REVIEW Effects of Insufficient Sleep on Myopia in Children: A Systematic Review and Meta-Analysis

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Abstract: Myopia is increasingly prevalent in children. Its association with insufficient sleep has been studied, yielding inconsistent findings. This review aims to assess the association of insufficient sleep with myopia and myopia-related refractive parameters in children. A total of 657 articles were identified, of which 40 were included in the systematic review and 33 were included in the metaanalysis. Results showed that insufficient sleep was significantly associated with an increased prevalence of myopia (odds ratio [OR] = 1.59; 95% confidence interval [CI] = 1.31, 1.95; I^2 = 99%), and an increased prevalence of high myopia (OR = 3.36; 95% CI = 1.26, 9.00; $l^2 = 96\%$). Shorter sleep duration was significantly linked to faster changes in axial length (AL) ($\beta = 0.05$; 95% CI = 0.02, 0.08; $I^2 = 0\%$). However, correlation between insufficient sleep and the incidence of myopia, spherical equivalent refraction, corneal curvature radius (CR) and AL/CR were insignificant. Moreover, the effect of insufficient sleep on premyopia and astigmatism was not well-studied. The results of this study suggest that insufficient sleep may be an important risk factor for the development of myopia in school-aged children. Therefore, in addition to ensuring sufficient outdoor activities and reducing near work, it is necessary to inform children and parents about the importance of adequate sleep to mitigate the risk of myopia. Keywords: insufficient sleep, myopia, children, axial length, refractive parameters

Introduction

Myopia has become a significant global public health concern,¹ and nearly 50% of the world's population would be myopic by 2050.² This alarming trend is especially relevant for children, a crucial life stage marked by rapid physical and cognitive growth, making it a pivotal period for myopia onset.^{3,4} The associated ocular complications, including retinal detachment, myopic maculopathy, and glaucoma, pose far-reaching consequences for future visual acuity.⁵ Identifying modifiable risk factors is crucial to prevent and manage myopia, ensuring ocular well-being for future generations.

Established risk factors for myopia include high education levels and prolonged near work, while protective factors involve extended outdoor activities.⁶⁻⁹ The association between sleep quality and myopia risk has also been demonstrated by some studies.^{10,11} However, the role of insufficient sleep as a potential risk factor remains inconclusive. Some studies suggest a correlation between short sleep duration and increased myopia risk, ^{12,13} while others fail to establish a clear connection.^{14–18} Experimental studies have revealed the circadian rhythm disruption induced by insufficient sleep and its potential role in childhood myopia.^{19,20} Moreover, some studies suggest that the occurrence and progression of myopia may be influenced by seasonal changes, with a faster progression in winter compared to summer.^{21,22} In addition to the effects of light exposure during different seasons, seasonal variations also affect sleep duration and patterns.²³ For instance, sleep time is significantly shorter in summer than in winter,²¹ indicating a potential association between sleep and myopia.

In previously published reviews, one study has scrutinized the implications of sleep duration and quality on the occurrence of childhood myopia.²⁴ Two studies have systematically examined the association between sleep duration and myopia, with varying conclusions.^{25,26} Previous relevant meta-studies included limited articles and did not yield significant results.^{27,28} Contrasting findings underscore the complex nature of the sleep-myopia relationship, necessitating further research.

As myopia develops and progresses, key refractive parameters undergo notable changes, including spherical equivalent refraction (SER), axial length (AL), radius of corneal curvature (CR), and AL/CR ratio.²⁹ Beyond assessing myopia risk, a comprehensive analysis of these parameters could offer profound insights into the relationship between insufficient sleep and myopia. This systematic review and meta-analysis focused on myopia and myopia-related factors in children, aiming to uncover modifiable risk factors for myopia prevention and management. The findings of this study will not only provide important evidence for understanding the relationship between insufficient sleep and myopia in children, but also have significant implications for clinical practice and policy-making. In clinical practice, healthcare providers should consider children's sleep patterns when treating myopia and offer parents and children important advice on healthy sleep habits. Additionally, the results can serve as a scientific basis for public health policymakers, promoting community and school-based health education and intervention programs to ensure adequate sleep, thereby helping to mitigate the rising prevalence of myopia.

Methods

In this systematic review and meta-analysis, we strictly followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (<u>Supplementary Table S1</u>),³⁰ and registered our study in the International Prospective Register of Systematic Reviews (PROSPERO registration number CRD42023439584).

Search Strategy

On October 7, 2023, we conducted a thorough search across five databases, namely PUBMED, Embase, Cochrane Library, Web of Science, and Medline. Our search strategy combined Medical Subject Headings (MeSH) terms, keywords, and text. The full search terms employed are included in <u>Supplementary Table S2</u>. We also manually screened the references of included articles for a comprehensive search. Our search encompassed articles from the database inception to the date of our search, with no language restrictions.

Eligibility Criteria

Two reviewers, X.Z and Y.M, independently screened titles and abstracts. Exclusion criteria covered reviews, case reports, conference papers, and studies lacking myopia-related outcomes or primarily addressing sleep disorders other than insufficient sleep. Duplicate articles were removed, with preference given to those with the largest sample size in cases of multiple publications using the same dataset.

Full-text articles and <u>Supplementary Materials</u> underwent thorough examination. Inclusion criteria were as follows: (1) the study population included individuals aged 18 or younger, with limited allowances for subjects aged 18–19; (2) risk factor analyses incorporated sleep duration, categorized as a specific time period or continuous variable, rather than relying on subjective judgments of sufficiency; and (3) myopia was defined using subjective refraction or auto-refraction, or denoted by the use of corrective spectacles or a prior confirmed diagnosis. For studies that rely on questionnaires to assess myopia in children, those that only asked whether the child had myopia without further details were excluded. However, if the questionnaire also inquired about specifics such as the degree of myopia or whether the child wore corrective lenses, those studies were included in the analysis. The characteristics of all included studies were tabulated and described in the systematic review. Studies lacking necessary data, such as odds ratios (OR), coefficients, or standard errors, were excluded from the meta-analysis. In cases of inclusion conflicts, consensus was reached through negotiation.

Data Extraction

Data extraction was carried out by two researchers, X.Z and Y.M. Extracted variables included study design, sample size, age, region, gender, myopia prevalence, methods for myopia measurement, refractive parameter assessment, sleep duration reporting, insufficient sleep definition and reference group criteria, covariates adjusted for multivariable analysis, odds ratios (OR), relative risks (RR), beta coefficients (β), and their associated 95% confidence intervals or standard errors. Additionally, information on study quality assessment was recorded.

Definition of Insufficient Sleep

We adhered to the American Academy of Sleep Medicine (AASM) guidelines for defining insufficient sleep, which stipulate less than 10 hours for 3 to 5-year-olds, less than 9 hours for 6 to 12-year-olds, and less than 8 hours for 13 to 17-year-olds,³¹ In cases where the original article presented sleep duration in multiple categories, we standardized them in accordance with AASM recommendations. When it was not feasible to merge categories as AASM guidelines, we designated the group with the shortest sleep duration as experiencing insufficient sleep, and the same approach was applied when extracting data from multivariate regression analyses.

Risk of Bias Assessment

Two researchers (X.Z and Y.M) independently evaluated methodological quality using the Downs & Black checklist,³² comprising 27 items (15 for longitudinal studies and 12 for cross-sectional studies). A 'yes' response scored 1 point, and "no" or "unclear" responses scored 0. Item 14 for intervention studies was excluded, and three follow-up questions (9, 17, 26) were omitted in cross-sectional study assessments. Percentages (items scored 'yes'/total items) were then calculated for each study. Quality classifications were high ($\geq 66.8\%$), moderate (33.4–66.7%), or low ($\leq 33.3\%$). Discrepancies were resolved through discussion, with a final decision made by a third reviewer, H.Z, when necessary.

Statistical Analysis

In our data analysis, for studies treating sleep duration as a continuous variable, we extracted outcomes and conducted separate pooling. Data meeting AASM criteria for insufficient sleep took precedence, followed by the latter in both unifactorial and multifactorial models. In multivariate models, we selected the one with the most adjusted covariates. When a study reported separate results for weekdays and weekends,³³ we chose the former for consistency due to potential variability in weekend sleep.³⁴ Additionally, for studies using insufficient sleep as the reference, we restructured the reference group to represent sufficient sleep following Hamling et al's statistical methodology.³⁵

Heterogeneity between studies was quantified using I^2 . The analysis methods were conducted in accordance with previously published meta-analyses, ensuring consistency with established practices in the field.^{36,37} A fixed-effects model was used if I^2 was <50%, indicating nonsignificant heterogeneity, and a random-effects model if I^2 exceeded 50%, signifying substantial heterogeneity. Potential publication bias was assessed via Egger's test (p < 0.05).

Leave-one-out sensitivity analyses assessed pooled estimate robustness. Meta-regression and subgroup analyses explored factors, including myopia definition (criterion: SER ≤ -0.50 D with cycloplegia, otherwise); sleep duration definition (specifying night sleep or total sleep hours, or unspecified); insufficient sleep criteria (conforming to AASM recommendations or not); study design (categorized as cross-sectional or longitudinal); region (differentiating between developed and developing countries); and covariate adjustment extent (models adjusted for outdoor time and hours of near work considered high quality). Gender was a continuous variable (male%) in meta-regression and a categorical variable (male <50%, >50%) in subgroup analyses. Sample size and myopia prevalence were included in the meta-regression. For conducting meta-regression 6.1 and ensured that at least 10 studies were included to provide reliable and robust results. For subgroup analyses, we aimed to include a minimum of 4 studies in each subgroup to ensure sufficient statistical power and meaningful interpretation of the results. Sensitivity analyses, meta-regression and sub-group analyses were conducted for the association between insufficient sleep as categorical variable and the prevalence of myopia. Review Manager 5.4.1 and Stata 16.0 were used for analyses.

Results

Study Selection

In our search, we initially found 657 manuscripts. After removing 331 duplicates and screening based on title and abstract (n=248), 78 articles underwent a full-text review. Ultimately, 40 papers, meeting eligibility criteria, were included in this systematic review, with 33 undergoing meta-analysis. Figure 1 visually outlines this stringent selection process.



Figure I Flow chart of the articles identified for the systematic review and meta-analysis.

Study and Participant Characteristics

The characteristics of the 40 studies in the systematic review are summarized in Table 1 and 2, with additional details in <u>Supplementary Table S3</u> and <u>S4</u>. Primary outcomes included myopia prevalence (n = 32), $^{12-15,33,38-55}$ myopia incidence (n = 4), 15,17,45,55 high myopia (n = 3), 12,47,53 premyopia $(n = 1)^{56}$ and refractive parameters (n = 8). $^{16-18,40,57-59}$ Studies were conducted in China (n = 36), Singapore (n = 2), France (n = 1) and Korea (n = 1). Of the studies, 33 were cross-sectional, and seven were longitudinal. Three studies involved participants under six years, while the remaining 37 focused on school-aged children aged 6 to 18 years.

Methodological Quality

Methodological quality assessment details are in <u>Supplementary Table S5</u>. Scores ranged from $44\%^{68}$ to 100%,¹⁵ averaging 81%. Sleep duration was mostly self-reported or parent-reported, defined as nighttime sleep in seven studies, nighttime sleep with naps in two, and unspecified in 31. Six studies analyzed sleep duration as a continuous variable, others used categorical variables. The definition of insufficient sleep varied, with 18 studies followed AASM recommendations. Myopia was mostly defined as SER \leq -0.50 D with cycloplegia (16 studies), using tropicamide (10) or

First	Region	n Study	Age	Sample size(n)	Prevalence of myopia	Sex (Male %)	Myopia Definition (Measure)	Sleep	Sleep Duration		Quality
author, year		Design	(Years)					Duration measurement	Insufficient	Ref	
Gong, 2014 ¹³	China	CS	6–18	15,316	53.40%	48.5	SER ≤−0.75 D (auto-refraction, without cycloplegia)	Self-reported	≤7h	≥9h	High
Zhou, 2015 ⁶⁰	China	CS	9.80±0.44	1902	30.91%	53.1	SER ≤−0.50 D (auto-refraction, 1% cyclopentolate)	Parent- reported	7–8h	≥9h	High
Guo, 2016 ⁶¹	China	CS	6–18	59,198	63.52%	52.3	Visual acuity < 20/20 ^a and subjective Parent- refraction reported		Continuous variable		Medium
Jee, 2016 ¹²	Korea	CS	12–19	3625	79.86%	52.9	SER ≤−0.50 D (auto-refraction, without cycloplegia)	Self-reported	<8h	≥8h	High
Xu, 2016 ⁴⁸	China	CS	8–18	8030	72.99%	49.9	Visual acuity < 20/20 ^a and subjective refraction	Self-reported	<7h	≥8h	High
Zhou, 2016 ⁵²	China	CS	6–18	57,904	55.70%	51.3	Visual acuity < 20/20 ^a and subjective refraction	Self/parent	<9h	≥9h	High
Qi, 2019 ⁴⁵	China	LS	14–16	522	27.01%	100.0	SER ≤−0.50 D (auto-refraction, 0.5% tropicamide)	Self-reported	≤7h	>7h	Medium
Cao, 2020 ³⁸	China	CS	6–15	6164	42.05%	50.3	Visual acuity < 20/20 ^a and SER (auto- refraction, without cycloplegia)	Self-reported	≤8h	>8h	Medium
Liu, 2020 ¹⁵	China	LS	7.2±0.7	5305	22.19%	53.2	SER ≤−0.50 D (auto-refraction, 0.5% tropicamide)	Parent- reported	<9.5h	≥9.5h	High
Wei, 2020 ¹⁷	China	LS	5.76–9.27	1887	27.72%	51.9	SER ≤−0.50 D (auto-refraction, 1% cyclopentolate)	Parent- reported	≤9.56h	>9.56h	High
Xu, 2020 ⁵⁴	China	CS	10–15	102,883	64.72%	0.0	Visual acuity < 20/20 ^a and subjective refraction	Self-reported	<7h	≥9h	High
Zhang, 2020 ⁶²	China	CS	6–9	2623	19.56%	53.2	SER ≤−0.50 D (auto-refraction, tropicamide)	Parent- reported	Continuous variable		High
Alexis, 2021 ⁵⁵	France	LS	2–5	1130	20.35%	52.6	Questionnaire of eye glasses prescription made by vision specialist doctor	Parent- reported	<10.5h	10.5-11h	High

(Continued)

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First	Region	Study	Age	Sample	Prevalence	Sex	Myopia Definition (Measure)	Sleep	Sleep Duration		Quality
author, year		Design	(Years)	size(n)	of myopia	(Male %)		Duration measurement	Insufficient	Ref	
Lai, 2021 ¹⁴	China	LS	6–18	4825	58.03%	54.8	Visual acuity < 20/20 ^a and SER ≤-0.50 D, auto-refraction, without cycloplegia Self-report		Based on grade level ^b		High
Lu, 2021 ⁴²	China	CS	9–12	556	63.67%	55.2	Visual acuity < 20/20 ^a and SER ≤−0.50 D, auto-refraction, without cycloplegia	Self-reported	≤8h	>8h	High
Zhang, 2021 ⁶³	China	CS	6–17	3072	55.50%	53.5	SER ≤−0.50 D (auto-refraction, 0.5% tropicamide)	Self-reported	Continuous variable		High
Chen, 2022 ³⁹	China	CS	<18	7948	59.55%	51.9	Visual acuity < 20/20 ^a and SER ≤−0.50 D (auto-refraction, tropicamide)	Self-reported	<7h	7–9h	High
Li, 2022 ³³	Singapore	CS	8–9	572	37.24%	49.9	SER ≤−0.50 D (auto-refraction, 1% Paren cyclopentolate) report		Continuous variable		High
Li, 2022 ⁶⁴	China	CS	7–12	10,700	21.20%	53.2	Questionnaire on whether their children have myopia and specific refractive values	Parent- reported	<9h	≥9h	High
Ma, 2022 ⁶⁵	China	CS	6–12	913	16.60%	50.1	SER ≤−0.5 D (auto-refraction, without cycloplegia)	Self-reported	Continuous variable	Medium	
Peng, 2022 ⁴⁴	China	CS	<18	6154	65.57%	53.4	Visual acuity < 20/20 ^a and SER <-0.50		<6h	>8h	High
Tian, 2022 ⁴⁶	China	CS	6–18	1622	61.34%	47.9	Visual acuity < 20/20 ^a and SER <-0.50 D (auto-refraction, without cycloplegia)	Self-reported	Based on grade level ^b		High
Wang, 2022 ⁵⁶	China	CS	5–6	23,930	10.70%	52.1	SER ≤−0.5 D (auto-refraction, 0.5% tropicamide)	Parent- reported	<9h	≥9h	High
Wang, 2022 ⁴⁷	China	CS	8–12	24,318	27.79%	51.2	Visual acuity < 20/20 ^a and SER ≤−0.50 D (auto-refraction, without cycloplegia)	Parent- reported	≤7h	>9h	High
Zhuang, 2022 ⁵³	China	CS	12.38±1.78	35,614	68.00%	51.9	SER ≤−0.50 D (auto-refraction, without cycloplegia)	Self-reported	<8h	≥8h	High
Huang, 2023 ⁴⁰	China	CS	6–18	1140	84.74%	48.4	SER ≤−0.50 D (auto-refraction, 0.5% tropicamide)	Self/parent	<8h	≥8h	High

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Lin, 2023 ⁴¹	China	CS	13.6±2.6	9530	73.78%	51.1	SER ≤−0.50 D (auto-refraction, without cycloplegia)	Self-reported	<8h	≥l0h	High
Mu, 2023 ⁴³	China	CS	7–9	7597	51.90%	44.6	44.6Visual acuity < 20/20 a and SER <-0.50Parent-<8hD (auto-refraction, without cycloplegia)reported		≥8h	High	
Shi, 2023 ⁶⁶	China	CS	7–18	876	37.56%	51.9	SER ≤−0.50 D (auto-refraction, 1% cyclopentolate)	Self-reported	Continuous variable		High
Xu, 2023 ⁴⁹	China	CS	11–18	30,188	49.80%	56.0	Questionnaire on type of glasses and the age at which they first started wearing them	Self/parent	<8h	≥8h	High
Zhang, 2023 ⁵⁰	China	CS	Median age 11.9	19,882	72.61%	51	Visual acuity < 20/20 ^a and SER <-0.50 D (auto-refraction, without cycloplegia)	Self-reported	<8h	≥8h	High
Zhao, 2023 ⁵¹	China	CS	5–13	1423	32.47%	37.1	Questionnaire on children's latest vision Parent- test results conducted by optometrists reported		<9h	≥9h	High

Notes: ^aSnellen visual acuity. ^bPrimary school students > 10h, middle school > 9h and high school > 8h as normal. Abbreviations: CS, cross-sectional; LS, longitudinal; SER, equivalent spherical refraction.

First author,	Region	Study	Age	Sample	Sex	Outcomes and Measurements	Sleep Duration	Sleep Duration (h)		Quality
Year		Design	(years)	Size(n)	(Male %)		Measurement	Insufficient	Ref	
Hua,2015 ⁵⁸	China	LS	6–14	317	47.9	SER: auto-refraction, 0.5% tropicamide AL: IOL Master	Both	Continuous variable		Medium
Sensaki,2018 ¹⁶	Singapore	LS	I–3	1236	50.3	SER: auto-refraction, 1% cyclopentolate AL: IOL Master	Parent-reported	Continuous variable		Medium
Wang, 2020 ⁶⁷	China	CS	66.8 ± 3.4 months	1327	53.2	Astigmatism was defined as a cylinder magnitude ≤1.0 D (auto-refraction, low- coherent reflectometer)	r Parent-reported Continuous variable ow-		s variable	High
Wei,2020 ¹⁷	China	LS	7.09 ± 0.41	1887	51.9	SER: auto-refraction, 1% cyclopentolate AL: Lenstar LS900	Parent-reported	Continuous variable		High
Zhao,2020 ⁵⁹	China	CS	6–12	1091	46.9	SER: auto-refraction, 0.5% tropicamide AL, AL/CR, K, CR: IOL Master	Parent-reported	Continuous variable		High
Cui,2021 ⁵⁷	China	CS	9.8± 2.5	566	53.4	SER: auto-refraction, 0.5% tropicamide AL, AL/CR, CR, VCD: Lenstar LS900	Both	≤7h	>9h	Medium
Cai, 2022 ⁶⁸	China	CS	9.60 ± 2.30	115	57.4	AL: IOL Master Self-reported Continuous variat		s variable	Medium	
Li, 2022 ¹⁸	Singapore	CS	8–9	572	49.5	SER: auto-refraction, 1% cyclopentolate AL: IOL Master	Parent-reported	Continuous variable		High
Huang, 2023 ⁴⁰	China	CS	6–18	1140	48.4	SER: auto-refraction, 0.5% tropicamide AL: AL-scan	Both	<8h	>9h	High

 Table 2 Characteristics of Studies Included in the Systematic Review of Insufficient Sleep and Refractive Parameters

Abbreviations: CS, cross-sectional; LS, longitudinal; SER, equivalent spherical refraction; AL, axial length; CR, radius of corneal curvature; K, corneal curvature; VCD, vitreous chamber depth.

cyclopentolate (6). Another 24 used different definitions, three relying on spectacle wear or prior diagnosis.^{33,51,55} Among the 24 articles with multifactorial analyses, eight used unifactorial results for the meta-analysis to align with insufficient sleep definition. The remaining sixteen used multifactorial results, with twelve adjusting for time outdoors and near work.

Insufficient Sleep and Myopia

Insufficient Sleep and Prevalence of Myopia

Results (Figure 2) from the meta-analysis of 27 studies, excluding participants with less than five hours of sleep to mitigate measurement errors,¹² indicated a significant increase in myopia prevalence with insufficient sleep (OR = 1.59; 95% CI = 1.31, 1.95; $I^2 = 99\%$; p < 0.001). No apparent publication bias was observed via funnel plot (Figure S1) and Egger's test (p = 0.219).

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Alovio 2021		0.5000	1.00		
Coo 2020	-0.1025	0.5000	2.0%		oj 21
Ca0,2020	0.4574	0.1200	3.970		J] ▲1
Cnen,2022	-0.1505	0.0430	4.170	0.00 [0.76, 0.9	4) 0) +
Gung,2014	0.6724	0.0470	9.170	3.37 [3.07, 3.7	
	0.0734	0.2100	3.0%	1.90 [1.20, 3.0	1) 2)
Jee,2010	0.4797	0.0074	4.0%	1.02 [1.30, 1.9	2) 5)
Lai,2021	0.7790	0.1317	3.9%	4.00 [3.01, 0.0	71
LI,2022	0.7709	0.0040	4.0%	2.10[1.00, 2.0	
Lin,2023 Sub1	0.5978	0.110	4.0%	1.02 [1.45, 2.2	oj 71
Lin,2023 Sub2	1.0033	0.3827	2.0%	2.73 [1.29, 5.7	7]
LIU,2020	0.1021	0.1291	3.9%		3]
LU,2021	-0.7985	0.4967	2.1%	0.45 [0.17, 1.1	9]
Wu,2023	0.7739	0.0525	4.1%	2.17 [1.90, 2.4]	
Peng, 2022 sub1	0.0862	0.2045	3.0%	1.09 [0.73, 1.6	3]
Peng,2022 Sub2	-0.0101	0.1992	3.0%	0.99 [0.67, 1.4	6]
QI,2019	0.0325	0.2535	3.3%	1.03 [0.63, 1.7	
11an,2022	0.5589	0.1141	4.0%	1.75 [1.40, 2.1	9]
vvang,2022	1.4258	0.0959	4.0%	4.16 [3.45, 5.0	2]
XU,2016	0.2231	0.0765	4.1%	1.25 [1.08, 1.4	5
XU,2020 SUD1	-0.0202	0.0213	4.2%	0.98 [0.94, 1.0]	2]
Xu,2020 sub2	0.0488	0.0148	4.2%	1.05 [1.02, 1.0	8]
Xu,2023	0.239	0.0418	4.1%	1.27 [1.17, 1.3	8]
Zhang,2023	0.7477	0.0341	4.1%	2.11 [1.98, 2.2	6]
Zhao,2023	-0.6931	0.065	4.1%	0.50 [0.44, 0.5	7] -
Zhou,2015	0.422	0.4331	2.4%	1.53 [0.65, 3.5]	6]
Zhou,2016	0.624	0.0213	4.2%	1.87 [1.79, 1.9	5]
Zhuang,2022	1.5102	0.0443	4.1%	4.53 [4.15, 4.9	4] +
Total (05% CI)			100.0%	1 50 11 21 1 0	
Total (95% CI)	- 0.05. 04.7-07.44	10 16-1	100.0%	1.59 [1.51, 1.9:	5]
Heterogeneity: Tau-	= 0.25; Chi ⁺ = 2741.	.43, 01 = . 004)	20 (P < 0.1	00001); 1- = 99%	0.01 0.1 1 10 100
rest for overall effec	ι. Z = 4.60 (P < 0.00	001)			Favours [experimental] Favours [control]
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D Study of Subaroup	log(Odde Datio)	6Г 1	Maight N	Odds Ratio	Odds Ratio
Study of Subgroup		<u>SE 1</u>		0.07 (0.72, 1.05)	
CI 2022	-0.139/	0.09/0	21.3%		
311,2023 Zhang 2020	0.1000	0.0015	30.970	1.21 [1.07, 1.30]	
znang,2020	0.122	0.0591	30.5%	1.13[1.01, 1.27]	Γ
Total (95% CI)		1	00.0%	1.08 [0.92, 1.26]	•
Heterogeneity: Tau ² =	= 0.02; Chi ² = 8.12, d	f=2(P=	0.02); I ^z =	75%	
Test for overall effect	Z = 0.89 (P = 0.37)				U.U1 U.1 1 1U 100
					Favours (experimental) Favours (control)

Figure 2 Forest plot showing the association between insufficient sleep and prevalence of myopia in children. (A) Studies using sleep duration as a categorical variable. (B) Studies using sleep duration as a continuous variable.

Four studies^{56,61,63,65} lacked data for inclusion. Among these, two in secondary school students reported higher myopia prevalence with insufficient sleep.^{61,65} A preschool study found myopic children slept less than hyperopes.⁵⁶ Another study explored sleep duration and family type jointly influencing childhood myopia prevalence, considering nuclear, extended, single-parent, and left-behind families, highlighting multifaceted factors in childhood myopia occurrence.⁶³

Insufficient Sleep and Incidence of Myopia

In the analysis involving data from four longitudinal studies (two to four years follow-up),^{15,17,45,55} insufficient sleep showed no significant association with myopia onset compared to normal sleep duration (Figure 3; RR = 1.05; 95% CI = 0.98, 1.13; $I^2 = 0\%$; p = 0.17).

Insufficient Sleep and Prevalence of High Myopia

In the analysis of three studies on high myopia (defined as SER ≤ -6.00 D),^{12,47,53} insufficient sleep was significantly associated with an increased risk of high myopia (Figure 4; OR = 3.36; 95% CI = 1.26, 9.00; $l^2 = 96\%$; p = 0.02).

Insufficient Sleep and Premyopia

Wang et al's study⁵⁶ defined premyopia as SER > -0.5 D and $\leq +0.75$ D based on the International Myopia Institute (IMI) report.⁶⁹ Cycloplegic autorefraction determined refractive error, while sleep duration data were collected through questionnaires, categorized as more than 9 hours or less than 9 hours of sleep. Results indicated that premyopic children, compared to hyperopic children, were more likely to spend less time sleeping (p = 0.032). However, the multivariate analysis in this study did not include sleep duration, introducing uncertainty about the association between insufficient sleep and pre-myopia after adjusting for covariates.

Insufficient Sleep and Refractive Parameters

Insufficient Sleep and SER

As shown in Figure 5, the analysis revealed no significant associations between insufficient sleep ($\beta = 0.00$; 95% CI = -0.03, 0.03; p = 0.95) or shorter sleep duration ($\beta = 0.06$; 95% CI = -0.36, 0.48; p = 0.78) and SER. Additionally, when examining changes in SER, calculated as the difference between final and baseline values, three studies were considered. The results indicated that neither insufficient sleep ($\beta = 0.01$; 95% CI = -0.07, 0.09; p = 0.36) nor shorter sleep duration ($\beta = 0.04$; 95% CI = -0.05, 0.13; p = 0.36) was associated with a significant change in SER.





				Odds Ratio	Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Rando	om, 95% CI	
Jee,2016	0.0998	0.2332	32.4%	1.10 [0.70, 1.75]	-	-	
Wang,2022	2.2813	0.181	33.3%	9.79 [6.87, 13.96]			
Zhuang,2022	1.2264	0.094	34.4%	3.41 [2.84, 4.10]		+	
Total (95% CI)			100.0%	3.36 (1.26, 9.00)			
Heterogeneity: Tau ² =	0.72; Chi ² = 56.49	. df = 2 (F	0.01 0.1	1 10	100		
restion overall ellect.	z = 2.42 (F = 0.02)		Favours [experimental]	Favours [control]			





Figure 5 Forest plot showing the association between insufficient sleep and SER in children. (A) SER, studies using sleep duration as a categorical variable. (B) SER, studies using sleep duration as a continuous variable. (C) Changes in SER, studies using sleep duration as a categorical variable. (D) Changes in SER, studies using sleep duration as a continuous variable.

Insufficient Sleep and AL

As seen in Figure 6, both insufficient sleep and shorter sleep duration did not show significant associations with AL when sleep duration was categorized ($\beta = -0.03$; 95% CI = -0.05, 0.00; p = 0.08) or treated as a continuous variable ($\beta = 0.06$; 95% CI = -0.36, 0.48; p = 0.78). However, a notable observation emerged: shorter sleep duration was significantly linked to a more rapid rate of change in AL, particularly when sleep duration was considered as a continuous variable ($\beta = 0.05$; 95% CI = 0.02, 0.08; p = 0.02).

Notably, one study⁶⁸ was excluded from the meta-analysis due to insufficient data. The study's univariate analysis indicated that the growth of AL appears to be accelerated in individuals with reduced sleep duration (r = -0.197, p = 0.040).

Insufficient Sleep and CR, AL/CR

Regarding other parameters, Zhao et al found that higher AL/CR values were associated with shorter sleep duration (p = 0.04). However, CR did not exhibit a significant correlation with sleep duration (p = 0.17).⁵⁹ Conversely, Cui et al utilized sleep duration as a categorical variable, revealing in their multivariate regression that students who slept \leq 7 hours per day had



Figure 6 Forest plot showing the association between insufficient sleep and AL in children. (A) AL, studies using sleep duration as a categorical variable. (B) AL, studies using sleep duration as a continuous variable. (C) Changes in AL, studies using sleep duration as a continuous variable.

a larger CR compared to those who slept more than 9 hours ($\beta = 0.11$; 95% CI = 0.01, 0.20). Furthermore, no significant correlation was observed between sleep duration and AL/CR ($\beta = 0.00$; 95% CI = -0.04, 0.04).⁵⁷

Insufficient Sleep and Astigmatism

Astigmatism is linked to the onset and progression of myopia.⁷⁰ In Wang et al's study,⁶⁷ the compensation factor (CF) was calculated as the negative ratio of internal astigmatism (IA) to anterior corneal astigmatism (ACA). The research involved measuring children's non-cycloplegic refractive parameters, and their sleep duration was assessed through questionnaires. The results from multivariate regression models indicated that having more overnight sleep on weekends was associated with a reduced risk of oblique internal compensation (CF45), with an OR of 0.84 for each additional hour of sleep (95% CI = 0.72, 0.97; p = 0.02). These findings suggest that children with less nighttime sleep on weekends may face a higher risk of developing oblique axial astigmatism.

Sensitivity Analysis

We first used an *P* threshold of 25% as a criterion for choosing between fixed-effect and random-effect models, and the research results did not change. Sensitivity analysis (Figure S2) demonstrated the consistent statistical significance of the pooled results even after systematically excluding each individual study, which underscores the robustness of the meta-analysis findings regarding the prevalence of myopia. Additionally, the analysis did not reveal any significant sources of heterogeneity, further enhancing the reliability of the results.

Meta-Regression

Analysis results indicated factors contributing to potential heterogeneity sources. Myopia definition (95% CI = 0.28, 0.83; p < 0.01), sleep duration definition (95% CI = 0.26, 0.80; p < 0.01), study design (95% CI = 0.21, 0.72; p < 0.01), covariate adjustment extent (95% CI = 0.03, 0.59; p = 0.03), and sample size (95% CI = 0.08, 0.70; p = 0.016) were identified as potential sources. However, insufficient sleep criteria, region, myopia prevalence, and gender did not significantly contribute to heterogeneity (Supplementary Table S6).

Subgroup Analysis

<u>Supplementary Table S7</u> results show significant correlations between insufficient sleep and myopia prevalence in various subgroups, including alternative myopia definitions (OR = 1.75; 95% CI = 1.38, 2.22; p < 0.01), unspecified sleep definitions (OR = 1.71; 95% CI = 1.35, 2.16; p < 0.01), adherence to AASM recommendations (OR = 1.78; 95% CI = 1.36, 2.34; p < 0.01), cross-sectional designs (OR = 1.59; 95% CI = 1.29, 1.97; p < 0.01), studies in developing countries (OR = 1.61; 95% CI = 1.31, 1.98; p < 0.01), studies with over 50% male participants (OR = 1.76; 95% CI = 1.35, 2.29; p < 0.01), and studies with high-quality covariate adjustment (OR = 1.76; 95% CI = 1.31, 2.36; p < 0.01).

Discussion

Summary of Findings

Results indicated a significant link between insufficient sleep and myopia/high myopia prevalence. Shorter sleep duration was associated with a faster change in AL. However, evidence did not strongly support a connection between insufficient sleep and myopia incidence or changes in SER in longitudinal studies. The association between insufficient sleep and SER, AL, CR, AL/CR, astigmatism, and premyopia in cross-sectional studies remained uncertain. Significant associations were found in subgroups using alternative myopia definitions, unspecified sleep definitions, following AASM recommendations, employing cross-sectional designs, conducting studies in developing countries, having over 50% male participants, and including high-quality covariate adjustment.

Interpretation of Results

The absence of a significant combined result in studies using sleep duration as a continuous variable in the meta-analysis could be due to several reasons. Firstly, the relatively small number of studies in this subgroup may limit the statistical power to detect significant associations. Secondly, the effect of a one-hour reduction in sleep duration on myopia might be weak, making it challenging to detect in the aggregated results. Lastly, there could be a non-linear relationship between sleep duration and myopia, requiring a certain threshold of sleep reduction to have a discernible effect. Further research is needed to validate these possibilities and gain a better understanding of the relationship.

The lack of an association between myopia onset and insufficient sleep in this analysis could be attributed to several factors. Firstly, the included studies were relatively small, with inconsistent large sample sizes, limiting the statistical power and precision of the analysis. Secondly, there was notable heterogeneity among the follow-up studies, arising from variations in myopia and sleep definitions and a lack of strict adherence to the AASM definition of insufficient sleep. The diversity in study populations, spanning preschool⁵⁵ to secondary school students,⁴⁵ could have contributed to observed heterogeneity. Quality issues, such as high follow-up loss¹⁷ and focus solely on male adolescents,⁴⁵ may also influence results.

Accelerated AL growth typically precedes myopia onset and continues as myopia progresses.^{71,72} While in our study, pooled results did not reveal a significant association between insufficient sleep and AL in observational studies. Short sleep duration was associated with changes in AL but not with SER, changes in SER, CR or AL/CR. Factors contributing to this include less accurate SER measurement without adequate cycloplegia⁵⁹ and the higher precision of AL measurements.⁷³ It is important to note that these results may also be influenced by heterogeneity in the methods used to measure refractive parameters.⁷⁴ First, the precision and repeatability of different devices used in the studies, such as autorefractors, manual refractors, and optical coherence tomography (OCT), can vary, potentially leading to systematic biases in the measurements.⁷⁵ Additionally, variations in the experience and skill levels of the operators may affect the

consistency of refractive parameter measurements. Moreover, the limited number of studies included and the heterogeneity in sleep measurement methods could also impact the stability and reliability of the study results.

The observed lack of significant correlations in certain subgroups could be attributed to various factors. Significant heterogeneity within subgroups, stemming from methodological variations, may contribute to diverse outcomes. Subgroups with fewer studies, particularly longitudinal and those in developed countries, may be more susceptible to the impact of heterogeneity.

Our study's findings differ from those of previously published meta-analyses. Zhou et al investigated the relationship between sleep duration and the risk of various major eye diseases but did not find a significant association between sleep duration and the risk of myopia.²⁵ Wang et al explored the relationship between sleep quality, bedtime, and myopia, and their analysis indicated a certain association between sleep duration and myopia.²⁶ Similarly, Dong et al's meta-analysis showed a significant correlation between myopia risk and both short and long sleep durations, though it did not specifically address the impact of insufficient sleep on the development of myopia and axial length changes.²⁸ Additionally, Jin et al's meta-analysis, which included six studies, concluded that there was no significant association between sleep and the prevalence of myopia.²⁷ Our study focuses on the pediatric population and provides a more comprehensive and detailed perspective by emphasizing the specific and significant impact of insufficient sleep on the prevalence, incidence, and changes in axial length and other refractive parameters related to myopia.

Potential Mechanisms

Physiologically, children's corneal radius, axial length, choroidal thickness, and intraocular pressure can undergo changes within a 24-hour period.⁷⁶ Insufficient sleep may disrupt circadian rhythms by exposing children to light at night, potentially increasing the risk of myopia development.⁷⁷

From a molecular and cellular perspective, dopamine plays a crucial role in regulating circadian rhythms and ocular growth in children.^{78,79} Basic research and animal experiments have shown that dopamine acts as a protective factor against myopia development.^{80–83} Light stimulation of the retina triggers dopamine release from secretory cells through short-wavelength-sensitive retinal ganglion cells (ipRGCs). ipRGCs play a crucial role in the mechanisms underlying the onset and progression of myopia. These cells, through their photopigment melanopsin, detect light and regulate corneal curvature and axial length, thereby influencing the progression of myopia. Research has shown that selective activation or inhibition of ipRGCs can induce myopic or hyperopic refractive changes in mice, highlighting their key role in refractive development.⁸⁴ Furthermore, ipRGCs influence myopia by modulating dopamine levels in the retina. Blue light stimulation of ipRGCs significantly increases retinal dopamine concentrations, which in turn suppresses the development of myopia.⁸⁵ These mechanisms suggest that ipRGCs not only affect ocular growth but may also regulate the physiological state of the retina through neurotransmitter modulation, thereby playing a significant role in myopia development.

Dopamine levels in the retina, especially in the photoreceptor-adapted retina, are modulated by ipRGCs' interaction with dopaminergic amacrine cells (DACs).⁸⁶ This interaction influences retinal electroretinogram responses, contrast sensitivity, and cone cell protein phosphorylation.^{87,88} Dopamine, in turn, inhibits melatonin synthesis in the pineal gland, suppressing axial length (AL) growth.^{64,89} Dopamine also regulates connexin-36, a gap junction protein in retinal cells, impacting photoreceptor coupling.⁹⁰ Notably, polymorphisms in GJD2, the gene encoding connexin-36, have been linked to myopia in genome-wide association studies.⁹¹ Light signals transmitted through ipRGCs to the optic nerve's supraoptic nucleus regulate melatonin release, impacting sleep and circadian rhythm by activating MT1 and MT2 receptors.^{92,93} Additionally, melatonin significantly increases gamma-aminobutyric acid (GABA) levels, crucial for sleep-wake cycle regulation.⁹⁴ Dopamine synthesis peaks during the day, while melatonin secretion peaks at night.⁹⁵ Interestingly, individuals with myopia exhibit nearly three times higher melatonin concentrations than those without myopia.⁹⁶ Figure 7 illustrates the potential mechanisms through which these signaling molecules influence ocular parameters.



Figure 7 Diagram illustrating the potential mechanisms underlying ocular circadian disruption leading to myopia. Abbreviations: ipRGCs, intrinsically photosensitive retinal ganglion cells; DACs, dopaminergic amacrine cells; DA, dopamine; SCN, suprachiasmatic nucleus; GABA, gamma-aminobutyric acid; AL, axial length; CT, choroidal thickness; IOP, intraocular pressure.

Implications

Insufficient sleep remains a prevalent public health issue in children,^{97,98} associated with risks such as anxiety, depression, and reduced quality of life.^{99,100} To prevent myopia, providing health education to parents and children with insufficient sleep is crucial.¹⁰¹ Additionally, it's essential to emphasize that adequate sleep does not equate to oversleeping, maintaining a balance is key for overall health and well-being.^{102,103}

The current studies on insufficient sleep and childhood myopia are primarily cross-sectional, featuring variations in defining and measuring myopia, unclear sleep duration definitions, and inconsistent insufficient sleep criteria. Recommendations for future research include: 1) Conducting additional high-quality longitudinal studies and more multi-regional and multi-ethnic studies. 2) Adhering to standardized definitions and measurements for myopia, specifying night or total sleep duration, following authoritative guidelines for insufficient sleep definitions, and correcting outcomes for key risk factors. 3) To more accurately assess the impact of sleep on myopia, future research could employ objective sleep monitoring methods to record sleep and wake times.¹⁰⁴ For instance, the use of actigraphy can provide detailed data on sleep patterns, including sleep onset and wake times, sleep cycle duration, and sleep quality.¹⁰⁵ Compared to self-reported sleep duration, actigraphy can capture subtle changes in sleep behavior more accurately. Additionally, combining actigraphy with polysomnography to validate the data could offer a more comprehensive picture of sleep.¹⁰⁶ These objective measurement techniques can reduce human error and enhance the accuracy of assessing the influence of sleep on myopia, thereby providing a solid evidence base for developing more effective intervention strategies.¹⁰⁷

Limitations

This review has limitations. Firstly, residual confounding factors may still exist in the included observational studies, uncertainty exists regarding whether observed myopia prevalence is primarily influenced by insufficient sleep or other confounding factors, as not all studies conducted multivariate regression analyses to adjust for key factors, future

research needs to carefully adjust for key confounding factors such as parental myopia, time spent in near work, and time outdoors. Secondly, varying definitions of insufficient sleep across studies raise questions about whether some children truly had insufficient sleep. Thirdly, the geographical focus of included studies, particularly in China,¹⁰⁸ limits generalizability to other regions. In addition, the majority of included studies were cross-sectional, resulting in limiting the ability to establish causality. To better understand the relationship between insufficient sleep and the occurrence and development of myopia, future studies should adopt more prospective cohort study designs. This will help establish causal evidence and further validate our findings. Lastly, the high heterogeneity in the study results also limits the interpretation of the outcomes. This heterogeneity may arise from various factors, including differences in study design, diversity in sample characteristics, and inconsistencies in measurement methods.¹⁰⁹ Future research should further explore these potential sources of heterogeneity and validate our findings within a more unified research framework to enhance the robustness and generalizability of the conclusions.

Conclusion

This systematic review and meta-analysis reveal significant associations between insufficient sleep in children and myopia prevalence, high myopia. Short sleep duration was found associated with more rapid changes in AL. While follow-up studies did not clearly establish links between insufficient sleep and myopia onset or progression, this may be due to limited and low-quality studies. Nevertheless, the overall evidence strongly suggests that insufficient sleep is an independent risk factor for childhood myopia, contributing to its mechanisms. Further research is vital to comprehend causal and biological aspects of the insufficient sleep-myopia relationship in children. Acknowledging the impact of insufficient sleep underscores the need for targeted interventions. Policymakers and educators should prioritize promoting healthy sleep habits in children, contributing to global public health initiatives to reduce myopia burden.

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Disclosure

The authors do not have any conflicts of interest to disclose.

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