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Systematic review and Meta Analysis

Low-level Red-Light Therapy for Myopia Control – A systematic review and Meta-Analysis of Randomized and Non-Randomized Controlled Studies

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Abstract

Myopia being a public health problem, its management has become a major focus in contemporary optometry and ophthalmology, with interest in innovative approaches to slow myopia progression. Low-level red-light therapy (RLRL) is one of recent non-invasive approaches to the myopic individuals exposed for certain period. This is a relatively recent approach, and the currently available evidence remains limited. This article provides a systematic insight into efficacy of red-light therapy in controlling myopia progression. Out of 173 results, a total of 20 studies with 16 Randomized controlled trials and 4 non-randomized control trials were included in this study after a thorough database search on PubMed, Scopus and Web of Science for all the literature related to red light therapy. Selected articles were thoroughly reviewed and the data containing both axial length and spherical equivalent values were included from the studies for the analysis. Risk of bias assessment was also carried out independently for all the studies included. Results showed that in treatment with RLRL the total pooled mean difference of Axial Length (AL) change between treatment and control groups was -0.29mm (95% CI: -0.36 to -0.22) I^2 = 98%; P<0.00001), and total pooled mean difference of Spherical Equivalent Refraction (SER) was 0.59D (95% CI: 0.49 to 0.69) I^2 = 96%; P<0.0001). Random effect model was used because included studies were differed in sample size, protocols and methodologies, and high heterogeneity was noted in both RCT and Non-RCT studies. This review showed that low- level-red-light therapy can significantly reduce myopia progression however, long-term studies are required to determine whether the effects are sustained over time and whether rebound occurs after cessation.

Keywords: Red Light Therapy, Combination Therapy, Myopia Management, Systematic Review, Meta-Analysis

1. Introduction

Myopia being a public health problem with 25% persons globally, is now a condition that is predicted to rise to 50% by the year 2050 if left untreated or uncontrolled [1, 2]. Therefore, tackling myopia progression and myopia preventive / control measures is now a topic of great interest among the eye care practitioners and researchers to investigate which interventions can lead to better control [3]. Eye elongation leads to several structural and functional changes within the myopic eye, especially in the retina and is associated with a change from a mostly spherical eye shape to a prolate ellipsoid form. It is combined with choroidal and scleral thinning, most pronounced at the posterior pole and less pronounced in the fundus midperiphery. Myopia occurs when the optical power of the eye causes image to focus anterior to the retina, often due to axial length elongation, continuing this results in myopia increase [4]. Myopia also increase as the age increases and is stated in a study published in France where prevalence of myopia was 19.6% among age of 0 to 9 years as compared to 52.4% among 20 to 29 years respectively [5]. Various strategies for managing myopia are available nowadays such as glasses, contact lenses or emerging therapies like red light therapy, which is also called Photo biomodulation, which uses near infra-red of 635 to 650nm

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wavelength to stimulate biological tissue and influence cellular function. However, there is no definite conclusion to say which strategy is more effective under which conditions. Therefore, approaches such as anti-myopia strategies require an in-depth investigation and analysis to ensure long term safety and efficacy or effectiveness. This review focuses on to know the efficacy of RLRL in myopia management [6, 7].

The exact mechanism of how red-light therapy alters the retinal structures is hypothesized and not yet well established, however there is a need to know the exact mechanism of how RLRL helps in myopia management. A study published in 2010, illustrated that choroidal vasculature serves as a major supply for retina to nourish and function smoothly, and that's the reason that RLRL influences the sub-foveal chorio-retinal thickness because of its secretory cells probably involved in altering the thickness thereby making the photoreceptors in the area of focus and defocus [8]. This sub-foveal choroidal thickness was also observed in the study conducted in 2024 leading to reduction in axial length over a 3-months treatment [9]. Another study reported positive correlation in chorio-capillaries luminal areas before and after RLRL [10]. This was further documented by study that talked about the association of light with myopia that may alter the expression of type 1 collagen human fibroblast to alter scleral modelling thereby altering progression of myopia [11]. Treating myopia is not only a medical solution but an opportunity to create a positive impact on life, education, work and leisure. Timely management of myopia can lead to economic cost as compared to those who are not treated in time and results in various unwanted complications. Higher the myopia, higher the incidence of pathologic complications due to myopia in adults and children with the impact on vision related quality of life. Some studies found the very strong parental effect on degree and incidence of myopia on their children's [12]. Although evidence exists, we intend to conduct this review because the evidence is inconsistent, incomplete and not yet globally applicable.

2. Methodology

The review aimed to understand evidence on low-level repeated red-light therapy using near infra-red with a wavelength of approximately 635nm as a non-invasive procedure to stimulate retina leading to structural and functional changes in the eye to manage myopia.

2.1. Databases, screening, inclusion and exclusion

In this review article, we followed and reported according to the PRISMA guidelines **(Figure 1)** for systematic review and meta-analysis [13]. For this systematic review we selected widely used major databases in medical literature, PubMed, Web of Science, and Scopus. A search was carried out by using Mesh terms such as Low-level red-light therapy OR LLRT, repeated low level red light OR RRLT AND Myopia control OR nearsightedness OR Axial length shortening OR SER. No filters, such as publication year, language, or article type were used while searching for studies on databases, however, the search terms used were in English only, and if articles published regarding the same study in other language are picked up by the search engine or not, but we tried to google translate it to get the maximum as we can. We also conducted a manual search in Google Scholar to find studies that might have been overlooked during the search. This was an independent review study conducted during June-July 2025.

We imported the extracted bibliography into the ZOTERO reference manager, which automatically detected duplicate studies. We removed these studies before screening. We included studies based on our PICOT (Population, Intervention, Comparator, Outcomes, Time Frame) where full study was available for getting an in-depth analysis and those having only abstract were not included. Population included myopic children of either gender with age between 4 to 16 years underwent for the therapy having minimum of two sessions per day for at least 5 continuous days. Further, criteria for the instrument for red-light therapy was checked for myopia control / management while keeping the wavelength in compliance solely intended for retinal stimulation. We included RCTs and non-RCTs irrespective of country of origin which focused on myopia control with RLRL in children or young adults with 6 months and 12 months follow-up protocols.

2.2. Data Extraction

We extracted the following data from the included studies

- Country of origin and publication data
- Study design
- Number of subjects in treatment and control groups
- RLRL protocol including session time, wavelength
- Duration of study
- Mean Axial length and Standard deviation
- Mean Spherical equivalent refraction and standard deviation

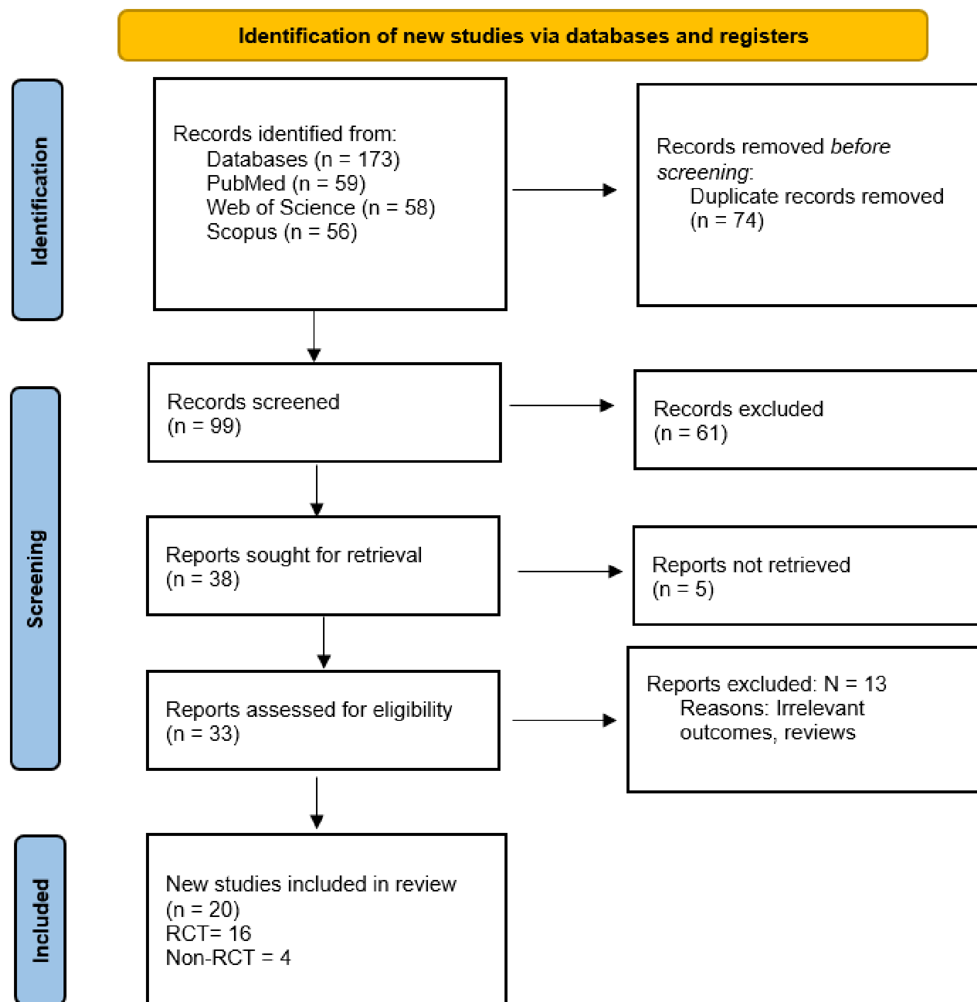

Figure 1: PRISMA Flow Chart diagram. *N or n – number of studies

2.3. Statistical Analysis

The meta-analysis was conducted by using Cochrane Review Manager. Random effect model was used to find the pooled mean AL and SER in different subgroups to find statistically the efficacy of red-light therapy in myopia control. Random effect model was used because the included studies differed in sample size and methodologies, and high heterogeneity was noted. Some of the studies did not report standard deviation we used the following formulas to get the standard deviation (SD). **SD = SE** $\times \sqrt{n}$ Where: - SE is the standard error & n is the sample size. **SE = (Upper CI - Lower CI) / (2** $\times$ **Z)**

- We found Standard Deviation with the following formula for studies reporting the Interquartile range. **SD** $\approx$ **IQR / 1.35**

- We conducted this meta-analysis using a random-effects model to account for variability across different studies, inverse variance, and 95% CI. We performed sensitivity analysis by removing individual studies to determine the change in heterogeneity and pooled estimates.

2.4. Risk of Bias Assessment

Risk of bias assessment was carried out by one reviewer independently and to ensure accuracy second reviewer did subset of studies. Any discrepancy between the reviewers was resolved through discussion and consultation with third and fourth reviewer. ROB-2 (Cochrane Risk of Bias) tool was used for randomized control trial studies while, ROBINS-I tool used for non-randomized control trial studies. The domain was randomization, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results. Each domain within respective tools was evaluated according to recommended guidelines of the tools. We assessed each domain of these tools for each study and reported them in **figure** 2 for RCTs and **figure** 3 for non-RCTs.

Table 1: Baseline characteristics of included studies

Patients N (T/C)	Age (yrs)	RLRL Protocol	RLRL session	Control Group	Duration (months)	Adverse Events	Included in Meta-analysis	Study site/year (Reference)
Study Design RCT								
248 (126/122)	6 to 11	650nm	2 sessions/day 5 days/week	No treatment	12	No structural damage	AL, SER, N	China/2023 [6]
86 (46/40)	6 to 13	635nm	2 sessions/day 5 days/week	SVS	12	None	AL, SER, N	China/2023 [14]
62 (31/31)	7 to 15	650 ±10 nm	3-minute session 2 sessions daily	LDA	12	None	AL, SER, N	China/2022 [15]
26(11/15)	8 to 15	—	3-minute session, 2 sessions/5 days/week	Ortho-K	12	None	AL, N	Spain/2025 [16]
111(56/55)	7 to 12	0.29mW	3-minute session 2 sessions daily	Sham light therapy	6	None	AL, SER, N	China/2023 [17]
246 (117/129)	8 to 13	650±10nm	2 sessions/day 5 days/week	SVS	12	None	AL, SER, N	China/2022 [18]
66(31/35)	4 to 8	650±10nm.	3-minute session 2 sessions daily	SVS	6	None	AL, SER, N	China/2025 [19]
198 (130/68)	7 to 12	650±10nm	3-minute session 2 sessions daily	SVS	12	None	AL, SER, N	China/2025 [20]
87(45/42)	6 to 12	650±10nm	3-minute session 2 sessions daily	LDA	6	None	AL, SER, N	China/2025 [21]
112(56/56)	6 to 12	650nm	3-minute session 2 sessions daily	No intervention	6	None	AL, SER, N	China/2023 [22]
47(30/17)	8 to 13	650 ±10nm	3-minute session 2 sessions daily	Ortho-K	12	26 cases reported	AL, N	China/2024 [23]
73(36/37)	6 to 14	650nm	3-minute session 2 sessions daily	SVS	6	None	AL, SER, N	China/2024 [24]
188(96/92)	6 to 16	650nm	3-minute session 2 sessions daily	SVS	12	None	AL, N	China/2024 [25]
52(26/26)	6 to 10	650nm	3-minute session, 2 sessions daily	SVS	12	None	AL, SER	China/2025 [26]
25(13/12)	8 to 14	650nm	3-minute session 2 sessions daily	PDMSL	12	None	AL, SER	China/2025 [27]
308 (157/152)	6 to 12	650nm	3-minute session, 2 sessions daily	No intervention	12	None	AL SE, N	China/2024 [28]
Study Design Non-RCT								
138(67/71)	6 to 14	635nm	3-minute session 2 sessions daily	Ortho-K	24	None	AL, N	China/2024 [29]
55(27/28)	5 to 15	635nm	Twice daily	SVS	12	None	N, AL, SER	China/2024 [30]
125(40/85)	5 to 16	650±10nm	3-minute session 2 sessions daily	DIMS	12	None	N, AL, SER	China/2025 [31]
108(53/55)	6 to 14	650±10nm	3-minute session 2 sessions daily	SVS	12	None	N, AL, SER	China/2024 [32]

**N – Number of subjects *T – Treatment Group *C- Control Group. SVS: Single vision spectacle; LDA: low dose atropine; Ortho-K: orthokeratology; PDMSL: Peripheral Defocus Modifying Spectacle Lenses; DIMS: Defocus Incorporated Multifocal Segment Spectacle Lenses*

Risk of bias domains

Study	D1	D2	D3	D4	D5	Overall
Chen H, 2023	+	-	-	+	-	-
Chen Y, 2022	+	-	+	+	-	-
Fernández, 2025	+	-	+	+	+	-
Dong J, 2023	+	+	+	+	+	+
He X, 2023	+	-	-	+	+	-
Jian Y, 2022	+	-	+	+	+	-
Li L, 2025	+	-	+	+	-	-
Liu G, 2025	+	-	+	+	+	-
Pang, 2025	+	-	+	+	+	-
Tian, 2023	+	-	+	+	+	-
Xiong R 2024	+	+	+	+	+	+
Xiong Y, 2024	+	+	+	+	+	+
Xu Y, 2024	+	-	+	+	+	-
Yang ke, 2025	+	-	+	+	+	-
Yu Jun, 2025	+	-	+	+	+	-
Cao K, 2024	+	-	+	+	+	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low

Figure 2: Risk of bias assessment in Randomized Controlled Trials

2.5. Study Characteristics

In this systematic review and meta-analysis, we included 16 randomized control trials (RCTs) [6, 14–28] and 4 non-randomized control trials [29–32] **(Table 1).** These studies were majorly performed in the age group 4 to 16 and most of the studies followed the same red light therapy session, 3 minutes session twice daily 5 days a week. Single vision (SVS) was the main control group used in most of the included studies, low dose atropine (LDA), orthokeratology (Ortho-K) and Defocus Incorporated Multiple Segments (DIMS) and Peripheral defocus modifying spectacle lens (PDMSL) were also used by some studies.

2.6. Study Quality Assessment

In all RCTs, participants were randomly allocated, but none of the RCTs implemented double blinding, introducing potential performance bias. 3 studies showed no low risk of bias and 13 RCTs showed some concerns of risk of bias. In non-randomized controlled trial, there were 4 studies, and all showed moderate risk of bias. In all studies there were clear intervention protocols. However, bias due to confounding was moderate in all studies introducing potential bias. To address differences in study design, both types of studies were analyzed and report separately and methodological quality of each study was carefully considered during interpretation.
We didn't exclude study based on risk of bias as it may introduce additional selection bias and reduce generalizability of findings. Instead, quality of studies is carefully assessed and incorporated into results during interpretation. Furthermore, we made subgroups and performed a sensitivity analysis to reduce the heterogeneity, but no major reduction was achieved.

3. Results

3.1. Axial length: Axial length analyzed based on duration of treatment 6 months and 12 months

Change in pooled mean difference in axial length between treatment group and control groups in 12 months duration RCT were -0.34mm (95% CI: -0.39 to -0.29). Pooled results showed high heterogeneity (I^2 = 88%; Z= 12.22; P<0.00001), while the

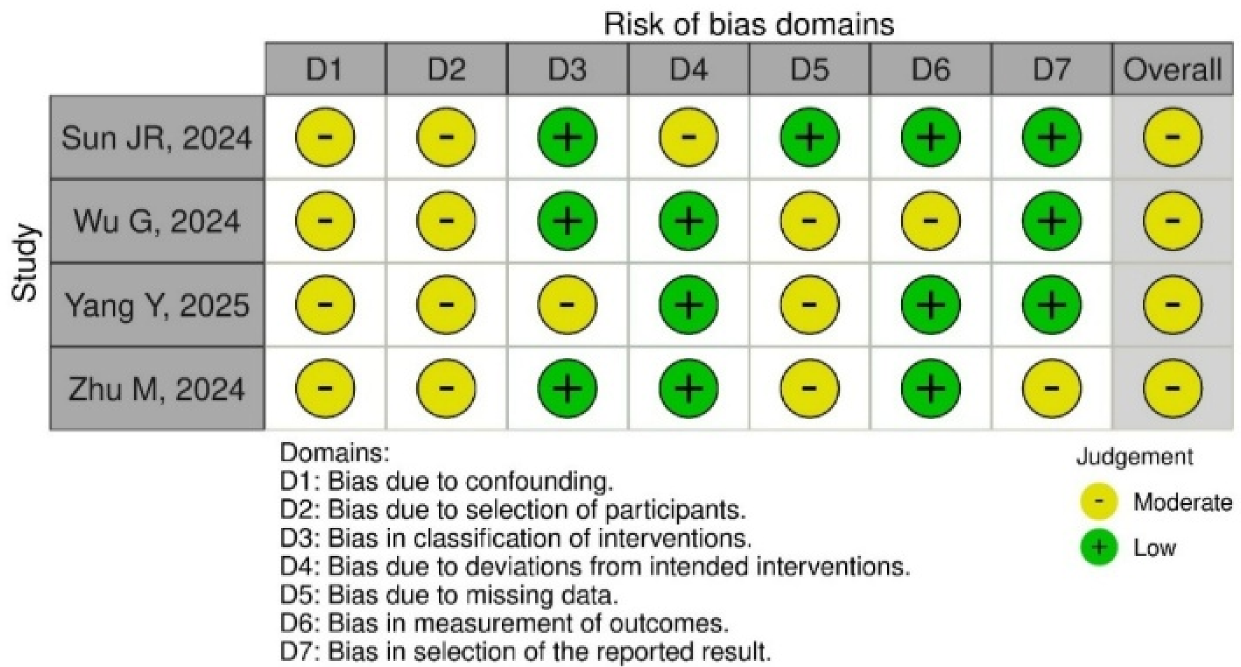

Figure 3: Risk of bias assessment in non-Randomized Controlled Trials

change in pooled mean difference in axial length between treatment group and control groups in 12 months duration non-RCT studies was -0.36mm (95% CI: -0.54 to -0.19). The pooled results showed high heterogeneity (I^2 = 97%; Z= 4.10; P<0.00001), pooled result for 6 months duration studies were -0.18mm (95% CI: -0.24 to -0.12). The heterogeneity was high (I^2 = 89%; Z= 5.75; P<0.00001). Sensitivity analysis was performed by removing individual studies to check the heterogeneity, but there was no significant difference found in heterogeneity **(Figure 4).**
There were 1368 participants in RLRT group (treatment) and 1339 participants in control group. The pooled mean difference of the change in axial length (AL) was -0.29mm (95% CI: -0.36 to -0.22). Heterogeneity analysis showed high heterogeneity (I^2=98%; Z=8.25; P<0.00001).
Figure 4 shows the forest plot of pooled mean difference of all the included studies.

3.2. Spherical Equivalent refraction (SER)

Change in spherical equivalent refraction was also analyzed based on 2 different durations i-e 12 months and 6 months. In 12 months, duration RCT studies, the pooled mean difference of change in SER was 0.69 D (95% CI: 0.60 to 0.79). High heterogeneity was observed in pooled results of SER (I^2=95%; Z=14.08; P<0.00001). Individual sensitivity analysis was done by removing studies to check the heterogeneity, but no significant effect was noticed. Non RCT 12-month studies showed the pooled mean difference of change in SER was 0.65 D (95% CI: -0.09 to 1.40). High heterogeneity was observed in pooled results of SER (I^2=98%; Z=1.72; P < 0.00001) **(Figure 5).**
In 6 months, studies the pooled mean difference of change in SER was 0.40 D (95% CI: 0.20 to 0.60). The heterogeneity was high (I^2=88%; Z=172; P<0.00001), different methods were used to lower the heterogeneity but here was no significant difference found.
There were 1098 participants in treatment group and 1077 participants in control group in SER analysis. The pooled mean difference of change in SER of both subgroups was a 0.59D (95% CI: 0.49 to 0.69). Heterogeneity analysis showed high heterogeneity (I^2=9%; Z=11.51; P < 0.00001).

3.3. Adverse Events

Some studies reported after-image symptoms, but no serious ocular damage. Xiong R [23] reported 26 cases with after image after red light therapy but no structural damage was noticed.

4. Discussion

This systematic review and meta-analysis demonstrate that RLRL can significantly slow progression of Axial length and SER in myopia control. We found that RLRL slowed significantly progression of axial length and SER in 12- and 6-months

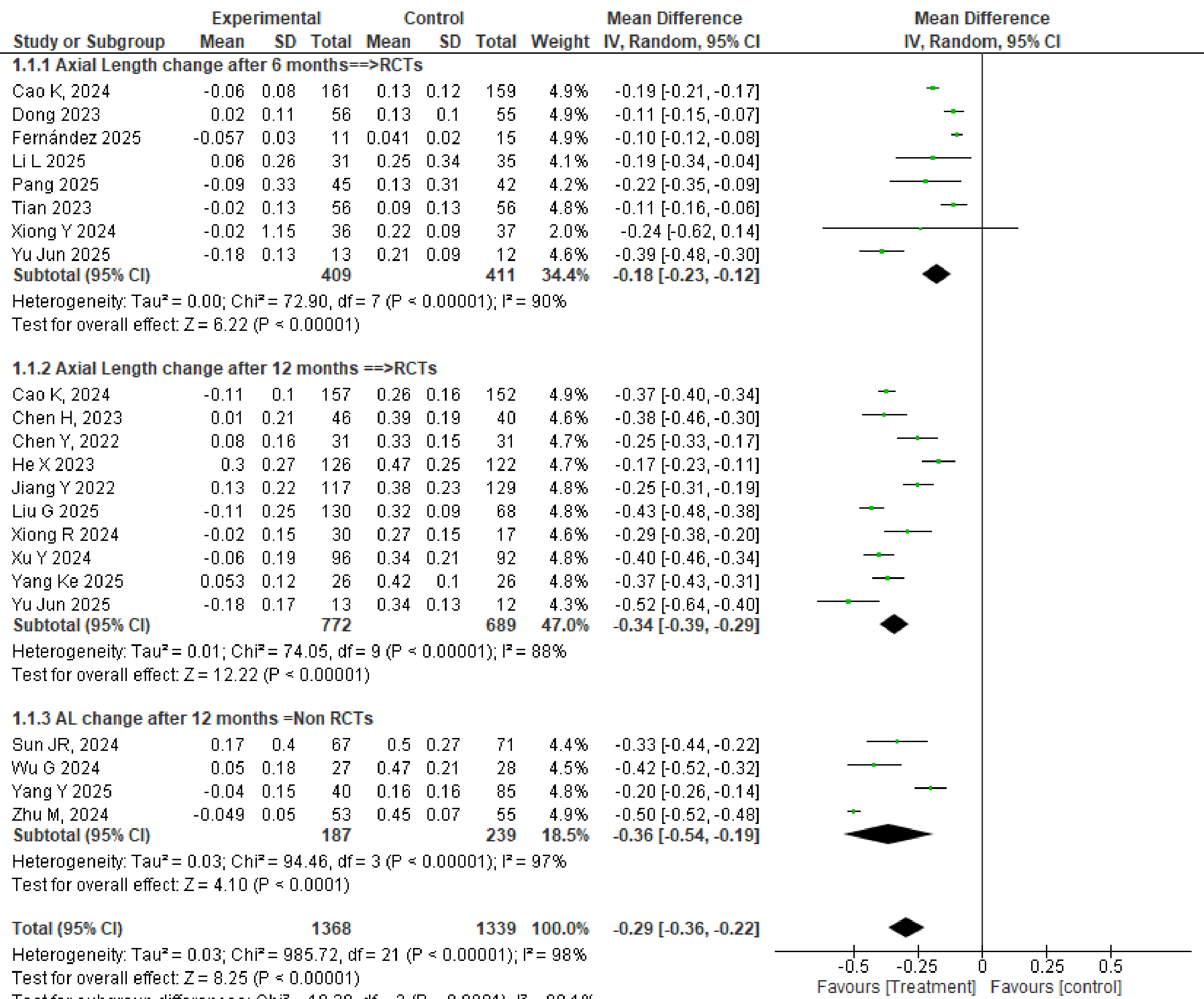

Figure 4: Forest plot showing pooled Mean difference of Axial length. **SD – Standard Deviation *CI – Confidence Interval*

duration. We reported all outcomes in different study durations, and we found that in longer-duration studies RLRL was more effective in controlling myopia progression. When pooling all studies the heterogeneity was high. We performed a sensitivity analysis to reduce the heterogeneity, but no significant reduction was noticed.

This study findings align with a previous meta-analysis by Wang F *et al* 2023 [33] discussing the efficacy of RLRL in myopia control. They reported the mean difference in axial length change between treatment and control groups was -0.25mm (95% CI: -0.32 to -0.17 P<0.001; I^2=13%) and SER mean difference was 0.60 D (95% CI: 0.44 to 0.76, P<0.001; I^2=20%). In our meta-analysis in total pooled mean difference of AL change between treatment and the control group in short and long-duration studies (6 and 12 months) was -0.29mm (95% CI: -0.36 to -0.22 P< 0.00001; I^2=98%), and pooled meant SER was 0.59 D (95% CI: 0.49 to 0.69). Heterogeneity analysis showed high heterogeneity (I^2 = 96%; P<0.00001). Wang F et al [33] included 7 RCTs and in our meta-analysis 16 RCTs and 4 non RCTs are included.

This study results are also consistent with another meta-analysis by Tang *et al* 2023 [34] the efficacy of RLRL in myopia control. They reported the mean difference of AL between the treatment and control group was -0.35 mm and SER change was 0.68 D per 6 months. However, this meta-analysis included non-randomized control which may affect the heterogeneity and validity of the results. Also, the Tang et al meta-analysis was based on 6 months of follow-up results while our review was based on a greater number of long follow-up studies. The duration of follow-up is critical consideration for myopia control. We included a detailed exploration of high heterogeneity by subgroup and sensitivity analysis.

This study results showed a greater reduction in AL with RLRL as compared to a recent meta-analysis to find the optimal concentration of atropine for myopia control by Wang XY *et al* 2024 [35] Their results showed the mean change in axial length and SER in different low concentrations were 0.01% (0.13mm,0.35D), 0.05% (-0.23mm, 0.57D), 0.025% (-0.16mm, 0.46D), and 0.02% (-0.21mm, 0.44D). In comparison our meta-analysis showed the mean change in AL was -0.29mm and SER was 0.59D, both of these findings surpass the effects observed with low concentration meta-analysis.

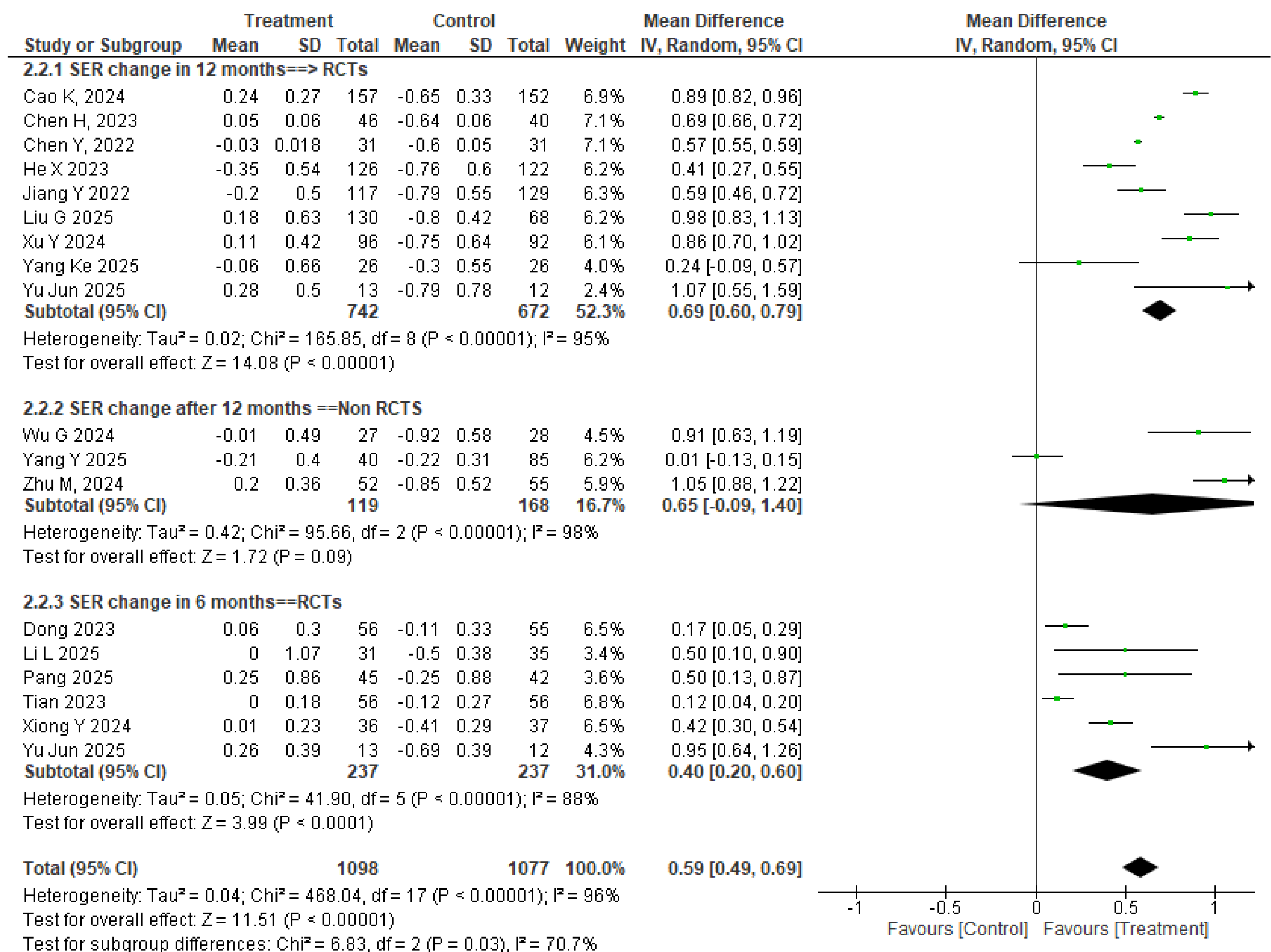

Figure 5: Forest plot shows pooled mean difference of change in SER *(Spherical Equivalent Refraction)*

In another recent meta-analysis by Wang Z 2023 [36] investigated the effects of 0.01% atropine alone and in combination with orthokeratology (AOK) on myopia control. Their results showed the combination of atropine with orthokeratology (AOK) over a 12-month follow-up significantly reduced axial elongation (WMD: -0.12 mm, 95% CI: -0.17 to -0.07, p=0.00001). However in our review the total pooled mean difference of AL change between treatment and control groups was -0.29mm (95% CI: -0.36 to -0.22 P<0.00001 ; I^2=98%), and pooled mean SER was 0.59 D (95% CI: 0.49 to 0.69).This larger effect suggests that RLRL combined therapy may offer superior control of axial elongation compared to the AOK approach, particularly in studies with longer follow-up periods and diverse treatment protocols.

Changes in axial length or choroidal thickness are permanent or temporary; it is still a question of debate. One study reported 40.8% decrease in incidence of myopia after being treated with low level red light as compared to the study controls. [18] Therefore, further study exploration needs to be conducted in these subjects over the upcoming time. It is also possible that it has not been reported because of the newer management therapy or short-term therapy or not including a follow-up study.

The safety Profile of RLRL is very critical in clinical application for myopia control. Our meta-analysis revealed no major adverse event in the included study while some studies like Xiong R *et al* [23] reported cases of temporary after image contributing to less than 1% of all the subjects included in this analysis (26 out of 2375 subjects) which supports the safety and tolerability of RLRL therapy over the study periods. However, it is important to note that individual cases of adverse events have been reported in the literature. For instance, 12-year-old female patient experienced symptoms of abnormal light sensitivity and prolonged afterimages one month prior to presentation. Clinical examination showed disruption of the ellipsoid zone and inter-digitation zone on optical coherence tomography along with hypo auto-fluorescent plaques on fundus auto-fluorescence imaging. Partial recovery of retinal integrity and visual acuity (20/25) was observed after discontinuation of RLRL therapy for 3 months. [37]. Although, such adverse events were not observed in the included studies, it is important to monitor for potential retinal toxicity associated with prolonged RLRL therapy in children with increased light sensitivity.

The findings of this review have significant implications for clinical practice. Clinicians should consider RLRL as a viable treatment option for myopia control, especially when combined with other myopia-controlling therapies. The observed reduction in axial elongation and improvement in spherical equivalent refraction indicate that RLRL may be especially

beneficial for children experiencing rapid myopia progression. Given the absence of major adverse events in the included studies, RLRL appears to have a favorable safety profile, although continued monitoring for rare retinal complications is recommended.

Despite these significant findings, several limitations should be addressed. First, high heterogeneity (I^2=97%) persisted in the pooled analysis, showing variability in study designs, participant characteristics, and treatment protocols. We made subgroups and performed a sensitivity analysis to reduce the heterogeneity, but no major reduction was achieved. Second, some included studies did not report standard deviations for key outcome measures, necessitating the use of imputation techniques, which may have introduced bias. Third, although no adverse events were reported in the included studies, reports of potential retinal toxicity from case studies in the literature warrant caution. Moreover, all studies were originated from China, only one study from Spain, and as instrument itself manufactured in China and only full text studies available from there at the time of review, which may limit generalizability of findings to other population which may restrict the external validity of the findings, as variations in genetic background, environmental exposures, and clinical practices could influence treatment outcomes. Plus, this study was not registered with registries like Prospero. Future studies should aim to standardize outcome reporting, employ longer follow-up durations, and assess long-term safety in larger, more diverse populations. Also, future studies should account for these regulatory developments from diverse contexts and geography to provide comprehensive understanding of this therapy effect.

5. Conclusion

RLRL shows promise but evidence is heterogeneous and largely from a limited geographic region (China); long-term efficacy and safety remain uncertain. This study adds into the comparative insights of short- and long-term efficacy (although data is very limited) as well as the combination therapy in these myopic subjects. Therefore, more studies and research are needed to see the efficacy, safety and long-term effects in the individuals opting for red-light therapy. There is also a dire need to validate the amount of exposure required for red light therapy in effective management of myopia.

6. Declarations

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Author Contributions

Conceptualization, MQ, JJ, PF; Methodology, MQ, JJ, PF; Software, MQ, MS.; Validation, MQ, MS, JJ, PF; Formal Analysis, MQ, MS.; Investigation, MQ, MS; Resources, MQ, MS, JJ, PF; Data curation, MQ, MS; Writing original draft, MQ; Writing—review and editing, MQ,JJ,PF,HM; Visualization, JJ,PF,HM; Supervision, JJ,PF.; Project administration, MQ,JJ,PF; Funding acquisition, None. All authors have read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not Applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Not Applicable.

Acknowledgments

Not Applicable.

AI declaration

The authors confirm that no content in this manuscript was generated using artificial intelligence (AI) tools and the authors take full responsibility for the accuracy and integrity of the work.

7. Abbreviations

RLRL	Repeated Low-Level Red-Light Therapy
AL	Axial Length
SER	Spherical Equivalent Refraction
RCT	Randomized Controlled Trial
Non-RCT	Non-Randomized Controlled Trial
Ortho-K	Orthokeratology
LDA	Low Dose Atropine
AOK	Atropine Orthokeratology
DIMS	Defocus Incorporated Multiple Segments
PDMSL	Peripheral Defocus Modifying Spectacle Lens
SD	Standard Deviation
CI	Confidence Interval
WMD	Weighted Mean Difference

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