# Ethnic and Dose-Dependent Differences in Atropine Efficacy for Myopia Control: A Systematic Review and Meta-analysis

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## Synopsis:

Atropine slows myopia progression in a dose-dependent manner across ethnicities, showing greater efficacy and pupil dilation in East Asian children compared to South Asian and White European children.

**Abstract**

Background/Aim: Clinical uncertainty remains regarding optimal atropine concentration, treatment duration, and potential differences in efficacy for myopia control between Asian and non-Asian children. This systematic review and meta-analysis evaluated the efficacy of different concentrations of atropine for myopia control, comparing outcomes among East Asian, South Asian, and White European children.

Methods: Five databases were searched for randomised controlled trials (RCTs) including children ≤16 years with myopia who received atropine treatment. Thirty-four RCTs with ≥12 months of follow-up were included. Weighted mean differences (WMD) in spherical equivalent refraction (SER) progression and axial length (AL) elongation were pooled by atropine concentration and ethnicity.

Results: Compared with controls, atropine significantly reduced myopia progression across all concentrations: <0.1% (WMD in SER: 0.44 [95% CI: 0.35, 0.52] D/year; AL: -0.20 [-0.24, -0.16] mm/year), 0.1% to <0.5% (0.81 [0.50, 1.13] D/year), and ≥0.5% (1.06 [0.88, 1.24] D/year; -0.36 [-0.40, -0.33] mm/year). The pooled effect on SER and AL progression across all concentrations were greater in East Asians (0.63 [0.50, 0.76] D/year; -0.26 [-0.31, -0.20] mm/year) than in South-Asians (0.40 [0.11, 0.70] D/year; -0.13 [-0.21, -0.05] mm/year) or White Europeans (0.18 [0.11, 0.25] D/year; -0.11 [-0.16, -0.05] mm/year).

Conclusion: Atropine slows myopia progression in a dose-dependent manner in studies with 1 to 5 years of follow-up. Efficacy appears greater in Asian children, particularly East Asians, who also exhibit greater photopic pupil dilation. These findings support the role of atropine in myopia control and highlight the importance of ethnicity-specific considerations when prescribing and tailoring treatment strategies.

**Keywords:** Myopia progression control, childhood myopia, atropine, RCT, meta-analysis, ethnic difference.

## Key messages

- What is already known on this topic

  Atropine reduces myopia progression in children, but uncertainty remains about the optimal dose and whether treatment efficacy varies among different ethnic populations.

- What this study adds

  This meta-analysis shows that atropine efficacy is dose-dependent, with East Asian children exhibiting greater reductions in myopia progression than South Asian or White European children.

- How this study might affect research, practice or policy

  These findings support personalised myopia control strategies considering ethnicity and dosage and emphasise the need for future studies on long-term safety, optimal dosing schedules, and mechanisms underlying inter-ethnic differences.

## Introduction

Myopia is a public health concern with increasing prevalence in East Asian countries [1 2]. In the past few decades, myopia prevalence also increased in Western countries, such as in the USA and Europe [3]. Now at pandemic levels among children [2] and teenagers [1], myopia carries a risk of severe ocular pathology and visual impairment in high myopes [4]. Thus, early prevention and control are crucial in tackling the myopia pandemic.

Atropine, a nonselective muscarinic acetylcholine receptor antagonist, has been the first line of treatment for myopia for many years [5], with low-dose concentrations (0.01% and 0.05%) commonly used in clinical practice. Previous systematic reviews reported short-term efficacy of atropine with different concentrations, mostly involving Asian populations [6-10]. However, a randomised controlled trial (RCT) conducted by the Pediatric Eye Disease Investigator Group (PEDIG) found 0.01% atropine no better than placebo for slowing myopia progression [11], while the Western Australia – Atropine for the Treatment of Myopia (WA-ATOM), the Myopia Outcome Study of Atropine in Children (MOSAIC) and the Childhood Atropine for Myopia Progression (CHAMP) showed non-significant or only modest control of myopia progression [12-14]. By contrast, The Low-Concentration Atropine for Myopia Progression (LAMP) studies reported superior effect of 0.05% in Asians [15-17]. The lack of benefit in the PEDIG study [11], compared with East Asian studies, may reflect racial differences in atropine response, since Asian children have higher myopia progression [9]. Thus, efficacy in Asian versus non-Asians, the optimal concentration and duration of treatment of myopia progression remains unclear. This systematic review and meta-analysis evaluated atropine's efficacy in the control of progression of myopia in children and compared outcomes between Asian and non-Asian regions.

## Methods

### Data Sources and Literature Searches

This meta-analysis of prospective RCTs followed the PRISMA (Preferred Reporting Items for Systematic Review and Meta-analyses) guidelines [18] and was registered in the International

Prospective Register of Systematic Reviews (PROSPERO: CRD42023454104). We searched PubMed, EMBASE, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials to yield relevant studies from their inception to July 31, 2025, using Medical Subject Headings (MeSH) and free words combined with myopia, refractive errors, and atropine. Additionally, we screened clinicaltrials.gov and the reference lists of published reviews to identify additional relevant studies. Only English-language RCTs were included. Details of search strategy, eligibility criteria, data collection, quality assessment, and bias assessment are in the supplemental file 1.

**Statistical analysis**

We calculated the weighted mean difference (WMD) and 95% confidence intervals (CIs) for different doses of atropine in SER changes and AL elongation vs the control group. Baseline and final SER and AL were summarized for each study and reported as mean ± SD for continuous variables. Statistical analysis was performed using STATA 19.0 (Stata Corporation, TX, USA) and Review Manager 5.4 (RevMan; Cochrane Collaboration). Additional details are provided in supplemental file 1.

**Outcomes**

The primary outcomes of this study were mean annual change in SER (in dioptres/year) and mean annual change in AL (in millimetres/year). Secondary outcomes were proportion of eyes showing overall myopia progression, adverse reactions, and side effects.

## Results

The search identified 4394 articles, of which 34 RCTs involving 7993 children (≤16 years) were included (Figure S1). Ethnic subgroups comprised 5593 East Asian, 1966 European and 337 South Asian participants. The characteristics of all the included studies are listed in Table 1 and supplemental file 1.

Table 1. Characteristics of the included studies.

| Source | Study Design | Country/ Region | Follow-up, months | Atropine dose, % | Age range, year | Baseline Refraction, Mean (SD) in Dioptre | Baseline axial length, mm |
|---|---|---|---|---|---|---|---|
| Chan et al, 2022 | RCT | Hong Kong | 12 | 0.01 | 7-10 | –1.82 (0.93) | 24.13 (0.76) |
| Chia et al, 2023 | RCT | Singapore | 12 | 0.01, 0.005, 0.0025 | 6-11 | –3.50 (1.2) | 24.64 (0.79) |
| Chua et al, 2006 | RCT | Singapore | 24 | 1.0 | 6-12 | –3.48 (1.28) | 24.80 (0.83) |
| Cui et al, 2021 | RCT | China | 24 | 0.01, 0.02 | 6-14 | –2.72 (1.45) | 24.57 (0.69) |
| Fu et al, 2020 | RCT | China | 12 | 0.01, 0.02 | 6-14 | –2.70 (1.49) | 24.57 (0.72) |
| Hansen et al, 2023 | RCT | Denmark | 12 | 0.01 | 6-9 | –2.99 (1.08) | 24.61 (0.84) |
| Hansen et al, 2024 | RCT | Denmark | 24 | 0.01 | 6-12 | –2.99 (1.27) | 24.60 (0.84) |
| Hieda et al, 2021 | RCT | Japan | 24 | 0.01 | 6-12 | –2.94 (1.25) | 24.45 (0.78) |
| Kumaran et al, 2015 | RCT | Singapore | 24 | 1.0 | 6-12 | –3.47 (Range, –6.00 to –1.00) | 24.8 (NR) |
| Lee et al, 2016 | RCT | Taiwan | 12 | 0.125, 0.25 | 6-12 | –1.34 (0.69) | NR |
| Lee et al, 2022 | RCT | Australia | 24 | 0.01 | 6-16 | –3.27 (1.25) | 24.63 (0.74) |
| Liang et al, 2023 | RCT | China | 12 | 0.01 | 6-12 | –2.56 (1.38) | 24.60 (0.89) |
| Loughman et al, 2023 | RCT | Ireland | 24 | 0.01 | 6-16 | –3.27 (1.77) | 24.88 (1.04) |
| Moriche-Carretero et al, 2021 | RCT | Spain | 24 | 0.01 | 5-11 | –2.15 (0.62) | 24.24 (0.79) |
| Moriche-Carretero et al, 2023 | RCT | Spain | 60 | 0.01 | 5-11 | –2.13 (0.62) | 24.32 (0.80) |
| Repka et al, 2023 | RCT | USA | 24 | 0.01 | 5-12 | –2.83 (1.10) | 24.40 (0.80) |
| Saxena et al, 2021 | RCT | India | 12 | 0.01 | 6-14 | –3.54 (1.35) | 24.66 (0.87) |
| Sen et al, 2022 | RCT | India | 24 | 0.01 | 5-15 | –3.96 (1.27) | 24.53 (0.68) |
| Sharma et al, 2023 | RCT | India | 12 | 0.01 | 5-12 | –3.17 (3.04) | 24.24 (1.51) |
| Shih et al, 1999 | RCT | Taiwan | 12 | 0.1 | 6-13 | –4.46 (1.67) | NR |
| Wang et al, 2017 | RCT | China | 12 | 0.5 | 5-10 | –1.25 (0.36) | 23.95 (0.96) |
| Wang et al, 2023 | RCT | China | 24 | 0.01, 0.02 | 6-14 | –2.75 (1.50) | 24.59 (0.70) |
| Wei et al, 2020 | RCT | China | 12 | 0.01 | 6-12 | –2.58 (1.39) | 24.59 (0.87) |
| Xia et al, 2023 | RCT | China | 12 | 0.01 | 6-16 | –2.78 (0.40) | 22.40 (1.56) |
| Xu et al, 2022 | RCT | China | 24 | 0.01 | 8-12 | Range, –6.00 to –1.00 | NR |
| Yam et al, 2019 | RCT | Hong Kong | 12 | 0.01, 0.05, 0.025 | 4-12 | –3.79 (1.84) | 24.77 (0.95) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Yam et al, 2020 | RCT | Hong Kong | 24 | 0.01, 0.05, 0.025 | 4-12 | –3.79 (1.84) | 24.77 (0.95) |
| Yam et al, 2022 | RCT | Hong Kong | 36 | 0.01, 0.05, 0.025 | 4-12 | –3.79 (1.84) | 24.77 (0.95) |
| Yi et al, 2015 | RCT | China | 12 | 1.0 | 7-12 | –1.19 (0.31) | 23.74 (0.12) |
| Zadnik et al, 2023 | RCT | North America & Europe | 36 | 0.01, 0.02 | 6-10 | –2.42 (1.16) | 24.32 (0.85) |
| Zhang et al, 2023 | RCT | China | 24 | 0.05 | 6-12 | –2.68 (1.14) | 24.56 (1.70) |
| Zhang et al 2024 | RCT | Hong Kong | 60 | 0.05 | 4-12 | –3.79 (1.84) | 24.77 (0.95) |
| Zhao et al, 2021 | RCT | China | 12 | 0.01 | 5-14 | –1.96 (0.61) | 24.23 (0.75) |
| Zhu et al, 2023 | RCT | China | 24 | 0.05 | 7-12 | –3.26 (0.27) | 23.70 (0.21) |
| RCT: randomised clinical trial; NR: Not reported; mm: millimetre; y: year. | | | | | | | |

**Spherical equivalent refraction**

Twenty-seven studies reported data on <0.1% atropine, 2 studies on 0.1% to <0.5% atropine and 4 studies on ≥0.5% atropine. The pooled data showed significantly less progression in SER for <0.1% (WMD, 0.44 D per year; 95% CI, 0.35-0.52 D per year; p<0.001), 0.1% to <0.5% (WMD, 0.81 D per year; 95% CI, 0.50-1.13 D per year; p<0.001), and ≥0.5% (WMD, 1.06 D per year; 95% CI, 0.88-1.24 D per year; p<0.001) atropine groups than controls after therapy (Subgroup difference, p<0.001; Figure 1). The ES pooling revealed a moderate to strong treatment effect for SER in <0.1% (ES, 0.70; 95% CI, 0.56-0.85; p<0.001), 0.1% to <0.5% (ES, 1.18; 95% CI, 0.58-1.78; p<0.001), and ≥0.5% (ES, 1.71; 95% CI, 0.70-2.72; p<0.001) atropine groups. We observed a significant correlation between dose and treatment effect for SER (r=0.318; p=0.031).

**Axial elongation**

Twenty-eight studies reported changes in AL between <0.1% atropine, no studies on 0.1% to <0.5% atropine, and 3 studies on ≥0.5% atropine and control groups. AL elongation was reduced for <0.1% (WMD, -0.20 mm per year; 95% CI, -0.24 to -0.16 mm per year; p<0.001), and ≥0.5% (WMD, -0.36 mm per year; 95% CI, -0.40 to -0.33 mm per year; p<0.001) atropine groups than control groups (Subgroup difference, p<0.001; Figure 2). ES pooling for AL had a medium to large treatment effect for <0.1% (ES, -0.65; 95% CI, -0.78 to -0.53; p<0.001), and

≥0.5% (ES, -1.43; 95% CI, -2.58 to -0.28; p=0.01) atropine groups than the controls. There was no significant correlation between dose and treatment effect for AL (r = -0.275; p=0.068).

**Ethnic Variation**

The pooled mean difference in SER of all concentrations of atropine versus placebo was 0.63 D per year (95% CI, 0.50 to 0.76, p<0.001) for East Asians, 0.40 D per year (95% CI, 0.11 to 0.70, p=0.008) for South Asians, and 0.18 D per year (95% CI, 0.11 to 0.25, p<0.001) for White Europeans (Subgroup difference, p<0.001; Figure S2). For AL, the pooled mean difference of all concentrations of atropine versus placebo was -0.26 mm per year (95% CI, -0.31 to -0.20, p<0.001) for East Asians, -0.13 mm per year (95% CI, -0.21 to -0.05, p=0.002) for South Asians, and -0.11 mm per year (95% CI, -0.16 to -0.05, p<0.001) for White Europeans (Subgroup difference, p<0.001; Figure S3).

The mean SER difference for <0.1% atropine was 0.54 D per year (95% CI, 0.42 to 0.66, p<0.001) in East Asians (n=16 studies), whereas it was 0.40 (95% CI, 0.11 to 0.70, p<0.001) for South-Asians (n=3), and 0.18 (95% CI, 0.11 to 0.25, p<0.001) for White Europeans (n= 8) (Subgroup difference, p<0.001; Figure 3). For 0.1% to <0.5% atropine, the mean difference in SER was 0.81 D per year (95% CI, 0.50 to 1.135, p<0.001) for East Asians (n=2). For higher doses ≥0.5%, the mean difference was 1.06 D (95% CI, 0.88 to 1.24, p<0.001) for East Asians (n=4). There were no South Asian or White European studies using moderate- and high-dose atropine.

Mean AL change for <0.1% dose atropine was -0.24 mm per year (95% CI, -0.30 to -0.19, p<0.001) for East Asians (n=17 studies), -0.13 mm per year (95% CI, -0.21 to -0.05, p=0.002) for South Asians (n=3), and -0.11 mm per year (95% CI, -0.16 to -0.05, p<0.001) for white Europeans (n=8) (Subgroup difference, p=0.001; Figure 4). No studies reported AL change with moderate-dose atropine. For atropine doses ≥0.5%, the mean difference was -0.36 mm (95% CI, -0.40 to -0.33, p<0.001) in East Asians (n=3), with no available data on South Asians or white Europeans.

ES pooling for SER in East Asian children indicated a large treatment effect for <0.1% atropine (ES, 0.80; 95% CI, 0.64 to 0.96; p<0.001), 0.1% to <0.5% (ES, 1.18; 95% CI, 0.58 to 1.78;

p<0.001) and ≥0.5% atropine (ES, 1.71; 95% CI, 0.70 to 2.72; p<0.001). Among white Europeans, the effect was small for <0.1% atropine (ES, 0.34; 95% CI, 0.17 to 0.51; p<0.001). South Asian studies (n=3) were focussed only on <0.1% dose with an observed large treatment effect (ES, 0.97; 95% CI, -0.08 to 2.02, p=0.07). For AL, East Asians showed moderate treatment effect for <0.1% atropine (ES, -0.74; 95% CI, -0.90 to -0.59; p<0.001), and ≥0.5% (ES, -1.43; 95% CI, -2.58 to -0.28; p=0.01) atropine showed large treatment effects. White Europeans demonstrated a small treatment effect for <0.1% atropine (ES, -0.38; 95% CI, -0.56 to -0.20; p<0.001) and 0.1% to <0.5% (ES, -0.30; 95% CI, -0.51 to -0.08; p=0.006) atropine. South Asian studies (n=3) were focussed only on <0.1% with an observed moderate treatment effect (ES, -0.70; 95% CI, -1.50 to 0.11, p=0.09).

**Ethnic variation in Asian populations outside Asia**

Inclusion of East and South Asian data from non-Asian regions in Asian data maintained the relationship between SER and AL observed in Asian populations. The changes in SER for low-dose atropine were 0.48 (95% CI, 0.36 to 0.61, p<0.001) for East Asians, 0.32 (95% CI 0.04 to 0.60, p=0.02) for South Asians and 0.20 (95% CI, 0.15 to 0.25, p<0.001) for white Europeans (Subgroup difference, p<0.001).

Similarly, the changes in AL for low-dose atropine were -0.24 mm per year (95% CI, -0.29 to -0.18, p<0.001) for East Asians, -0.09 mm per year (95% CI, -0.19 to 0.00, p=0.06) for South Asian and -0.13 mm per year (95% CI, -0.17 to -0.09, p<0.001) for White Europeans (Subgroup difference, p=0.003).

Results on pupil size, heterogeneity test, sensitivity analysis, publication bias, proportion of eyes showing myopia progression, and adverse events are provided in supplementary file 2.

## Discussion

Our meta-analysis shows that atropine at all concentrations slows myopia progression in children over 1 to 5 years of follow-up. Higher doses yield greater efficacy, with reductions in SER and AL progression showing a dose-dependent relationship. While several meta-analyses corroborated a dose-dependent effect on SER progression [6 7 19 20], others did

not [10 21 22]. Our findings support greater efficacy of higher concentrations in mitigating refractive changes and axial elongation in children.

We found a difference in treatment effect of atropine among ethnic groups. Atropine slowed myopia progression more in East Asians (SER: 0.63 D, AL: -0.26 mm) than their South-Asian (0.40 D, -0.13 mm) and White European counterparts (0.18 D, -0.11 mm) across all three concentrations. A previous meta-analysis reported stronger atropine effects in Asian (0.55 D per year) than White children (0.35 D per year) [9], suggesting ethnicity influences treatment efficacy, potentially due to faster baseline myopia progression in Asian children. One study showed mean axial elongation was 38% greater in Asian than non-Asian children, though both decline 15% per year with age [23]. Similarly, previous research has shown faster myopia progression and axial elongation in East Asian than European children [24], particularly in younger East Asian children that are twice as fast [24].

For atropine <0.1%, East Asian children showed the greatest effect on SER (0.54 D) and AL (−0.24 mm), compared with South Asians (0.40 D; −0.13 mm) and White Europeans (0.18 D; −0.11 mm), with significant subgroup differences. For 0.1% to <0.5% and ≥0.5% atropine we found large treatment effects in East Asians only, whereas no comparable data were available for South Asian or White European populations. Effect size estimates showed consistently large effects observed in East Asians, small effects in White Europeans, and moderate effects in South Asians based on limited studies. Ethnic variation in myopia progression and treatment response is influenced by a complex interplay of genetic and environmental factors. Our subgroup analysis suggests that although lifestyle and environment contribute substantially, East and South Asian children living outside Asia continue to show treatment responses and progression patterns more similar to those of Asian populations than to White Europeans, highlighting the contribution of genetic predisposition alongside environmental exposure.

In our study, adverse events were more frequent in East Asians, lower in White Europeans, and absent in South-Asians, with no clear dose-response relationship. This suggests tolerability may depend on factors beyond dose, such as compliance, demographics, or formulation differences. Previous research found similar levels of adverse events across

ethnicities [10 25], whereas our findings showed higher adverse events in Asians, possibly linked to higher treatment efficacy in this group. Notably, all non-Asian studies reported side effects versus 85% of Asian studies. Differences may also reflect differences in age ranges (East Asians 4–16, South Asians 5–15, White Europeans 5–16) (see table 1) and darker iris colour among Asians.

In low-dose atropine trials, East Asian children showed greater changes in both mesopic (0.35 mm) and photopic (0.61 mm) pupil size compared with White Europeans (0.15 mm and 0.23 mm, respectively) and South Asians (0.17 mm and 0.08 mm, respectively). While subgroup differences were not significant for mesopic pupil size ($p=0.30$), they were significant for photopic pupil size ($p<0.001$). Importantly, only one RCT provided pupil data for South Asians, and no studies reported changes with moderate- or high-dose atropine. These differences may relate to darker iris pigmentation and genetic factors. Other studies reported mixed findings, with MOSAIC study showing stronger effects in lighter colour eyes (e.g., blue) but not in brown eyes [13]. A German study found no effect of iris colour on myopia progression [26] and the WA-ATOM study reported no interaction between treatment, ancestry or eye colour on pupillary measures [27]. Pupil diameter may influence myopia control efficacy [28 29]. One possible theory is that a larger pupil size in untreated children is responsible for an increase in peripheral defocus increasing myopia progression. However, evidence is mixed, with some studies reporting no link [30 31], while others found reduced pupil sizes in pre-schoolers with untreated myopia compared with emmetropes [32]. Another theory is that reduced pupil diameters receive less effective light exposure outdoor, a known mechanism to prevent myopia. These mechanisms remain unclear warranting further research across ethnic groups. Smaller pupil size changes in White European children may also reflect compliance differences. Pupil size outcomes in this meta-analysis were derived exclusively from low-dose atropine studies, limiting our ability to examine the dose–response relationship with higher concentrations. While both mesopic and photopic measurements indicated consistent changes across East Asian, South Asian, and European cohorts, the absence of higher-dose

data from European and US trials restricts conclusions about potential ethnic or regional differences in pupil response at medium or high concentrations.

Most studies had short follow-ups of 1 to 3 years, with only two extending to 5 years (See table 1). The Atropine Treatment Long-term Assessment Study (ATLAS) found that 2 to 4 years of topical atropine (0.01% to 1.0%) use did not change final SE significantly after 10-20 years compared to controls [33], highlight the need for research on optimal dosage and duration of treatment to prevent rebound and ensure sustained myopia control. The five-year LAMP study showed high retreatment rates, with 87.9% of children in the cessation group requiring retreatment after year 3 [34]. Retreatment with 0.05% achieved similar efficacy as continuous treatment, supporting its long-term application and retreatment if progression resumes. Although, the trial underscores the value of prolonged treatment in younger children, further studies are needed to understand the most appropriate age of cessation. While short-term outcomes of atropine are well-documented, long-term data on sustained efficacy and rebound remain limited.

Rebound occurs when myopic progression increases after treatment cessation compared to controls. A previous meta-analysis covering several treatments for myopia progression found that rebound varied by modality with high concentrations of atropine and red-light therapy showing significant rebound [35]. Further studies on the rebound phenomenon after cessation of atropine and differences between Asians and non-Asians are necessary.

There are several limitations of this study. We found high heterogeneity in SER analysis, except for SER in moderate dose ($I^2$ = 36%) and White European ($I^2$ = 48%) and AL in high dose ($I^2$ = 0%). Previous systematic reviews reported similarly high values of heterogeneity [6 8 9 55]. Those results may arise from variability in study design and population demographics. Interestingly, while SER outcomes exhibit high heterogeneity, AL changes were more consistent, particularly for studies involving high dosages of atropine. High heterogeneity could stem from differences in study design, patient population, or measurement techniques, indicating that the overall effect is not uniform across studies. This may suggest that AL is a more reliable and objective measure for evaluating the efficacy of atropine. However, we did

not find replicable results regarding heterogeneity across the broader spectrum of atropine doses. The data from non-Asians showed lower heterogeneity compared to Asians, difference that could stem from genetic and environmental factors influencing treatment response. In addition, the predominance of Asian-based studies may skew the results, limiting the applicability of findings to non-Asians. For the missing placebo group, we used projected values based on a prediction model [34], approach that relies on assumptions and can over- or under-estimate treatment effects, as it does not fully capture real-world variability in myopia progression. Historical information if sufficiently similar to the current control data, increases power and reduces type I error [36]. The absence of placebo groups in many recent myopia RCTs reflects ethical concerns around withholding treatment from myopic children, given the long-term risks associated with myopia progression. This shift poses challenges in meta-analyses, as the lack of untreated controls necessitates reliance on projected or historical data, which may introduce bias and variability.

## Conclusions

The results from this meta-analysis of RCTs confirmed that atropine, at all doses effectively reduces the progression of myopia (measured by both SER and AL) in a dose-dependent manner in children aged 4 to 16 years. Additionally, East Asian children showed greater reduction in both SER and AL compared to South-Asian and White European children. East Asian children also experienced greater dilation of the pupils in photopic lighting conditions compared to White European counterparts. Our findings emphasize atropine's potential as a viable intervention to control myopia progression. Further studies should explore long-term effects and specific mechanisms behind ethnic differences in treatment response. Investigating duration of the treatment, concentration, tapering, rebound in a wider range of racial backgrounds and ethnicities is important to help to uncover efficacy of atropine in different populations.

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## Figure Legends

Figure 1: Forest plot of mean differences in SER change between different doses of atropine and control groups.

Figure 2: Forest plot of mean differences in AL change between different doses of atropine and control groups.

Figure 3: Forest plot of mean differences in SER change between <0.1% atropine and control groups, stratified by ethnicity.

Figure 4: Forest plot of mean differences in AL change between <0.1% atropine and control groups, stratified by ethnicity.

## Ethics Statement

As this study is a systematic review and meta-analysis of previously published data, no new patient data were collected, and therefore ethical approval and patient consent were not required.

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**Data availability statement**

All data relevant to the study are included in the article or uploaded as supplementary information. All the data included in our study are from published studies.