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Original Article

Causal Association of Educational Attainment with Myopia: A Two-sample Mendelian Randomization Study

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Abstract

Background and objectives: Observational studies have shown that educational attainment is associated with the risk of myopia, but the causality of this relationship is unclear. The aim of the present study was to investigate the causal association between educational attainment and myopia.

Methods: Using publicly available data from genome-wide association studies, single nucleotide polymorphisms associated with educational attainment (college/university completion and years of education) were selected as instrumental variables. Causal associations with myopia risk were examined using two-sample Mendelian randomization (MR) analyses. Sensitivity analyses were conducted to assess the robustness of the results in terms of violations of MR assumptions.

Results: The inverse variance–weighted analysis revealed potential causal associations of college/university completion (odds ratio (OR) = 1.102; 95% confidence interval (CI): 1.085–1.119; $P < 0.001$) and years of education (OR = 1.009; 95% CI: 1.007–1.010; $P < 0.001$) with myopia risk. MR-Egger and weighted median methods yielded similar results for both educational attainment measures.

Conclusions: MR evidence supports a potential causal association between educational attainment and myopia. This evidence highlights the need for careful management of myopia risk in individuals with higher educational attainment.

Introduction

In recent years, the social determinants of health have gained increasing attention and significance among scholars in various fields, including social medicine, public health, and clinical medicine.[1-3] Myopia has become a highly prevalent global public health issue, particularly in East and Southeast Asian populations.[4] The development of myopia is attributed to the combined effects of genetic (single nucleotide polymorphisms (SNPs), DNA methylation, and non-coding RNA) and environmental factors (e.g., near work, outdoor activities, education, classroom environments, and population density).[5] Because the gene pool changes minimally across generations, whereas natural and social environments evolve rapidly, identifying the key environmental exposures driving the rapid increase in the prevalence of myopia is imperative. Identifying modifiable environmental risk factors can provide crucial insights for the development of preventive interventions.[6]

Educational attainment (EA), a crucial indicator of socioeconomic status, has garnered significant attention from clinicians, epidemiologists, and other medical researchers in recent years. Studies have revealed a close association between EA and individuals' lifelong health status, as well as strong correlations with various health behaviors and disease outcomes.[7]

The recent introduction of Mendelian randomization (MR) methods has provided new approaches for conducting reliable causal inference studies based on observational data and for avoiding confounding and reverse causation problems in traditional observational epidemiological studies.[8,9] In MR analyses, genetic variations robustly associated with exposure factors (most commonly SNPs) serve as instrumental variables (IVs) for inferring the causal effects of those factors on disease outcomes.[8-10] Individuals are grouped based on these genetic

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variations, and the groups are compared in a manner similar to randomized controlled trials. This allocation method helps reduce confounding biases arising from individual characteristics and behaviors, enabling more reliable inference of causal relationships.[11-13] Two-sample MR analysis leverages summary statistics from genome-wide association studies (GWASs), avoiding the need to directly analyze individual-level data. It enables the assessment of causal relationships between socioeconomic exposures and disease risk in large-scale populations, thereby providing more representative and reliable research results.

Despite recent advances in MR research, the causal pathways linking EA and myopia remain incompletely understood. Emerging evidence suggests that EA is embedded within a more complex causal framework involving both upstream determinants and downstream behavioral mediators. For example, obesity-related traits may influence myopia partly through EA, and time spent outdoors may partially mediate the effect of education on myopia. These findings highlight the need for further investigation using robust causal inference approaches.[14,15] Thus, the aim of the present study was to investigate the causal association of EA with myopia, independent of potential confounding and reverse causality, using a two-sample MR design.

Materials and methods

Study design

This analysis was conducted using summary-level data from published GWASs, and all studies included in the GWASs were approved by the relevant review boards and conducted with participants' informed consent. The present MR analyses were conducted in accordance with the STROBE-MR guidelines.[16] The study was conducted in accordance with the three fundamental assumptions underlying MR analysis: (1) strong association of IVs (EA-related SNPs) with the exposure (EA); (2) independence of confounding factors from the exposure–outcome (myopia) relationship; and (3) influence of genetic variants on the outcome only through the exposure, not through other pathways. The overall study design is illustrated in Figure 1. Figure 2 presents a standardized flowchart detailing participant inclusion, SNP screening, harmonization, quality control, and statistical analysis procedures, constructed in full compliance with the STROBE-MR reporting guidelines.

Data sources

Summary-level data for educational attainment (EA) were obtained from the Social Science Genetic Association Consortium (SSGAC) 2018 genome-wide association study (OpenGWAS IDs: ebi-a-GCST90029012 for college/university completion and ebi-a-GCST90029013 for years of schooling; total N ≈ 1,131,881 individuals of European ancestry). These GWAS summary statistics were derived from a large multi-cohort meta-analysis that included UK Biobank participants as one of several contributing cohorts (Table 1: N = 470,941 for college completion; N = 461,457 for years of education; https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90029012/; https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90029013/).

Summary-level data for myopia were obtained from the Medical Research Council Integrative Epidemiology Unit (MRC IEU) OpenGWAS database (OpenGWAS ID: ukb-b-6353; N = 460,536 individuals of European ancestry; https://gwas.mrcieu.ac.uk/datasets/ukb-b-6353/), which were derived exclusively from UK Biobank participants.

Inclusion and exclusion criteria

The following inclusion criteria were applied: (1) GWAS conducted in populations of European ancestry; (2) large sample size with publicly available complete summary statistics; (3) clear and standardized phenotype definitions for EA (college/university completion or years of education) and myopia; and (4) study approval by an ethics committee and provision of informed consent by all participants. Datasets with low genotyping quality or incomplete summary statistics (lacking SNP IDs, effect alleles, β values, standard errors, or *P*-values) were excluded.

IV selection

To explore the causal relationship between EA and myopia, SNPs associated with EA were selected as IVs. To ensure IV independence and relevance, eligible SNPs were associated with EA at a significance threshold of $P < 5 \times 10^{-8}$, with linkage disequilibrium removed ($r^2 < 0.001$, kb = 10,000). SNP harmonization and quality control were performed by aligning effect alleles between exposure and outcome datasets, removing palindromic SNPs or correcting them according to allele frequencies, and excluding SNPs with missing data in the outcome GWAS.

MR analysis

The inverse variance–weighted (IVW), MR-Egger, and weighted median methods were used in the analysis. With the IVW method, commonly used in meta-analyses, Wald estimates for individual SNPs were combined to assess the overall effect of EA on myopia.[17] The results were used as the primary outcome measure. The MR-Egger and weighted median methods were used to complement the IVW results, providing a more robust and comprehensive evaluation. The MR-Egger method allows for pleiotropy in genetic IVs but requires that pleiotropic effects are independent of the variant–exposure association. The weighted median method permits the use of invalid IVs in an MR analysis under the assumption that at least half of the instruments are valid. In cases of inconsistency in results across methods, a stricter significance threshold for the *P*-value was applied. We used the MR-Egger intercept test, funnel plots, and leave-one-out analysis to assess horizontal pleiotropy, and Cochran's *Q* test to detect heterogeneity. To account for possible horizontal pleiotropy, we supplemented the primary IVW analysis with Simple Mode and Weighted Mode estimations. The F-statistic was used to evaluate IV strength. The mean F values were 32.64 for college/university completion and 35.17 for years of education, both well above 10, indicating no evidence of weak instrument bias. All analyses were conducted using the TwoSampleMR package (version 0.5.5) in R (version 4.0.3; https://www.r-project.org/). To account for potential confounding effects, we also conducted a multivariable MR analysis adjusting for time spent outdoors, near-work intensity, and obesity-related anthropometric traits using the MVMR package in R.

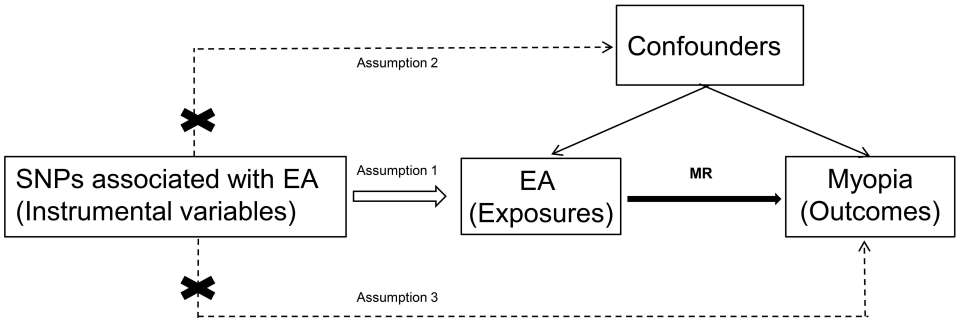

Fig. 1. Overview of the study design according to the three key Mendelian randomization (MR) assumptions: (1) strong association between instrumental variables and exposure factors, (2) no confounding factors affecting the association between exposure and outcome (i.e., no genetic pleiotropy), and (3) effects of instrumental variables on the outcome only through exposure. EA, educational attainment; SNP, single nucleotide polymorphism.

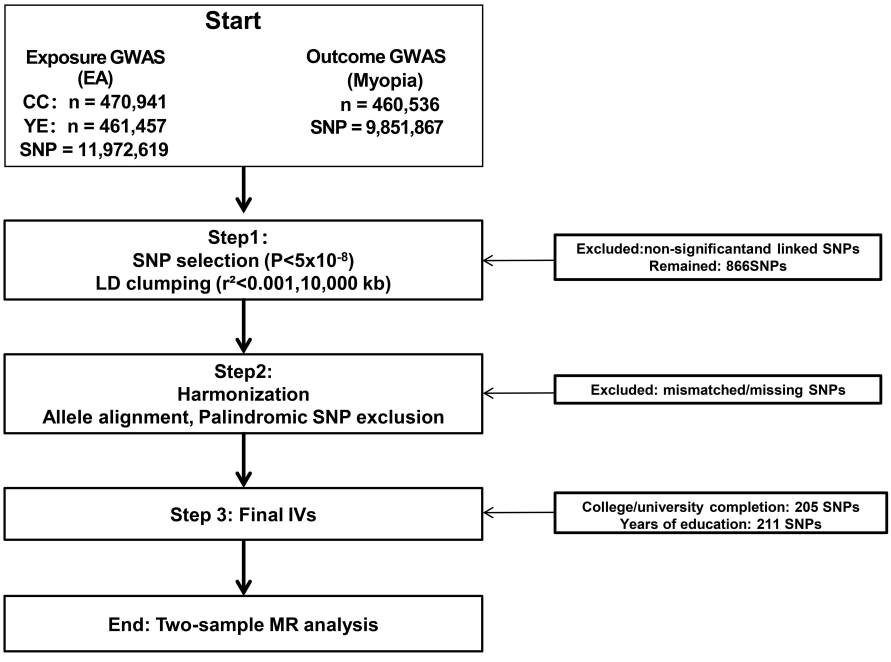

Fig. 2. Flowchart of study design, SNP selection, and analytical procedures following the STROBE-MR guidelines. CC, college completion; EA, educational attainment; GWAS, genome-wide association studies; IV, instrumental variable; LD, linkage disequilibrium; MR, Mendelian randomization; SNP, single nucleotide polymorphism; YE, years of education.

Results

MR estimates

For the EA phenotypes of college/university completion and years of education, 205 and 211 SNPs, respectively, were included in the analysis. The SNP data for the most significantly associated EA phenotypes are detailed in Supplementary Table. 1. The characteristics of the selected EA phenotype-associated SNPs are also presented there. IVW analysis demonstrated that college/

Table 1. Details of the GWAS summary statistics used in this study

Variable type	Trait	Sample size	No. of variants	Population	Data type	GWAS ID	Year of publication
Exposure	College/university completion	470,941	11,972,619	European	Binary	ebi-a-GCST90029012	2018
	Years of education	461,457	11,972,619	European	Continuous	ebi-a-GCST90029013	2018
Outcome	Myopia	460,536	9,851,867	European	Binary	ukb-b-6353	2018

GWAS, genome-wide association studies.

Table 2. Associations of educational attainment with myopia risk

Exposure	Method	No. of SNPs	β	SE	OR	95% CI	*P*
College/university completion	MR Egger	205	0.100	0.032	1.105	1.038-1.178	0.002
	Weighted median	205	0.102	0.010	1.107	1.084-1.130	<0.001
	IVW	205	0.097	0.008	1.102	1.085-1.119	<0.001
	Simple mode	205	0.106	0.031	1.114	1.045-1.188	0.001
	Weighted mode	205	0.105	0.027	1.110	1.055-1.169	0.0001
Years of education	MR Egger	211	0.008	0.003	1.008	1.001–1.014	0.029
	Weighted median	211	0.008	0.001	1.008	1.006-1.010	<0.001
	IVW	211	0.009	0.001	1.009	1.007-1.010	<0.001
	Simple mode	211	0.008	0.002	1.008	1.003-1.014	0.005
	Weighted mode	211	0.008	0.002	1.008	1.004-1.013	0.001

CI, confidence interval; IVW, inverse variance–weighted; MR, Mendelian randomization; OR, odds ratio; SE, standard error; SNP, single nucleotide polymorphism.

university completion increased the risk of developing myopia (odds ratio (OR) = 1.102; 95% confidence interval (CI): 1.085–1.119; $P < 0.001$) (Table 2). College/university completion was associated with a 10.2% increased risk of myopia compared with no tertiary education. Comparable causal estimates were obtained from the WM analysis (OR = 1.107; 95% CI: 1.085–1.130; $P < 0.001$). The MR-Egger analysis also indicated a consistent directional result (OR = 1.105; 95% CI: 1.038–1.178; $P = 0.002$) (Fig. 3a). The IVW method also revealed a consistent association between years of education and an increased risk of myopia (OR = 1.009; 95% CI: 1.007–1.010; $P < 0.001$). A one-standard-deviation increase in years of education was associated with a 0.9% increase in myopia risk. Meanwhile, WM analysis yielded comparable risk estimates (OR = 1.008; 95% CI: 1.007–1.010; $P < 0.001$). MR-Egger also showed similar causal estimates (OR = 1.008; 95% CI: 1.001–1.014; $P < 0.05$) (Fig. 3b). The causal associations remained significant in the multivariable MR analysis (college/university completion: OR = 1.094, 95% CI: 1.028–1.163, $P = 0.005$; per-standard-deviation increase in years of education: OR = 1.007, 95% CI: 1.001–1.014, $P = 0.032$), suggesting an independent causal effect of EA on myopia development.

Sensitivity analyses

Cochran's Q test and the MR-Egger intercept test were performed to assess the robustness of the results (Table 3). The Cochran's Q test revealed heterogeneity for the college/university completion measure ($P < 0.05$), but this heterogeneity was deemed acceptable under the random-effects IVW model (Table 3). The *P*-values from the MR-Egger intercept tests were all >0.05, indicating the absence of horizontal pleiotropy.

The MR estimates from the random-effects IVW method remained valid. Additionally, the MR-Egger intercept test found no evidence of pleiotropy, suggesting that the MR estimates were unbiased despite the heterogeneity (Fig. 3; Supplementary Fig. 1). In support of this result, the leave-one-out analysis and funnel plots suggested that the results were not driven by individual SNPs (Supplementary Fig. 2 and 3).

Discussion

This MR study provides compelling evidence for a causal relationship between EA and the risk of myopia development. College/university completion and years of education were significantly associated with increased susceptibility to myopia. These results were consistently supported across IVW, weighted median, and MR-Egger analyses.

This study builds upon and extends previous research on the association between EA and myopia risk. Although cross-sectional and longitudinal studies have consistently shown this association,

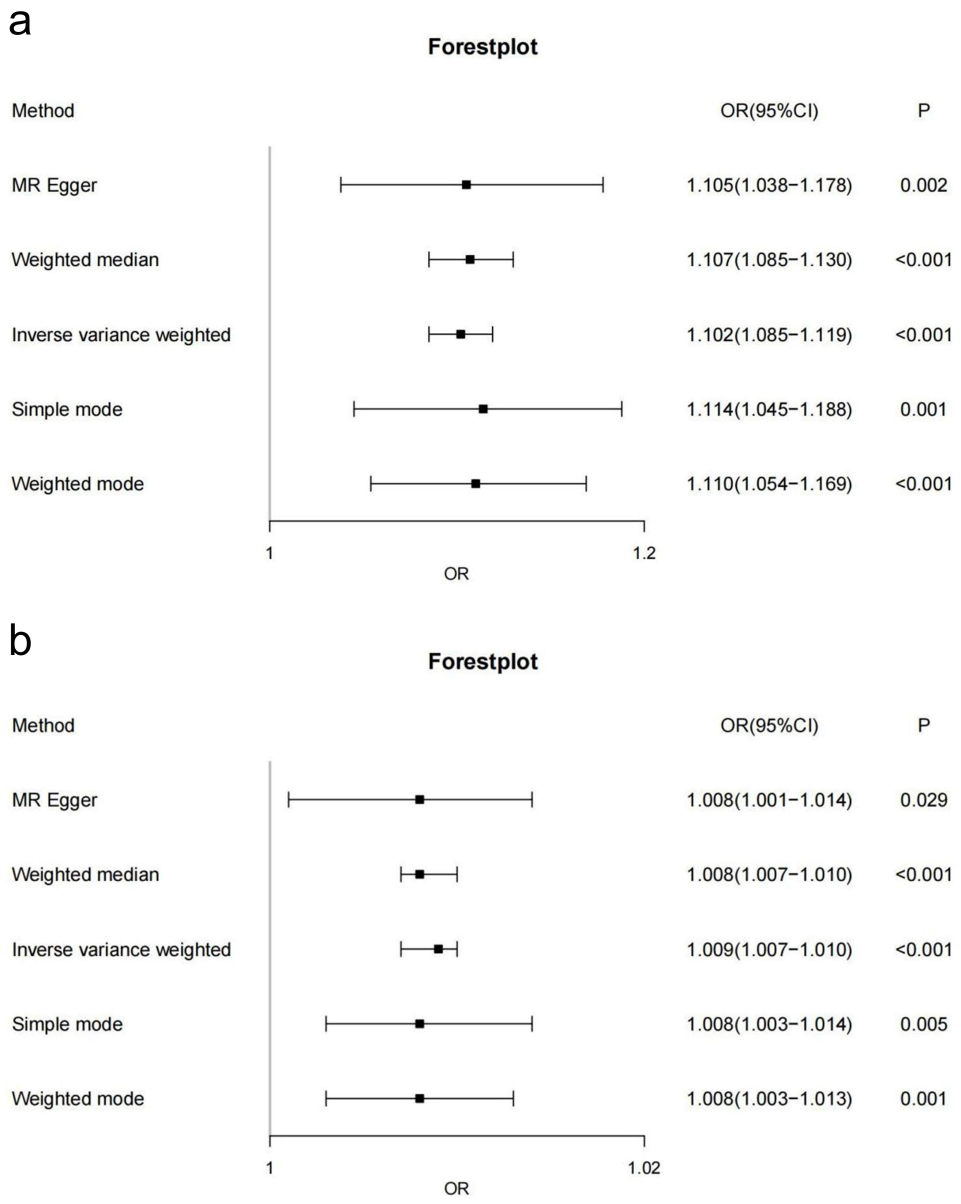

Fig. 3. Forest plots of causal effects of (a) college/university completion and (b) years of education (exposures) on myopia risk (outcome). CI, confidence interval; MR, Mendelian randomization; OR, odds ratio.

they have been limited by potential confounding factors such as socioeconomic status and parental EA. The use of MR analysis in our study helped mitigate these limitations by leveraging genetic variants as IVs, providing stronger evidence for a causal relationship.[18] Although some studies have suggested that years of education or increases in grade level increase the risk of myopia, others have found no significant association between EA and myopia risk.[19] The findings of our study align with those of Mountjoy *et al*.,[20] who used MR analysis to demonstrate that more years of education contribute to the rising prevalence of myopia. However, we examined not only years of education but also college/university completion as an EA measure. This comprehensive approach provides a more nuanced understanding of the relationship between education and myopia risk.

This MR study revealed associations between two EA measures (college/university completion and years of education) and the risk of myopia development. Myopia has been associated with higher education.[21] Several mechanisms have been proposed to explain this association. Primarily, increased engagement in near-work activities (e.g., intensive reading) associated with higher educational levels, as well as increased screen time and prolonged near-work duration, are thought to contribute significantly to myopia development.[20-25] These activities may lead to sustained accommodation and peripheral hyperopic defocus, which are

Table 3. Heterogeneity and horizontal pleiotropy of EA-associated SNPs

Exposure	Outcome	Heterogeneity			Horizontal pleiotropy			
		IVW Cochran Q	IVW *P*	MR Egger Cochran Q	MR Egger *P*	Egger regression intercept	SE	Intercept *P*
College/university completion	Myopia	329.5	<0.001	329.5	<0.001	<0.001	<0.001	0.915
Years of education	Myopia	391.3	<0.001	391.1	<0.001	<0.001	<0.001	0.773

EA, educational attainment; IVW, inverse variance–weighted; MR, Mendelian randomization; SE, standard error; SNP, single nucleotide polymorphism.

hypothesized to stimulate axial elongation of the eye. Additionally, the indoor learning environments typically associated with higher education may reduce exposure to natural light, which is believed to protect against myopia progression. Recent MR evidence further supports this behavioral pathway. For example, Clark *et al*.[15] demonstrated that time spent outdoors may partially mediate the effect of EA on myopia, accounting for a substantial proportion of the total causal effect. In one study, each additional year of education was associated with a refractive error change of –0.18 diopters,[20] highlighting the cumulative effect of prolonged academic pursuits on ocular health. Findings from population-based and intervention studies suggest that a key strategy to reduce the development of myopia is to encourage children to spend more time engaged in outdoor activities.[26-28] Reducing study burden, especially after class, has been found to effectively prevent myopia.[25]

Gene–environment and gene–gene interaction effects are also recognized as contributors to myopia,[29] and the genetic factors involved in refractive error development may also influence EA.[30] In a cohort of unrelated UK Biobank participants of European ancestry, five genetic variants located near GJD2, RBFOX1, LAMA2, KCNQ5, and LRRC4C showed evidence of genotype–education interaction; the effects of variants involved in axon guidance, synapse formation, and neural circuit development were enhanced with additional years of education.[31] However, some scholars believe that increased near work, rather than genetic factors, is the primary factor driving the relationship between education and myopia.[32] These findings underscore the complex interplay between genetic predisposition and environmental factors in the etiology of myopia, highlighting its multifactorial nature and the need for comprehensive approaches to prevention and management. Furthermore, EA may also act as an intermediate factor within a broader causal framework. Obesity-related anthropometric traits have been found to influence myopia partly through EA,[14] suggesting that biological and socioeconomic factors may be integrated within the causal pathway.

The causal relationship between EA and myopia has been further supported by studies in which genetic risk scores for education served as IVs. Cuellar-Partida *et al*.[12] demonstrated that education significantly affects myopia, with a –0.35-diopter change per standard deviation increase in the genetic risk score. Mountjoy *et al*.[20] observed an even stronger causal effect, with a –0.27-diopter change per year of education ($P = 4 \times 10^{-8}$).

Our study provides valuable insights, but it is not without limitations. Recent methodological studies have highlighted potential limitations of MR analyses of myopia, demonstrating that causal estimates may vary substantially depending on the choice of GWAS summary statistics, with some datasets producing inconsistent or even contradictory findings. Thus, our findings should be interpreted with caution, particularly given the reliance on a single set of GWAS data sources.[33] Moreover, although the escalating prevalence of myopia in East and Southeast Asia needs to be addressed, most currently available data—including those used in the present study—are from European populations. A comprehensive analysis of the applicability of the current findings to Asian populations is needed before definitive conclusions can be drawn and robust recommendations for the Asian context can be made. Furthermore, genetic pleiotropy, whereby factors beyond EA (e.g., ethnic background and birthplace) may influence the likelihood of myopia development, is a pertinent issue. Identifying such factors is essential for a comprehensive understanding of the multifaceted etiology of myopia and for tailoring interventions and preventive strategies accordingly. Several avenues for future research emerge from our findings. Longitudinal studies combining genetic data with detailed information on educational experience and environmental factors could provide deeper insights into the mechanisms underlying the relationship between education and myopia. Additionally, investigating the potential protective effects of outdoor activities, as suggested by population-based and intervention studies, could lead to the development of practical strategies for myopia prevention in educational settings.[34]

Future directions

In future studies, the generalizability of the present findings should be validated in non-European populations, particularly East and Southeast Asian populations, where myopia is highly prevalent. Well-designed longitudinal studies using individual-level data are needed to further clarify the biological and behavioral mechanisms underlying the causal relationship between EA and myopia. Further research is also warranted to explore potential mediating factors, including time spent outdoors, near-work intensity, learning environments, and light exposure, which may help identify actionable targets for myopia prevention. In addition, large-scale cohort studies and randomized controlled trials focusing on eye health interventions in educational settings are needed to support the development of evidence-based strategies for myopia control among students and individuals with higher EA.

Conclusions

Our data suggest that EA is causally associated with myopia. These findings have important implications for public health strategies and educational policies. Although education is undoubtedly beneficial, our results suggest that measures to mitigate the associated myopia risk should be considered. Incorporating more outdoor activities into educational programs, optimizing learning environments to reduce eye strain, and implementing regular vision screening in schools may be beneficial. By addressing these factors, it may be possible to balance the benefits of education with the preservation of ocular health.

Supporting information

Supplementary material for this article is available at https://doi.org/10.14218/ERHM.2026.00007.

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Conflict of interest

The authors have no conflict of interest related to this publication.

Author contributions

Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, visualization (RW), writing - original draft (RW, ZW), supervision, validation, writing - review & editing (ZW). Both authors have made significant contributions to this study and have approved the final manuscript.

Ethical statement

This analysis was conducted using summary-level data from published GWASs, and all studies included in the GWASs were approved by the relevant review boards and conducted with participants' informed consent. Because no individual-level data were used and no new human participants were recruited, additional ethical approval and informed consent were not required for the present study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2024).

Data sharing statement

The exposure and outcome data were obtained from the UK Biobank (https://www.ukbiobank.ac.uk/). Data on educational attainment (measured by years of education and college/university completion) were obtained from the Social Science Genetic Association Consortium database (https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90029012/; https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90029013/), which was published in 2018 and contains data on 470,941 individuals of European ancestry (Table 1). Data on myopia (ukb-b-6353, https://gwas.mrcieu.ac.uk/datasets/ukb-b-6353/) were sourced from the Medical Research Council Integrative Epidemiology Unit Open GWAS database, published in 2018, which contains data on 460,536 individuals of European ancestry.

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