ortho-k	1 year	Atropine = ortho-k	Zhao and Hao (Oph Epi 2021b)
CL based	Ortho-k	SVS	1 year	Ortho-k > SVS	Zhang, Sun, et al. (2023)
CL based	Ortho-k	SVS	13 months	Ortho-k > SVS	Zhu, Yin, et al. (2023)
Others	LLRL	Atropine 0.01%	1 year	LLRL > atropine	Chen et al. (2022)
Others	Elevated light	Placebo	1 year	Elevated light > Placebo	Hua and Zhou (2015)
Others	LLRL	SVS	1 year	LLRL > SVS	Jiang et al. (2022)
Others	7-methylxanthine tablet	Placebo	3 years	7-methylxanthine tablet = Placebo	Trier et al. (2008)
Others	Myopia song	No treatment	3 years	Myopia song > No treatment	Tong et al. (2024)
Others	LLRL	SVS	1 year	LLRL > SVS	Zhou et al. (2023)

Abbreviations: add, addition; CARE, cylindrical annular refractive element; CL, contact lens; D, diopter; DIMS, defocus incorporated multiple segments; DOT, diffusion optics technology; EDOF, extended depth of focus; HAL, highly aspherical lenslets; LLRL, low-level red light; ortho-k, orthokeratology; PAL, progressive addition lenses; PA-PAL, positively aspherized progressive addition lenses; SAL, slightly aspherical lenslets; SMC, Sharmir Myopia Control; SVCL, single-vision contact lens; SVS, single-vision spectacle; VL, violet light-transmission; vs., versus.

from intended interventions, 81% of studies for missing outcome data, 99% of studies for the measurement of the outcome and 100% of studies for the selection of the reported results. The main source of risk of bias scores across studies was from participants and study personnel being aware of the intervention, and the nature of interventions being of such sort that potential deviations could have arisen (i.e., systematic preference or dislike of certain type of intervention such as spectacle lenses/CL) although actual deviations within individual studies seemed to be limited. Overall bias was deemed low across studies in 62%, with some concerns in 34% and high in 4%. Our summary of the risk of bias within studies is available in Figure 2.

3.4 | Availability of outcomes of interest within studies

Axial length was reported after 1 year (n = 71 studies), after 2 years (n = 29) and after 3 years (n = 8). Some studies reported adverse effects such as corneal infiltrates (n = 18), photophobia (n = 17) and allergic response (n = 22) and some reported visual acuity for distance (n = 17) or near (n = 14). The adherence to allocation was reported in 61 studies. The availability of outcomes of interest from individual studies, including follow-up studies, is reported in Table 3.

3.5 | Analyses of outcomes of interest

3.5.1 | Axial length progression after 1 year

Data for the meta-analysis of change in axial length from baseline to 1 year was available from 71 studies as three studies only reported either 2- or 3-year outcomes. For the analysis of change in axial length, we pooled the groups of single-vision spectacles, single-vision CL and placebo treatment. There was a complete network across the various interventions which allowed for a network meta-analysis (File S3). The network meta-analysis was made with the single-vision spectacles/single-vision CL/placebo as the reference group (Figure 3). This analysis highlighted a statistically significant effect of the following interventions on axial length elongation at 1 year:

- Atropine:
  - 1.0%: −0.28 (95% CI: −0.30 to −0.26) mm
  - 0.1% and Ortho-K: −0.24 (95% CI: −0.37 to −0.11) mm
  - 0.05%: −0.21 (95% CI: −0.30 to −0.13) mm
  - 0.5%: −0.20 (95% CI: −0.26 to −0.14) mm
  - 0.1%: −0.18 (95% CI: −0.24 to −0.12) mm
  - 1.0% for 6 months followed by 0.01%: −0.17 (95% CI: −0.23 to −0.11) mm

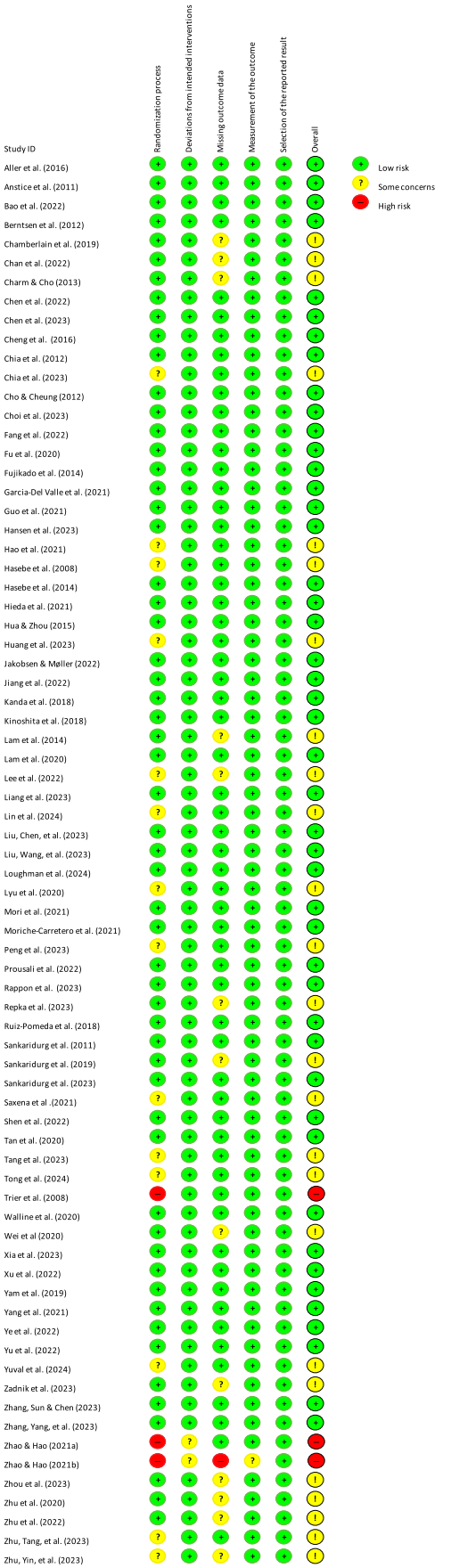

FIGURE 2 Risk of bias of individual studies.

- 0.025%: −0.13 (95% CI: −0.21 to −0.05) mm
- 0.02%: −0.12 (95% CI: −0.20 to −0.04) mm
- 0.1% for 6 months followed by 0.01%: −0.10 (95% CI: −0.17 to −0.03) mm
  - 0.01%: −0.10 (95% CI: −0.18 to −0.01) mm
  - 0.005%: −0.08 (95% CI: −0.14 to −0.02) mm
- CL based therapy:
  - Ortho-K with 5 mm treatment zone: −0.32 (95% CI: −0.41 to −0.24) mm
  - Ortho-K with aspheric base curve: −0.29 (95% CI: −0.37 to −0.22) mm
  - Atropine 0.1% and Ortho-K: −0.24 (95% CI: −0.37 to −0.11) mm
  - Ortho-K with increased compression factor 1.75 D: −0.23 (95% CI: −0.28 to −0.17) mm
  - Bifocal CL: −0.19 (95% CI: −0.26 to −0.12) mm
  - CL with positive spherical aberration (+SA): −0.14 (95% CI: −0.20 to −0.08) mm
  - MiSight CL: −0.14 (95% CI: −0.18 to −0.10) mm
  - Multifocal CL with addition +2.50 D: −0.13 (95% CI: −0.16 to −0.10) mm
  - Multifocal CL with addition +2.00 D: −0.12 (95% CI: −0.17 to −0.07) mm
  - Ortho-K: −0.11 (95% CI: −0.20 to −0.03) mm
  - Multifocal CL with addition +1.50 D: −0.07 (95% CI: −0.11 to −0.03) mm
  - Extended depth of focus (EDOF) +1.75 D CL: −0.10 (95% CI: −0.13 to −0.07) mm
  - EDOF +1.25 D CL: −0.10 (95% CI: −0.13 to −0.07) mm
- Spectacle-based therapy:
  - Highly aspherical spectacle lenslets (HAL): −0.23 (95% CI: −0.26 to −0.19) mm
  - Defocus incorporated multiple segments (DIMS): −0.21 (95% CI: −0.27 to −0.15) mm
  - Diffusion optics technology (DOT) 0.365: −0.15 (95% CI: −0.19 to −0.11) mm
  - DOT 0.240: −0.11 (95% CI: −0.16 to −0.06) mm
  - Slightly aspherical lenslets (SAL): −0.11 (95% CI: −0.15 to −0.08) mm
  - Sharmir Myopia Control (SMC): −0.11 (95% CI: −0.17 to −0.05) mm
  - Cylindrical annular refractive element (CARE): −0.10 (95% CI: −0.17 to −0.03) mm
  - Progressive addition lenses (PAL): −0.05 (95% CI: −0.08 to −0.01) mm
  - Others:
  - LLRL: −0.33 (95% CI: −0.40 to −0.26) mm
  - Elevated light: −0.07 (95% CI: −0.10 to −0.04) mm

Overall results and conclusions remained unchanged in the sensitivity analysis (File S4). The Consistency H was 1.514 for axial length, indicating minimal inconsistency within the network.

3.5.2 | Axial length progression after 2 and 3 years

Data for axial length progression after 2 years were available in 28 studies, though the data were insufficient for the network meta-analysis. Nine studies included atropine 0.01% (Chia et al., 2023; Hieda et al., 2021; Lee et al., 2022; Loughman et al., 2024; Moriche-Carretero et al., 2021; Repka et al., 2023; Tan et al., 2020, 2023; Xu et al., 2023; Zadnik et al., 2023).

TABLE 3 Availability of outcomes of interest within individual studies in review.

Reference	AL 1 year	AL 2 years	AL 3 years	Corneal infiltrates	Photophobia	Allergic response	Distance VA	Near VA	Adherence to allocation
Aller et al. (2016)	Yes	No	No	No	No	No	No	No	No
Anstice & Phillips (2011)	Yes	No	No	No	No	No	Yes	No	Yes
Bao, Huang, et al. (2022)	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
Berntsen et al. (2012)	Yes	No	No	No	No	No	No	No	Yes
Chamberlain et al. (2019)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Chan et al. (2022)	Yes	No	No	No	No	No	No	No	Yes
Charm and Cho (2013)	Yes	Yes	No	Yes	No	No	No	No	Yes
Chen et al. (2022)	Yes	No	No	No	Yes	Yes	No	No	Yes
Chen et al. (2023)	Yes	No	No	No	No	No	No	No	Yes
Cheng et al. (2016)	Yes	No	No	No	No	Yes	No	No	Yes
Chia et al. (2012)	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes
Chia et al. (2023)	Yes	No	No	No	No	Yes	Yes	Yes	Yes
Cho and Cheung (2012)	Yes	Yes	No	Yes	No	No	No	No	Yes
Choi et al. (2023)	Yes	Yes	No	No	No	No	No	No	No
Fang et al. (2022)	Yes	No	No	No	No	No	No	No	Yes
Fu et al. (2020)	Yes	No	No	No	Yes	Yes	No	No	Yes
Fujikado et al. (2014)	Yes	No	No	No	No	No	No	No	No
Garcia-Del Valle et al. (2021)	Yes	No	No	Yes	No	No	No	No	Yes
Guo et al. (2021)	Yes	No	No	Yes	No	No	No	No	Yes
Hansen et al. (2023)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Hao and Zhao (2021)	Yes	No	No	Yes	No	No	No	No	No
Hasebe et al. (2008)	No	No	Yes	No	No	No	No	No	Yes
Hasebe et al. (2014)	Yes	Yes	No	No	No	No	No	No	Yes
Hieda et al. (2021)	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
Hua and Zhou (2015)	Yes	No	No	No	No	No	No	No	No
Huang et al. (2023)	Yes	Yes	No	No	No	No	No	No	Yes
Jakobsen and Møller (2022)	Yes	No	No	Yes	No	No	No	No	Yes
Jiang et al. (2022)	Yes	No	No	No	No	No	Yes	No	Yes
Kanda et al. (2018)	Yes	Yes	No	No	No	No	No	No	Yes
Kinoshita et al. (2018)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Lam et al. (2014)	Yes	Yes	No	No	No	No	No	No	Yes
Lam et al. (2020)	Yes	Yes	No	No	No	No	Yes	Yes	Yes

(Continues)

TABLE 3 (Continued)

Reference	AL 1 year	AL 2 years	AL 3 years	Corneal infiltrates	Photophobia	Allergic response	Distance VA	Near VA	Adherence to allocation
Lee et al. (2022)	Yes	Yes	No	No	No	No	Yes	Yes	Yes
Liang et al. (2023)	Yes	No	No	No	Yes	Yes	No	No	Yes
Lin et al. (2024)	Yes	No	No	No	No	No	No	No	No
Liu, Chen, et al. (2023)	Yes	No	No	Yes	No	No	Yes	No	Yes
Liu, Wang, et al. (2023)	Yes	No	No	No	No	No	No	No	Yes
Loughman et al. (2024)	Yes	Yes	No	No	No	No	Yes	Yes	Yes
Lyu et al. (2020)	Yes	No	No	No	No	No	No	No	Yes
Mori et al. (2021)	Yes	Yes	No	No	No	No	No	No	Yes
Moriche-Carretero et al. (2021)	No	Yes	No	No	No	No	No	No	Yes
Peng and Jiang (2023)	Yes	No	No	Yes	No	Yes	No	No	Yes
Prousali et al. (2022)	Yes	No	No	No	No	No	No	No	Yes
Rappon et al. (2023)	Yes	No	No	No	No	Yes	No	No	No
Repka et al. (2023)	Yes	Yes	No	No	No	Yes	No	No	Yes
Ruiz-Pomeda et al. (2018)	Yes	Yes	No	No	No	No	No	No	Yes
Sankaridurg et al. (2011)	Yes	No	No	No	No	No	No	No	Yes
Sankaridurg et al. (2019)	Yes	Yes	No	No	No	No	No	No	Yes
Sankaridurg et al. (2023)	Yes	No	No	No	No	No	No	No	Yes
Saxena et al. (2021)	Yes	No	No	No	Yes	No	No	No	Yes
Shen et al. (2022)	Yes	No	No	Yes	No	No	No	No	Yes
Tan et al. (2020)	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes
Tang et al. (2023)	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes
Tong et al. (2024)	No	No	Yes	No	No	No	Yes	Yes	Yes
Trier et al. (2008)	Yes	No	No	No	No	No	No	No	No
Walline et al. (2020)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Wei et al. (2020))	Yes	No	No	No	Yes	Yes	No	No	Yes
Xia et al. (2023)	Yes	No	No	No	No	No	No	No	No
Xu et al. (2023)	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes
Yam et al. (2019)	Yes	No	No	No	No	No	No	No	No
Yang et al. (2021)	Yes	No	No	No	No	No	No	No	No
Ye et al. (2022)	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes
Yu et al. (2022)	Yes	No	No	No	Yes	No	No	No	Yes
Yuval et al. (2024)	Yes	No	No	No	No	No	No	No	Yes

TABLE 3 (Continued)

Reference	AL 1 year	AL 2 years	AL 3 years	Corneal infiltrates	Photophobia	Allergic response	Distance VA	Near VA	Adherence to allocation
Zadnik et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Zhang, Sun, et al. (2023)	Yes	No	No	No	No	No	No	No	Yes
Zhang, Yang, et al. (2024)	Yes	Yes	No	No	Yes	Yes	No	No	Yes
Zhao and Hao (Int Oph 2021a)	Yes	No	No	No	No	No	No	No	No
Zhao and Hao (Oph Epi 2021b)	Yes	No	No	No	No	No	No	No	No
Zhou et al. (2023)	Yes	No	No	Yes	Yes	No	No	No	Yes
Zhu et al. (2020)	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes
Zhu et al. (2022)	Yes	Yes	No	No	No	No	No	No	Yes
Zhu, Tang, et al. (2023)	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes
Zhu, Yin, et al. (2023)	Yes	No	No	No	No	No	No	No	Yes

Abbreviations: AL, axial length; VA, visual acuity.

Five studies compared the use of atropine 0.01% to a control or placebo group and found a significant difference in axial length progression at 2 years (Hieda et al., 2021; Loughman et al., 2024; Moriche-Carretero et al., 2021; Xu et al., 2023; Zadnik et al., 2023) while two studies did not find any difference (Lee et al., 2022; Repka et al., 2023). Chia et al. compared different doses of atropine (0.5%, 0.1% and 0.01%) and found that atropine 0.01% was less effective than the two higher doses (Chia et al., 2023). Other studies found an effect of atropine 0.025%, 0.05% and 1% (Zadnik et al., 2023; Zhang, Yang, et al., 2024; Zhu et al., 2020; Zhu, Tang, et al., 2023). Combined atropine 0.01% and ortho-K were more effective than either treatment alone (Tan et al., 2020, 2023; Xu et al., 2023). Ortho-K, particularly with increased compression factor, MiSight CL, CLs inducing peripheral myopic defocus and multifocal CL with +2.50 spherical addition, reduced axial length progression compared to single-vision CL (Berntsen et al., 2023; Chamberlain et al., 2019; Charm & Cho, 2013; Cho & Cheung, 2012; Choi et al., 2023; Lam et al., 2014; Ruiz-Pomeda et al., 2018; Sankaridurg et al., 2019; Tang et al., 2023; Walline et al., 2020). Spectacle interventions, including highly aspherical spectacle lenslets (HAL), positively aspherical progressive addition spectacle lenses (PA-PAL) with +1.50 D addition, progressive addition spectacle lenses and defocus incorporated multiple segments (DIMS) spectacle lenses, reduced the axial length compared to single-vision spectacles (Bao, Huang, et al., 2022; Hasebe et al., 2014; Huang et al., 2023; Lam et al., 2020; Zhu et al., 2022). Myovision spectacles and violet light-transmitting spectacles did not affect the axial elongation (Kanda et al., 2018; Mori et al., 2021).

Axial length progression after 3 years was reported in seven studies. Atropine 0.01%, 0.02%, 0.05% and 1.0%, MiSight CL, HAL spectacles and progressive addition spectacle lenses remained effective after 3 years (Chamberlain et al., 2019; Walline et al., 2020; Zadnik et al., 2023; Zhu et al., 2020; Zhu, Tang, et al., 2023). Singing a 'myopia ballad' twice daily showed efficacy after 3 years (Tong et al., 2024).

3.5.3 | Corneal infiltrates

Data on the 1-year incidence of corneal infiltrates were reported in 18 studies, of which 16 reported incidences of corneal infiltrates according to the study group and were thus eligible for our meta-analysis. These 16 studies did not have a complete network for comparison, and two separate networks were constructed for comparison. Network diagrams for both networks are shown in File S5. The network meta-analyses were made with single-vision spectacles as the reference in one network and single-vision CL as the reference group in the other smaller network. Consistency $H = 1.000$ suggested minimal inconsistency in the network. None of the treatment groups were associated with a statistically significantly higher risk of corneal infiltrates within the two networks (Figure 4). Using a prevalence meta-analysis, we found

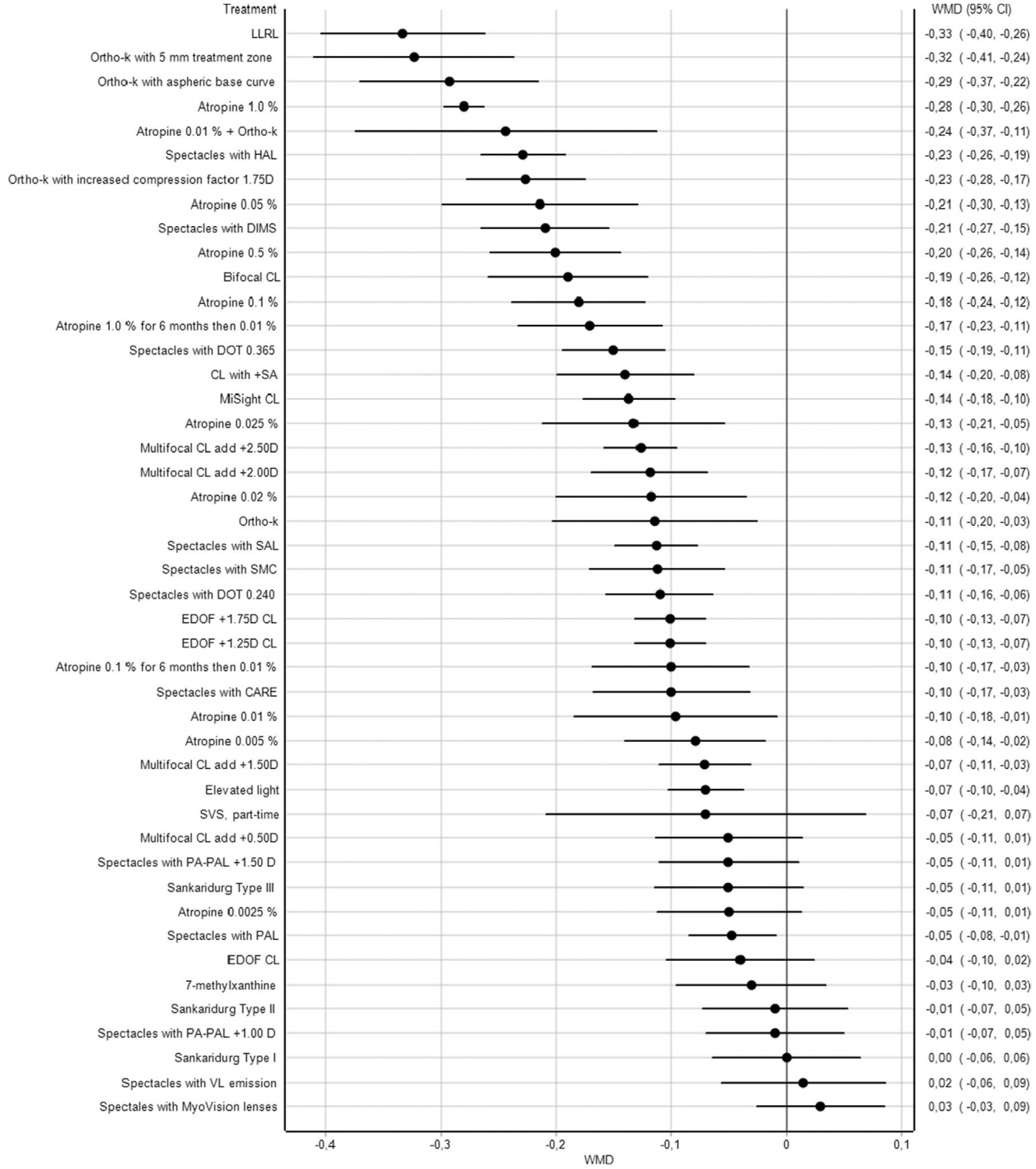

FIGURE 3 Network meta-analysis on the effect of interventions for myopia control on the axial length elongation at 1 year from baseline. Negative values indicate slower axial length elongation (i.e., the desired treatment effect). Summary estimates (dots and whiskers) for each type of intervention are provided as weighted mean difference (WMD) and 95% confidence interval, both in mm. The vertical black line indicates the reference, which is the use of single-vision spectacles. Treatment does not yield statistically significant different outcomes compared to the reference when the confidence interval includes the reference line.

the overall incidence of corneal infiltrates across all study groups at 1 year to be 1.2% (95% CI: 0.4 to 2.5%) (Figure 5). Heterogeneity statistics suggested moderate heterogeneity levels at I^2=69 and Cochran's Q=49. The Funnel plot did not suggest publication bias (File S6). Sensitivity analyses suggested robustness, as the summary estimate did not change significantly (0.8%–1.4%) (File S7).

3.5.4 | Photophobia

Data on the 1-year incidence of photophobia were reported in 17 studies, of which 14 reported incidences of photophobia according to the study group and were thus eligible for our meta-analysis. These 14 studies had a complete network for comparison (File S8). The network meta-analysis was made with the single-vision spectacles

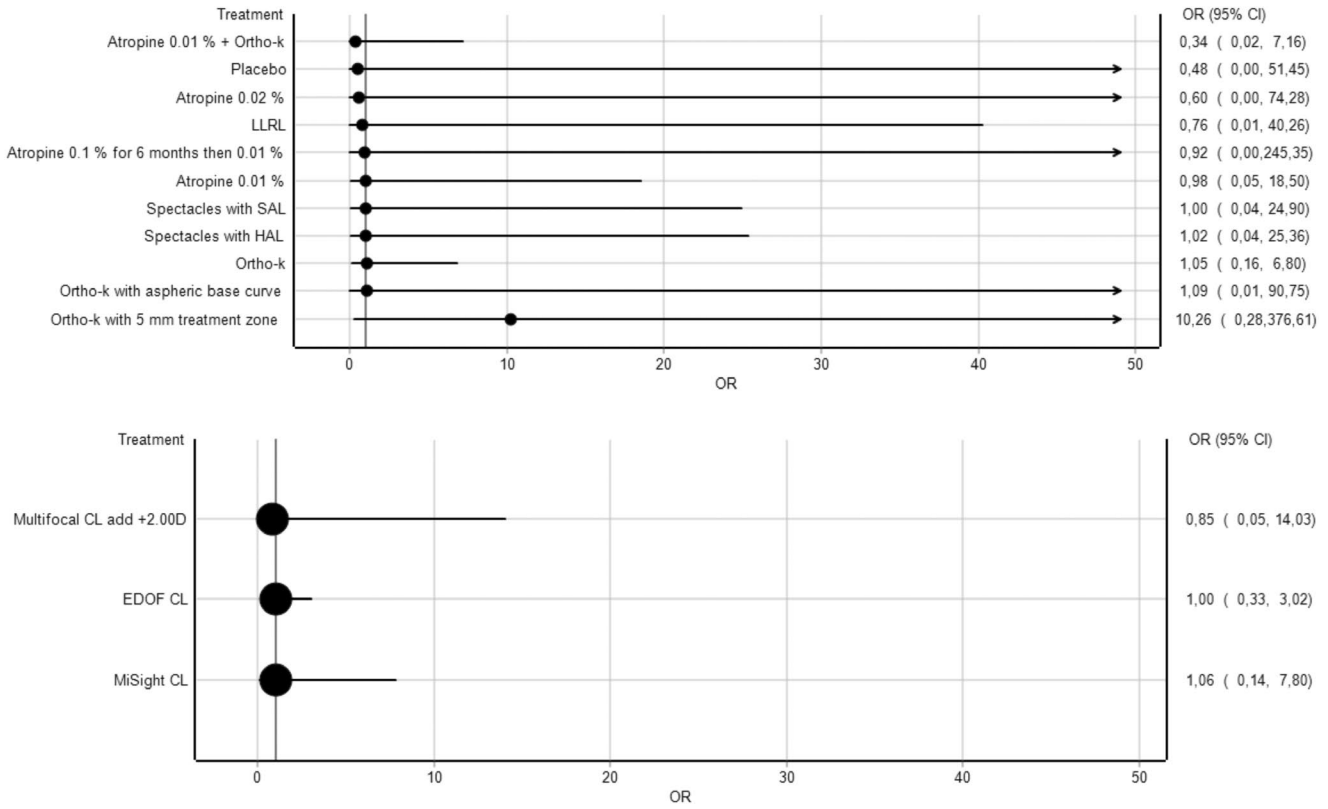

FIGURE 4 Network meta-analyses on the 1-year incidence of corneal infiltrates with interventions for myopia control. Values higher than 1 indicate a higher odds ratio (OR) for corneal infiltration with the specific intervention. Summary estimates (dots and whiskers) for each type of intervention are provided as OR and 95% confidence interval. The vertical black line indicates the reference, which is the use of single-vision spectacles (top) and single-vision contact lenses (bottom). Treatment does not yield statistically significant different outcomes compared to the reference when the confidence interval includes the reference line.

as the reference. Consistency $H=1.000$ suggested minimal inconsistency in the network. We found statistically significant higher OD of photophobia among those in atropine 0.01% (OR 10.5; 95% CI: 3.7 to 29.7), atropine 0.02% (OR 37.0; 95% CI: 5.2 to 265.5) and atropine 0.05% (OR 23.2; 95% CI: 4.9 to 111.3) (Figure 6). Using a prevalence meta-analysis, we found the overall incidence of photophobia at 1 year to be 3.5% (95% CI: 1.0 to 7.2) (Figure 7). Heterogeneity statistics suggested a high level of heterogeneity at $I^2=94$ and Cochran's $Q=217$. The Funnel plot did not suggest publication bias (File S9). Sensitivity analyses suggested robustness as the summary estimate did not change significantly (0.8%–1.4%) (File S10).

3.5.5 | Allergic response

Data on the 1-year incidence of allergic responses were reported in 22 studies, of which 17 reported incidences of allergic response according to the study group and were thus eligible for our meta-analysis. These 17 studies had a complete network for comparison (File S11). The network meta-analysis was made with the single-vision spectacles as the reference. Consistency $H=1.000$ suggested minimal inconsistency in the network. None of the treatment groups were associated with a statistically significantly higher risk of an allergic response (Figure 8). Using a prevalence meta-analysis, we found the incidence of any allergic response at 1 year to be 1.8% (95% CI: 1.0 to 2.9) (Figure 9). Heterogeneity statistics suggested a high level of heterogeneity at $I^2=73$ and Cochran's $Q=62$. The Funnel plot did not suggest publication bias (File S12). Sensitivity analyses suggested robustness, as the summary estimate did not change significantly (1.6%–2.1%) (File S13).

3.5.6 | Visual acuity

Seventeen studies assessed distance visual acuity, and 14 evaluated near visual acuity. Chia et al. (2012, 2023) found no effect of atropine 0.0025%, 0.005%, 0.01%, 0.1% and 0.5% on distance best-corrected visual acuity (BCVA), although doses of 0.1% and 0.5% atropine affected near vision (Chia et al., 2012, 2023). Hansen et al. (2023) reported blurred near vision in 1/33 of children receiving the 0.1% atropine loading dose and the 0.01% dose at 12 months, but no blurring of distance vision (Hansen et al., 2023). Other studies (Lee et al., 2022; Loughman et al., 2024) found no difference in BCVA at distance or near for atropine 0.01%; however, one study reported decreased near BCVA (Hieda et al., 2021). Ye et al. (2022) found a difference in BCVA in children receiving atropine 1% in the first 6 months tapered to 0.01% compared to children solely receiving 0.01% (Ye et al., 2022). Ortho-K treatments showed no difference in uncorrected or best-corrected distance and near acuity between lens designs (Kinoshita et al., 2018; Liu, Chen, et al., 2023; Tang et al., 2023). Dual-focus lenses, MiSight lenses and multifocal lenses performed comparably to single-vision CL in near and distance BCVA

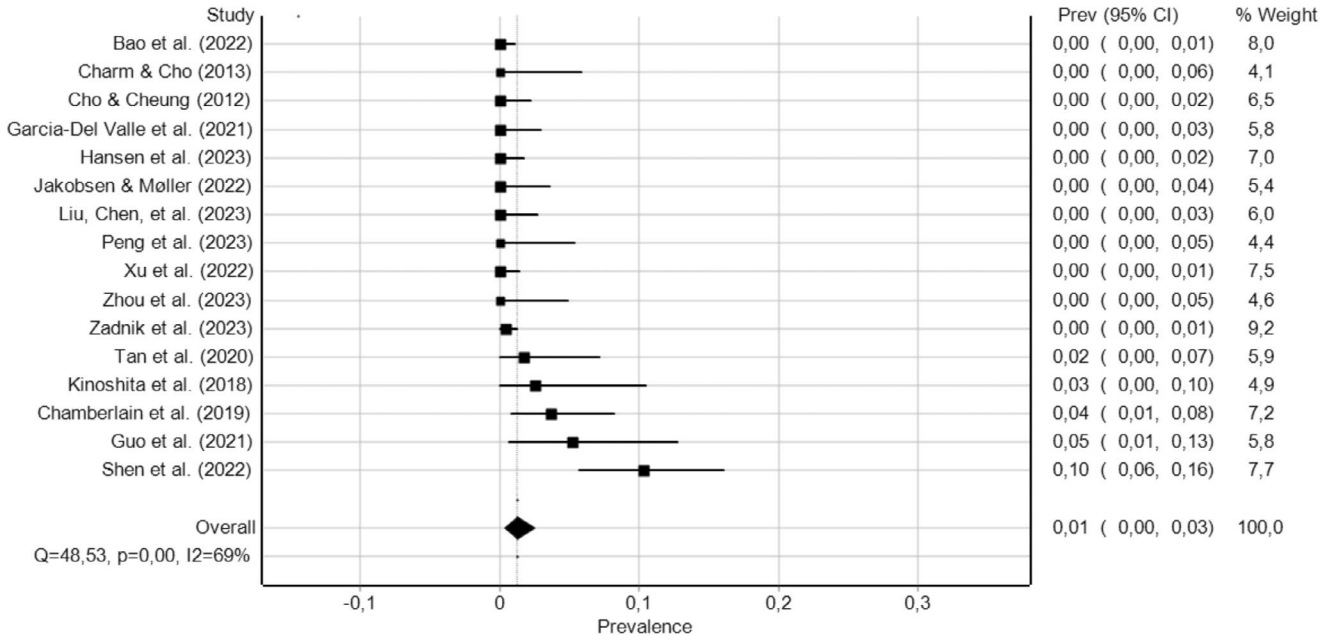

FIGURE 5 Prevalence meta-analysis on the 1-year incidence of corneal infiltrate across studies. Dots and whiskers represent study-specific incidence rates and the 95% confidence interval for the incidence. Calculated summary effect is provided at the bottom. *X*-axis is in rate decimal, i.e., a rate of 0.01 means that 1% develop any corneal infiltrate throughout 1 year.

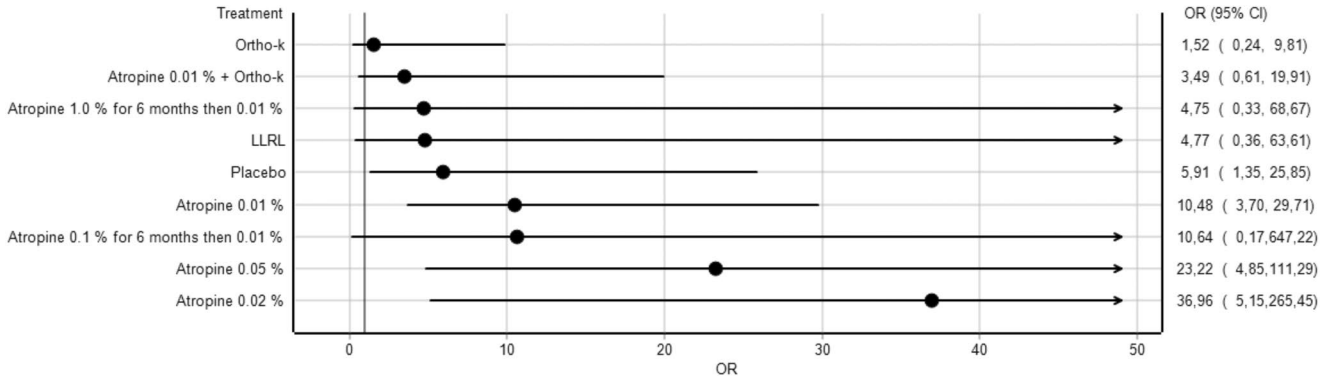

FIGURE 6 Network meta-analysis on the 1-year incidence of photophobia with interventions for myopia control. Values higher than 1 indicate a higher odds ratio (OR) for photophobia with the specific intervention. Summary estimates (dots and whiskers) for each type of intervention are provided as OR and 95% confidence interval. The vertical black line indicates the reference, which is the use of single-vision spectacles. Treatment does not yield statistically significant different outcomes compared to the reference when the confidence interval includes the reference line.

(Anstice & Phillips, 2011; Chamberlain et al., 2019; Walline et al., 2020). Spectacle interventions, including HAL, SAL and DIMS spectacle lenses, showed no difference in BCVA compared to single-vision spectacles (Bao, Yang, et al., 2022; Lam et al., 2020). Jiang et al. reported improved uncorrected distance acuity after LLRL compared to children in the single-vision spectacles group (Jiang et al., 2022); however, BCVA was equal between the two groups. Lastly, a behavioural intervention including singing a 'myopia ballad' had no effect on BCVA (Tong et al., 2024).

3.5.7 | Adherence to allocation

Data on the 1-year adherence to allocation were reported in 61 studies, of which 60 reported adherence to allocation for specific interventions and were thus eligible for our meta-analysis. These 60 studies had a complete network for comparison (File S14). The network meta-analysis was made with the placebo group as the reference, as known allocation to no active treatment/single-vision products potentially may lead to withdrawal of consent/no-show from the study. Consistency $H = 1.008$ suggested minimal inconsistency in the network. We only found a statistically significant OD of lower adherence to allocation for atropine 1.0% (OR 0.3; 95% CI: 0.2 to 0.5) (Figure 10). Using a prevalence meta-analysis, we found the overall lack of adherence to allocation at 1 year to be 1.8% (95% CI: 1.0 to 2.9) (Figure 11). Heterogeneity statistics suggested a high level of heterogeneity at $I^2 = 73$ and Cochran's $Q = 62$. The Funnel plot did not suggest publication bias (File S15). Sensitivity analyses suggested robustness as the summary estimate did not change significantly (1.6%–2.1%) (File S16).

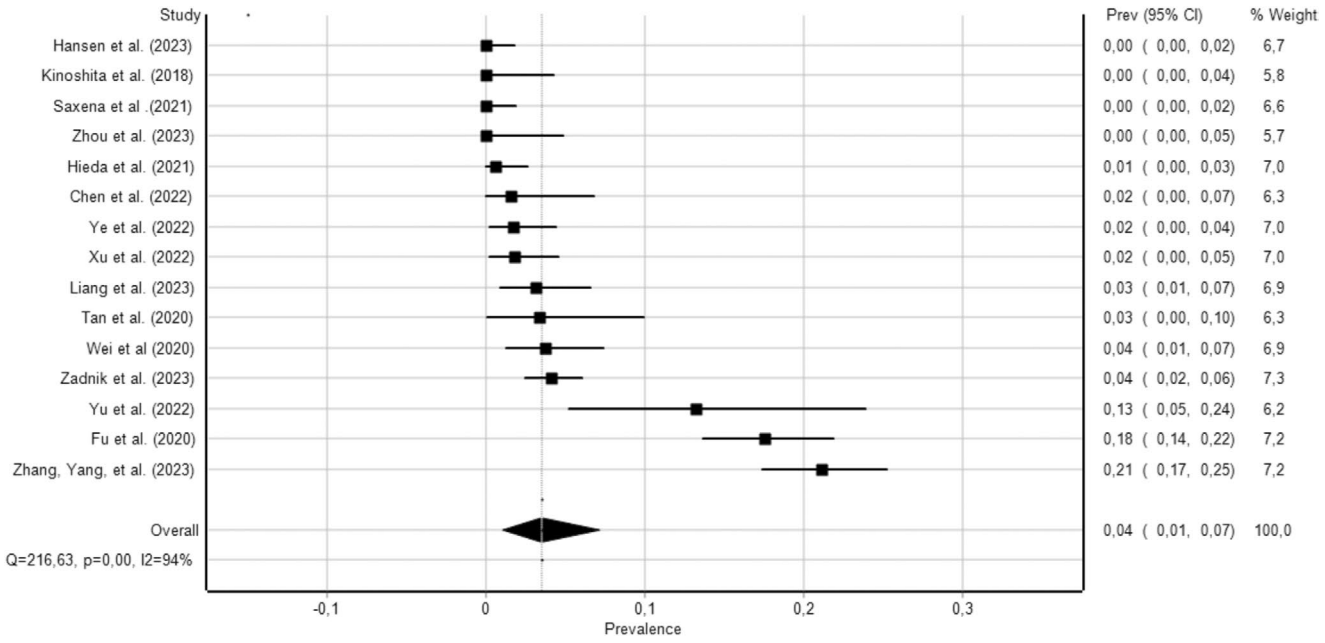

FIGURE 7 Prevalence meta-analysis on the 1-year incidence of photophobia across studies. Dots and whiskers represent study-specific incidence rates and the 95% confidence interval for the incidence. Calculated summary effect is provided at the bottom. The *X*-axis is in rate decimals, i.e., a rate of 0.01 means that 1% develop photophobia at any point throughout 1 year.

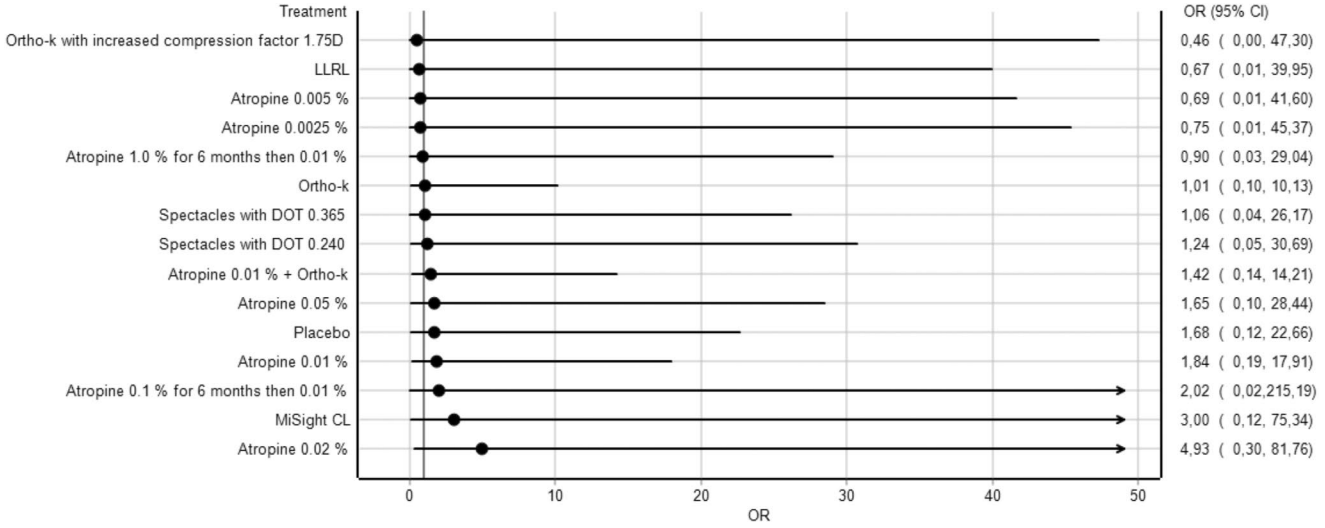

FIGURE 8 Network meta-analysis on the 1-year incidence of allergic response with interventions for myopia control. Values higher than 1 indicate a higher odds ratio (OR) for allergic response with the specific intervention. Summary estimates (dots and whiskers) for each type of intervention are provided as OR and 95% confidence interval. The vertical black line indicates the reference, which is the use of single-vision spectacles. Treatment does not yield statistically significant different outcomes compared to the reference when the confidence interval includes the reference line.

4 | DISCUSSION

This systematic review with network meta-analyses included 74 studies comprising 12 154 participants aged 6–18 years. Over 70% of the studies were conducted in Asian populations. Axial length measurements after 1 year of treatment were reported in 71 studies. The interventions yielding the most significant effects included low-level red light, orthokeratology lenses, atropine and spectacles with highly aspherical lenslets.

Ortho-K are rigid, gas-permeable CLs with a reverse geometry design that are worn during sleep. The design enables the flattening of the central and steepening of the mid-peripheral cornea. Hereby, central refractive errors are eliminated or reduced while myopic defocus on the peripheral retina is induced (Bullimore & Johnson, 2020). Ortho-K significantly reduced the axial length growth, with the most pronounced effect in lenses with a 5 mm treatment zone. Lenses with an aspheric base curve, combined treatment with atropine 0.01%, lenses with an increased compression factor of 1.75 D, and standard ortho-K also showed measurable efficacy. Previous studies have reported cases of microbial keratitis during CL wear (Bullimore & Johnson, 2020; Kam et al., 2017); however, we could not confirm a significant association between

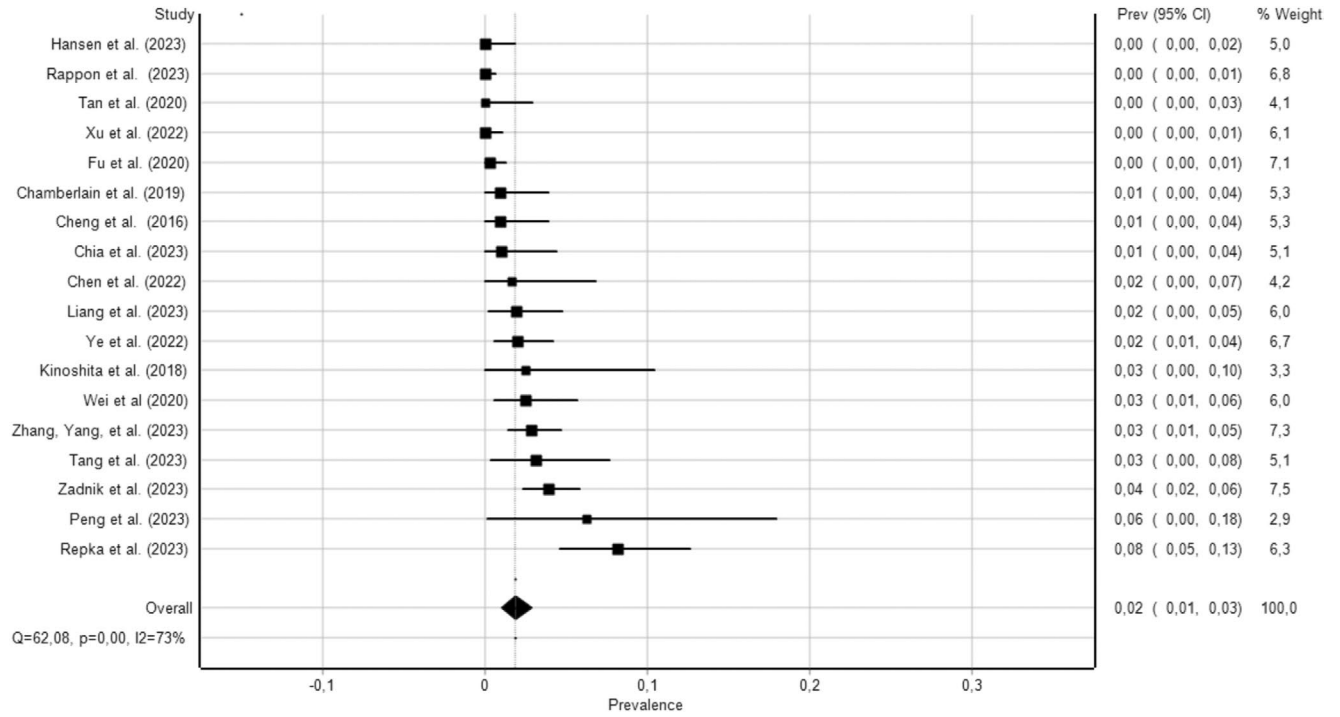

FIGURE 9 Prevalence meta-analysis on the 1-year incidence of allergic response across studies. Dots and whiskers represent study-specific incidence rates and the 95% confidence interval for the incidence. Calculated summary effect is provided at the bottom. *X*-axis is in rate decimal, i.e., a rate of 0.01 means that 1% develop allergic response at any point throughout 1 year.

corneal infiltrates and any of the interventions that were tested. Transient choroidal thickening has been reported following retinal defocus induced by optical interventions, which might be measured as a shortening of the axial length and overestimate treatment efficacy. However, the maximum effect has been reported to be 0.013 mm, thus minor compared to the reduction in axial elongation found in studies on ortho-K (Brennan et al., 2021; Read et al., 2010). Additionally, ortho-k lenses have been found to decrease corneal thickness, thereby reducing the axial length (Alharbi & Swarbrick, 2003). However, few studies examining the effect of ortho-k lenses have considered this factor (Jakobsen & Møller, 2022; Kinoshita et al., 2018; Yu et al., 2022; Zhao & Hao, 2021a, 2021b).

Atropine is a non-selective muscarinic cholinergic receptor antagonist. Its mechanisms in myopia prevention are not fully understood, but atropine is thought to influence biological mechanisms such as dopamine signalling in the retina and extracellular matrix remodelling in the sclera (Upadhyay & Beuerman, 2020). This network meta-analysis found that increasing atropine concentrations yielded higher efficacy, while the lowest concentration of 0.0025% did not have a significant effect compared to single-vision spectacles or placebo. Ten studies found persistent efficacy of atropine after 2- and 3-year periods, although two studies reported no effect after 2 years. However, a rebound phenomenon following treatment cessation has been reported (Chia et al., 2014). Photophobia was reported for concentrations of atropine 0.01%, 0.02% and 0.05%, but lower adherence was only observed in the 1.0% group. Additionally, most studies using atropine concentrations above 0.01% reported reduced near-visual acuity but unaffected distance vision. No interventions were significantly associated with allergic reactions.

HAL spectacles provide optimal central correction for distance vision while inducing peripheral myopic defocus and inhibiting ocular elongation (Bao, Yang, et al., 2022). Peripheral hyperopic defocus is known to stimulate eye growth, whereas peripheral myopic defocus counteracts this effect (Wallman & Winawer, 2004). HAL spectacles had the most significant effect on axial length growth; however, spectacles with DIMS and DOT 0.365 were also significantly better than single-vision spectacles.

LLRL treatment is thought to enhance cellular metabolism through cytochrome c oxidase in mitochondria, promoting retinal and neural health (Zhu, Cao, et al., 2023). In this analysis, including three trials with LLRL, the treatment seemed to significantly reduce axial elongation. However, LLRL devices have been found to surpass the maximum permissible exposure limits, risking photochemical and thermal retinal damage (Ostrin & Schill, 2024), resulting in changes in the photoreceptor outer segments and the relative reflectance of the ellipsoid zone (Zhu et al., 2024), and leading to permanently decreased visual acuity (Liu, Yang, et al., 2023). Further studies are needed to investigate the long-term efficacy and safety of LLRL.

In the category of soft CL, the highest effect in myopia control was reported with bifocal CL, followed by CL with positive spherical aberration, MiSight lenses and multifocal CL (higher efficacy observed with higher addition powers, such as +2.50 D and +2.00 D). However, the study on bifocal CL was limited to a population of myopic children with associated esophoria at near (Aller et al., 2016). Myopic children with large accommodative lags and near esophoria have previously been found to have statistical and clinical effects of treatment with progressive additional spectacle lenses in contrast to

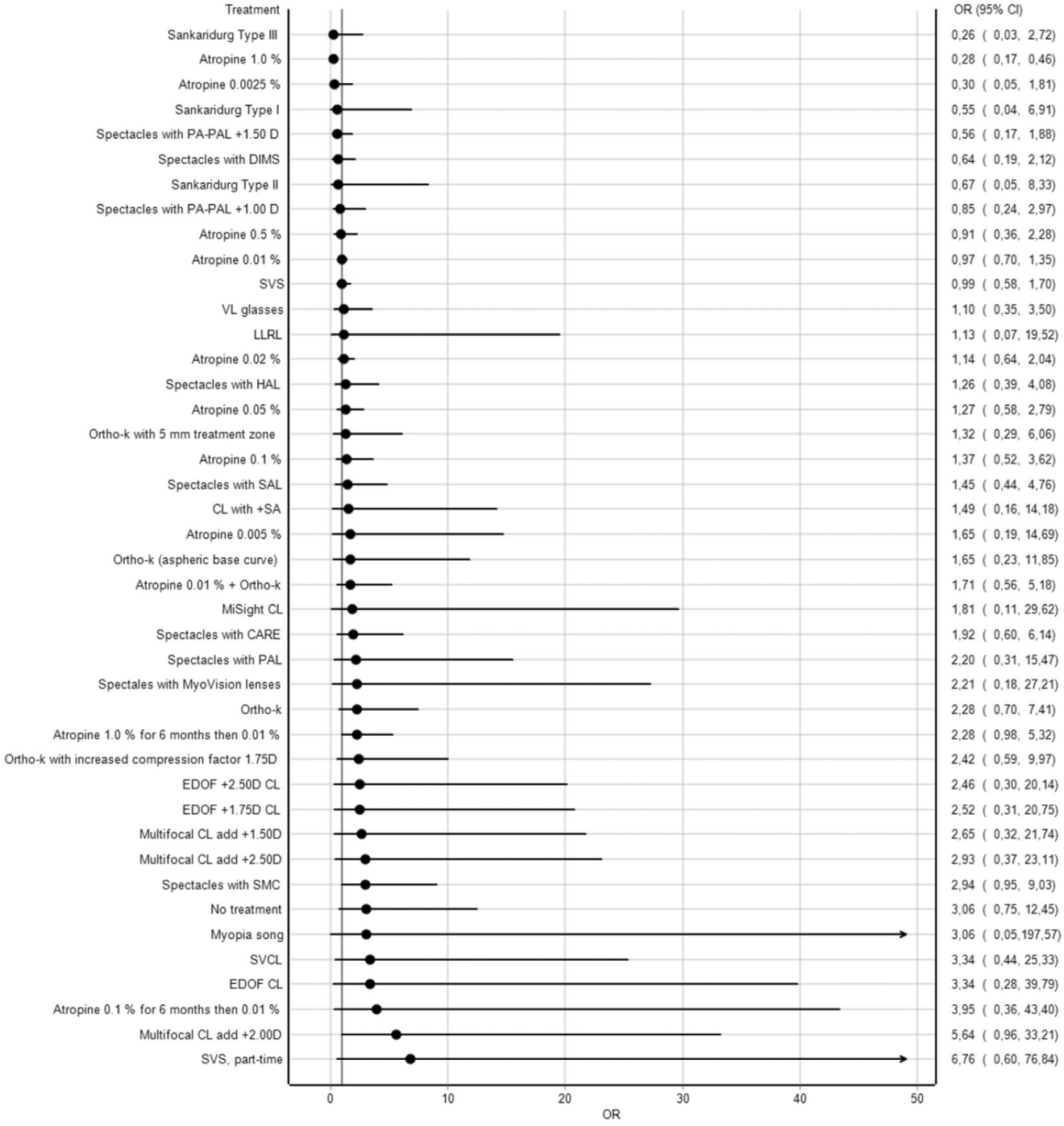

FIGURE 10 Network meta-analysis on the 1-year adherence to allocation for interventions for myopia control. Values higher than 1 indicate a higher odds ratio (OR) for adherence to allocation with the specific intervention. Summary estimates (dots and whiskers) for each type of intervention are provided as OR and 95% confidence interval. The vertical black line indicates the reference, which is placebo. Treatment does not yield statistically significant different outcomes compared to the reference when the confidence interval includes the reference line.

myopic children without these characteristics (Gwiazda et al., 2004). Hence, it is doubtful that the results of the study on bifocal CL apply to broad populations of myopic children.

Results from previous systematic reviews and network-meta analyses have shown that a range of interventions can slow axial length progression similar to our results (Huang et al., 2016; Lawrenson et al., 2023). Previous network meta-analyses have suggested a synergistic effect of combination therapy with ortho-K and atropine, demonstrating efficacy comparable to high-dose atropine or a greater effect than ortho-K monotherapy (Lawrenson et al., 2023; Tsai et al., 2022). One analysis identified the combination treatment as the most effective option (Zhang et al., 2023). However, the wide confidence interval of the combination therapy prevents us from confirming its superiority over monotherapy.

Two systematic reviews on myopia progression after treatment cessation found a rebound phenomenon following optical treatments (spectacles with HAL, DIMS, soft bifocal CLs and ortho-K lenses) as well as atropine and LLRL treatments (Chiu et al., 2023; Sánchez-Tena et al., 2024). Higher doses of atropine, LLRL and ortho-K treatment exhibited more pronounced rebound effects

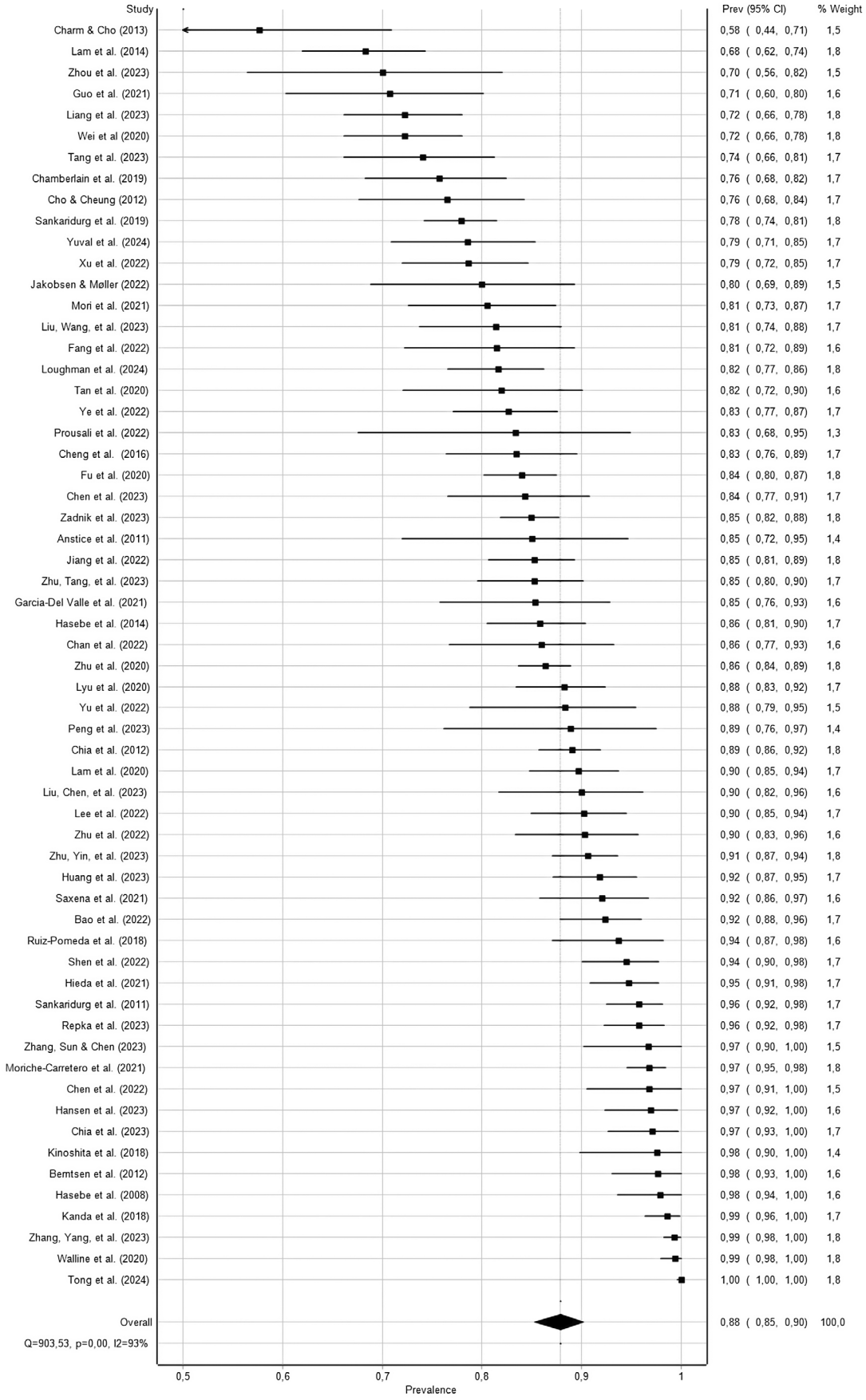

FIGURE 11 Prevalence meta-analysis on the 1-year adherence to allocation across studies. Dots and whiskers represent study-specific incidence rates and the 95% confidence interval for the 1-year adherence rate. Calculated summary effect is provided at the bottom. *X*-axis is in rate decimal, i.e., a rate of 0.99 means that 99% adhere to the allocation throughout 1 year.

than DIMS spectacles and soft bifocal CL. However, differences in treatment duration, cessation period and age at intervention likely influence the magnitude of the reported rebound effect and complicate direct comparisons between interventions.

The strength of our network meta-analyses lies in the differentiation between various groups of optical modalities based on their distinct optical principles. Furthermore, we solely included studies that measured axial length using light-based methods, ensuring accurate measurements with high repeatability.

This review has some limitations. In some studies, double-blinding was not possible, and the predominance of Asian populations may limit the generalizability of our findings, as Asian children appear more susceptible to the development of myopia. Subgroup analysis based on ethnicity could not be conducted due to the limited number of studies available for non-Asian populations, and an analysis of hazard ratios between genders was not feasible due to insufficient data. Additionally, the wide age range of the participants could influence the rate of axial elongation, as myopia progresses more rapidly in younger children. Variability in baseline myopia severity and progression rates may also influence the effectiveness of interventions, along with various environmental factors such as the intensity of near work and the duration of time spent outdoors, which we were unable to adjust for in this review (Jones-Jordan et al., 2011; Pärssinen & Kauppinen, 2022; Saw et al., 2001). Unfortunately, sufficient data for network meta-analysis was available only for the 1-year results, limiting the clinical applicability of the 2- and 3-year data, as the treatment modalities could not be ranked.

This systematic review and network meta-analyses found that multiple interventions were effective in preventing axial elongation. However, clinicians must distinguish between statistically significant effects and clinically meaningful effects, as some treatments result in only negligible slowing of axial elongation. The predominance of Asian participants and the variability in study designs underscore the need for future research involving diverse populations and standardized treatment protocols to improve generalizability and comparability.

5 | CONCLUSION

This systematic review and network meta-analyses highlight the efficacy of various interventions, including orthokeratology lenses, atropine, highly aspherical lenslets and defocus incorporated multiple segments spectacles in slowing axial elongation in children. Low-level red-light therapy also slowed axial length progression; however, further research is needed to assess the potential side effects. Future studies should include diverse populations and standardized methodologies to enhance the applicability and comparability of results.

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CONFLICT OF INTEREST STATEMENT

Author Y.S. declares to have received a speaker fee for lectures from Bayer and Roche, not related to this study. Remaining authors declare no potential conflicts of interest.

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Additional supporting information can be found online in the Supporting Information section at the end of this article.

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