

Association between asthma and myopia: the NHANES database and Mendelian randomization analysis

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Abstract

• **AIM:** To comprehensively assess the relationship between asthma and myopia based on the National Health and Nutrition Examination Survey (NHANES) database combined with Mendelian randomization (MR).

• **METHODS:** Initially, 20 497 subjects from the complete questionnaire cycle in the NHANES database from 2005 to 2008 were included. By exclusion criteria, 8460 subjects were screened with 1676 myopia samples and 6784 control samples. Subsequently, baseline characteristics, association analyses, risk stratification analyses, and receive operating characteristic curve (ROC) were used to investigate the associations between covariates and myopia. Then, the causal relationship was explored in depth by MR analysis, and was estimated the reliability by sensitivity analyses and directionality tests.

• **RESULTS:** Baseline characteristics illustrated a significant difference between myopia and controls for both asthma and covariates (excluding gender; $P<0.05$). The results in all three models indicated that asthma was strongly associated with myopia and the effect on myopia was not significantly confounded by other covariates [model 3: odd ratio (OR)=1.31; 95%CI=1.07-1.62; $P=0.0133$]. The risk stratification analysis again verified that asthma remained strongly associated with myopia and was a risk factor for myopia ($P<0.05$, $OR>1$). ROC proved that the model was accurate in its prediction [area under curve (AUC)=0.7]. Subsequently, the causal relationship between them was statistically significant ($P<0.05$) according to the inverse variance weighted (IVW) method in MR. Scatterplot showed that asthma and myopia had significant positive

causality and were not affected by confounders. Forest plot displayed an increasing risk of myopia on asthma ($OR>1$). The funnel plot demonstrated compliance with Mendel's second law. Sensitivity analysis and directional analysis further confirmed the confidence of the MR analysis results and a unidirectional causal relationship between them.

• **CONCLUSION:** A significant association and causality between asthma and myopia is found through the NHANES database and MR analysis, which is important implications for public health policy development and clinical practice.

• **KEYWORDS:** asthma; myopia; National Health and Nutrition Examination Survey; Mendelian randomization

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INTRODUCTION

Myopia is a refractive error primarily caused by the mismatch between the optical power of the cornea and lens and the axial length of the eye, leading to blurred vision for distant images^[1]. With the increase in indoor activity time and the amount of near work, this condition has become a relatively common and increasingly serious public health issue^[2]. It is estimated that by 2050, the prevalence of myopia and high myopia will significantly increase, affecting nearly 5 billion and 1 billion people globally, respectively^[3]. The etiology of myopia can be attributed to the complex interplay between environmental exposure and genetic susceptibility. Environmental and lifestyle factors, such as behavioral impacts, play a significant role in the development of myopia^[4-5]. Factors including outdoor exposure time, lighting environment, light levels, timing, duration, and patterns all influence the onset of myopia^[6-7]. Therefore, based on existing research, there is growing interest in methods to slow down the progression of myopia.

Asthma is a chronic inflammatory disease that primarily affects the airways, characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. The etiology of asthma is complex, encompassing both genetic predisposition

and environmental exposures^[8]. Genetic factors, such as variations in certain genes, can increase the susceptibility to asthma. Environmental factors include exposure to allergens, air pollution, and viral infections. Although myopia and asthma belong to different systems of diseases, recent studies have suggested that there may be a certain association between the two.

Asthma is a chronic inflammatory disease caused by abnormal immune system responses. Similarly, the development of myopia may also be associated with the immune system. Some studies have shown that there are immune system-related inflammatory markers present in the ocular tissues of individuals with myopia^[9], suggesting that the immune system might play a role in the association between the two conditions. Changes in modern lifestyles, such as prolonged indoor activities and the use of electronic devices, are high-risk factors for myopia and also contribute to the triggers of asthma. Furthermore, air pollution not only increases the incidence of asthma but may also indirectly lead to myopia by affecting eye health^[10]. This finding suggests that there may be a link between myopia and asthma. Although current research provides some preliminary evidence, further in-depth studies are needed to clarify the specific relationship and mechanisms between the two.

Mendelian randomization (MR) is a data analysis technique used in epidemiological studies to assess causal inference, utilizing genetic variants as instrumental variables (IVs) to estimate the causal relationship between an exposure of interest and an outcome of concern in non-experimental data. In epidemiological studies, MR is often employed to evaluate causal inference. Despite being based on non-experimental data, it is reliable due to its ability to overcome potential confounding and reverse causality. In recent years, the application of MR in observational studies has become increasingly widespread^[11-13].

In this study, we, for the first time, combined data from the National Health and Nutrition Examination Survey (NHANES) with MR analysis to investigate the correlation between asthma and the risk of myopia, aiming to provide ideas and strategies for early detection and prevention of myopia.

MATERIALS AND METHODS

Data Selection and Study Design Established in 1999, the NHANES database was a continuous cross-sectional survey designed to assess the health and nutritional status of people living in American communities. Each year, nearly 5000 people across the country were interviewed, examined, and lab tested by NHANES. The data collected were uploaded to the National Center for Health Statistics website (<https://www.cdc.gov/nchs/nhanes/>). Because the NHANES protocol was approved by the Ethics Review Board of the National Center

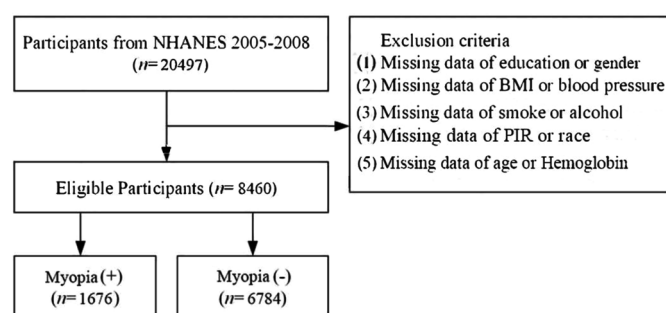


Figure 1 Flowchart of sample selection NHANES: National Health and Nutrition Examination Survey; BMI: Body mass index; PIR: Poverty income ratio.

for Health Statistics and Research, all participants provided informed consent. Inclusion criteria for this analysis were 20 497 subjects from the complete questionnaire cycle from 2005 to 2008. Exclusion criteria were subjects with missing key clinical information; the main missing information included education, gender, body mass index (BMI), hypertension, smoke, alcohol, poverty income ratio (PIR), race, age, and hemoglobin. Finally, 8460 subjects were screened from 20 497 subjects (Figure 1).

Variables Definition and Baseline Statistics In the questionnaire (No.MCQ010), as to the question “Has a doctor or other health professional ever told {you/SP} that {you have/ s/he/SP has} asthma”, respondents who answered “yes” were in the asthma group, and those who answered “no” were in the control group.

In the questionnaire (No.VIQ031), for the question “At the present time, would you say (your/SP’S) eyesight, with glasses or contact lenses if (you/he/she) wear them is...” The respondents who answered “1, 2” were in the control group, and those who answered “3, 4, 5” were in the myopic group.

The following clinical characteristics were selected as covariates in this study, mainly gender, race, age, education, PIR, alcohol, smoke, BMI, hypertension, and hemoglobin. Gender was divided into male and female. Race was categorized as Mexican American and other race. Age was split into two groups: age<40y and age≥40y. Education included below high school and high school or above. PIR was PIR<1.00 and PIR≥1.00. Alcohol was alcohol (yes) and alcohol (no). Smoke was smoke (yes) and smoke (no). BMI was grouped into BMI<25, BMI 25-29.9 and BMI≥30.0. Hypertension was hypertension (yes) and hypertension (no). Hemoglobin was hemoglobin<11 g/dL and hemoglobin≥11 g/dL. The information table for covariates was detailed in Table 1.

Subsequently, Student’s *t*-tests and Chi-square tests were compared whether there were differences between the myopic and control groups for the covariates, and the results were presented in a table of baseline characteristics of the covariates.

Table 1 Information sheet on covariates

| Variable | Subgroup variables/continuous variables | Dataset |
|----------------------------|--|----------|
| Gender | Male/female | RIAGENDR |
| Race | Mexican American/other race | RIDRETH1 |
| Age (y) | <40/≥40 | RIDAGEYR |
| Education | Below high school/high school graduate or above | DMDEDUC2 |
| Poverty income ratio (PIR) | Below poverty level (<1.00)/poverty level or above (≥1.00) | INDFMPIR |
| Alcohol | Yes/no | ALQ101 |
| Smoke | Yes/no | SMQ020 |
| Body mass index (BMI) | <25/25 to 30/30 kg/m ² or higher | BMXBMI |
| Hypertension | Yes/no | BPQ020 |
| Hemoglobin | <11/≥11 g/dL | LBXGH |

Risk Association Analysis To investigate whether there was a significant association between asthma and myopia, three successive multifactorial GLM regression models were constructed for the relationship between asthma and myopia by the survey package (version 4.2.1)^[14]. Model 1 was an unadjusted model with only asthma put in to study its relationship with myopia. Model 2 was added age, race, and gender based on model 1. Model 3 was added education, PIR, alcohol, smoke, BMI, hypertension, and hemoglobin based on model 2.

Risk Stratification Analysis To further confirm the stability of the correlation between asthma and myopia across populations, the following covariates were stratified by weighted logistic regression analyses, including age (≥40y), sex (male), race (other race), PIR (≥1.00), education (high school or above), alcohol (yes), smoke (yes), BMI (25-29.9), BMI (≥30.0), hypertension (yes) and hemoglobin (≥11 g/dL).

ROC to Assess Predictive Performance in Asthma To estimate the predictive efficiency of asthma in myopia risk, the receive operating characteristic curve (ROC) of model 3 was plotted by the pROC package (v 1.18.5)^[15] and the area under curve (AUC) was calculated; the closer AUC was to 1, the more accurate the diagnosis.

Data Sources for MR Experiments After the results of NHANES database, MR analysis was performed further to understand the causal relationship between asthma and myopia. First, using asthma as a keyword to search in the genome-wide association Study (GWAS) catalog database (<https://gwas.mrcieu.ac.uk/>), relevant eQTL data (ebi-a-GCST90038616) were obtained, as an exposure factor. This dataset included 9 587 836 SNPs with 484 598 samples, of which 56 087 were disease samples and 428 511 were control samples. Then, myopia was searched in this database using myopia as a keyword to obtain the relevant GWAS ID (ukb-b-6353), as an outcome. It included 9 851 867 SNPs with 460 536 samples, of which 37 362 were disease samples and 423 174 were control samples.

Screening of Instrumental Variables Initially, the exposure factor data were read and screened for single nucleotide polymorphism (SNPs) by `extract_instruments` function^[16]. SNPs significantly associated with the exposure factor were found according to the screening condition $P < 5 \times 10^{-6}$. Subsequently, SNPs with chain imbalance were removed according to the criterion `Clump=TRUE`, $r^2=0.001$, `kb=50`. On the basis of this, SNPs that were not relevant to the outcome but related to the exposure factors were obtained. For the above, SNPs were used as IVs. Later, the exposure factor-IVs-outcome was matched by harmonizing the effect alleles and effect sizes through the `harmonise_data` function for performing MR analysis^[16]. In addition, the *F*-value ($F = \text{beta}^2 / \text{SE}^2$) was calculated for each SNP. *F*-value was greater than 10, meaning strong and effective IVs.

MR Analysis In order to explore the causal relationship between exposure factor and outcome, MR analysis was performed by MR function combined with five algorithms, including MR Egger^[17], weighted median^[18], inverse variance weighted (IVW)^[19], simple mode^[20], and weighted mode^[21]. Since IVW was the most robust analysis method, its result was mainly referred to here for MR analysis. Afterwards, scatter plot was determined the correlation between exposure factor and outcome. Next, the diagnostic efficacy of the SNP loci of the exposure factor on the outcome was judged by plotting a forest plot. Eventually, funnel plot was drawn based on the SNP distribution of the exposure factor to determine whether the analysis complied with Mendel's second law.

Sensitivity Analysis Sensitivity analyses were carried out to understand whether the results of the MR analysis were reliable. Primarily, the MR_Heterogeneity function^[22] was used to assess whether there was heterogeneity in the results. If the *P*-value was greater than 0.05, it indicated the absence of heterogeneity, and the fixed-effects IVW method was more appropriate for the analysis; if the *P*-value was less than 0.05, it indicated the presence of heterogeneity, and the random-effects IVW needed to be used for the MR analysis. Second, the

MR_Pleiotropy_Test and Run_MR_Presso functions^[23] were tested to evaluate whether there was horizontal pleiotropy, and if *P*-value was greater than 0.05, it meant that there was no horizontal pleiotropy and no confounders. Afterwards, the effect size of individual SNPs on the whole was examined using a leave-one-out (LOO) analysis^[24]. If the results changed significantly after the exclusion of an SNP, it was necessary to re-analyze the results after its exclusion.

Directionality Test To detect the direction of causality between exposure factor and outcome, MR steiger filtering analysis was utilized to remove exposure factors with SNP $r^2_{\text{exposure}} < \text{SNP } r^2_{\text{outcome}}$ ^[25]. If correct causal direction was TRUE and the Steiger *P*-value was less than 0.05, it suggested a unidirectional causal relationship between exposure factor and outcome.

Statistical Analysis The R software (version 4.2.2) was employed for all analyses. NHANES database-related analyses were performed using the rhanesR software package (v 1.0)^[26], while MR-related analyses were prepared using the Two Sample MR package (v 0.5.7)^[16]. All tests were two-tailed with a significance level of *P*<0.05. When *P* was less than 0.05, it demonstrated there was a statistically significance. Odd ratio (OR) was larger than 1, meaning a protective factor, while less than 1, meaning a risk factor.

RESULTS

Demographic Differences Between Myopic Patients and Controls After going through the exclusion criteria and variable definitions, 8460 subjects were included in this study, with 1676 in the myopia group and 6784 in the control group. The baseline characteristics illustrated the differences between the myopia group and the control group in terms of the covariates (Table 2). The covariates (race, age, education, PIR, hemoglobin, BIM, alcohol, hypertension, smoke) differed significantly (*P*<0.05) between the myopic and control groups. Obviously, asthma was also significantly different with myopic (*P*=0.002).

Correlation Established Between Asthma and Myopia Asthma had a *P*-value of less than 0.05 in all three models, demonstrating that asthma was strongly associated with myopia and that the effect on myopia was not significantly confounded by other covariates [Model 1: OR=1.29; 95% confidence interval (CI)=1.07-1.57; *P*=0.0106; Model 2: OR=1.42; 95%CI=1.17-1.73; *P*=0.0010; Model 3: OR=1.31; 95%CI=1.07-1.62; *P*=0.0133; Table 3]. Results of the risk stratification analysis subsequently showed that age (≥40), race (other race), PIR (≥1.00), education (high school or above), alcohol (yes), smoke (yes), hypertension (yes), and hemoglobin (≥11 g/dL) had a significant effect on the outcome of myopia (*P*<0.05). Specifically, asthma remained strongly linked to myopia and was a risk factor for myopia (OR=1.31;

Table 2 Baseline characteristics of subjects by presence or absence of myopia

| Parameters | Myopia, n (%) | | <i>P</i> |
|------------------------|---------------|-------------|----------|
| | No | Yes | |
| <i>n</i> | 6780 | 1674 | |
| Asthma | | | 0.002 |
| No | 5921 (87.3) | 1413 (84.4) | |
| Yes | 859 (12.7) | 261 (15.6) | |
| Race | | | <0.001 |
| Mexican American | 1115 (16.4) | 428 (25.6) | |
| Other | 5665 (83.6) | 1246 (74.4) | |
| Gende | | | 0.468 |
| Female | 3454 (50.9) | 870 (52.0) | |
| Male | 3326 (49.1) | 804 (48.0) | |
| Age | | | <0.001 |
| <40y | 2581 (38.1) | 375 (22.4) | |
| ≥40y | 4199 (61.9) | 1299 (77.6) | |
| Education | | | <0.001 |
| Below high school | 1557 (23.0) | 814 (48.6) | |
| High school or above | 5223 (77.0) | 860 (51.4) | |
| PIR | | | <0.001 |
| <1.00 | 1065 (15.7) | 511 (30.5) | |
| ≥1.00 | 5715 (84.3) | 1163 (69.5) | |
| Haemoglobin | | | <0.001 |
| <11 g/dL | 6746 (99.5) | 1638 (97.8) | |
| ≥11 g/dL | 34 (0.5) | 36 (2.2) | |
| BMI, kg/m ² | | | 0.041 |
| <25 | 2024 (29.9) | 450 (26.9) | |
| 25-29.9 | 2292 (33.8) | 574 (34.3) | |
| ≥30.0 | 2464 (36.3) | 650 (38.8) | |
| Alcohol | | | <0.001 |
| No | 1958 (28.9) | 566 (33.8) | |
| Yes | 4822 (71.1) | 1108 (66.2) | |
| Hypertension | | | <0.001 |
| No | 4641 (68.5) | 948 (56.6) | |
| Yes | 2139 (31.5) | 726 (43.4) | |
| Smoke | | | <0.001 |
| No | 3636 (53.6) | 749 (44.7) | |
| Yes | 3144 (46.4) | 925 (55.3) | |

BMI: Body mass index; PIR: Poverty income ratio.

Table 3 Association between asthma and myopia

| Model | OR | 95%CI | <i>P</i> |
|---------|------|-----------|----------|
| Model 1 | 1.29 | 1.07-1.57 | 0.0106 |
| Model 2 | 1.42 | 1.17-1.73 | 0.00104 |
| Model 3 | 1.31 | 1.07-1.62 | 0.0133 |

OR: Odd ratio; CI: Confidence interval.

95%CI=1.07-1.62; *P*=0.0133; Figure 2A). Furthermore, Model 3 had an AUC=0.7 for myopia risk prediction, suggesting an accurate prediction (Figure 2B).

Asthma as a Risk Factor for Myopia According to the results of IVW method, the causal relationship between

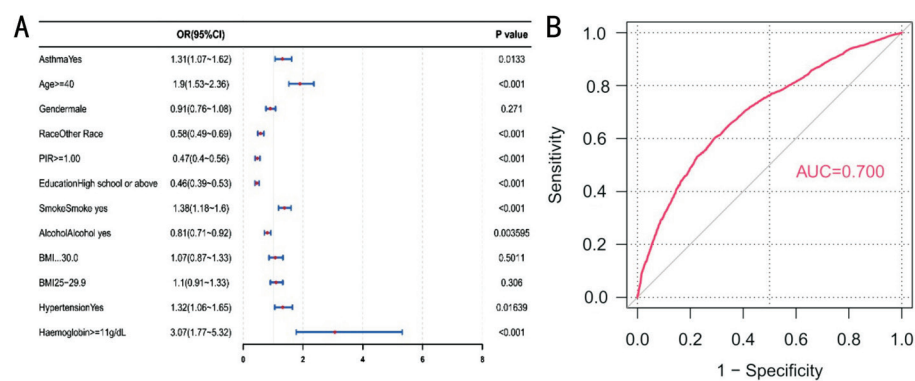


Figure 2 Stratified analysis of asthma and myopia (A) and ROC curve for risk prediction (B) OR: Odd ratio; ROC: Operating characteristic curve; AUC: Area under curve.

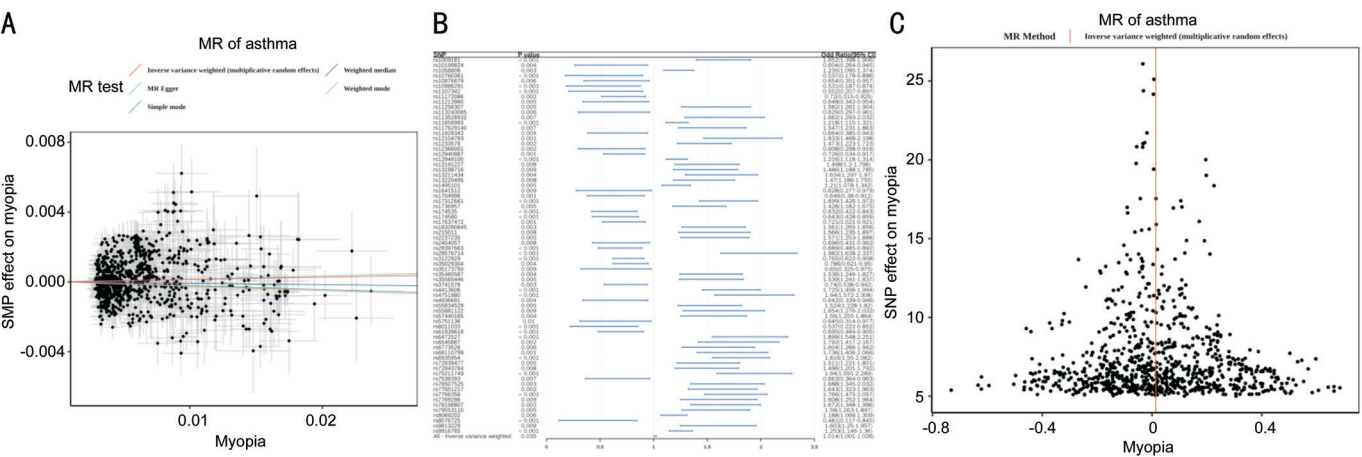


Figure 3 Asthma as a risk factor for myopia A: Scatter plot for correlation analysis. The x-axis represents the effect of SNPs on the exposure factor, and the y-axis represents the effect of SNPs on the outcome. B: Forest plot for diagnostic performance. The x-axis values represent the effect size estimates for each SNP, and y-axis represents SNPs, each entry represents one SNP. C: Funnel plot. Each point represents the effect size of one SNP, the x-axis typically represents the effect size, and the y-axis represents precision. MR: Mendelian randomization; SNP: Single nucleotide polymorphism.

Table 4 Results of MR analysis

| Exposure | ID.outcome | Method | nSNP | b | OR | P |
|--------------------|------------|---|------|---------|--------|--------|
| ebi-a-GCST90038616 | ukb-b-6353 | MR Egger | 855 | 0.01897 | 1.0191 | 0.1941 |
| ebi-a-GCST90038616 | ukb-b-6353 | Weighted median | 855 | -0.0080 | 0.9920 | 0.3186 |
| ebi-a-GCST90038616 | ukb-b-6353 | Inverse variance weighted (multiplicative random effects) | 855 | 0.0134 | 1.0136 | 0.0348 |
| ebi-a-GCST90038616 | ukb-b-6353 | Weighted mode | 855 | -0.0254 | 0.9749 | 0.0641 |
| ebi-a-GCST90038616 | ukb-b-6353 | Simple mode | 855 | -0.022 | 0.9781 | 0.4239 |

OR: Odd ratio; MR: Mendelian randomization; SNP: Single nucleotide polymorphism.

asthma and myopia was statistically significant (OR=1.014; 95%CI=1.001-1.026; $P=0.035$; Table 4). The scatterplot of the IVW method had a positive slope of the line, showing a significant positive causality between asthma and myopia, and an intercept of 0, signifying that it was not influenced by confounders (Figure 3A). Correspondingly, the forest plot revealed that the combined SNP was greater than 0, implying that asthma had a positive effect on myopia and increased the risk of developing myopia (Figure 3B). The funnel plot illustrated that the distribution of SNPs in asthma was generally symmetric and homogeneous overall, in accordance

with Mendel's second law (Figure 3C). The results of the MR study were further confirmed by sensitivity analyses. Cochran's Q assessment implied that the P value was less than 0.05, which was suitable for a random effect, and that there was heterogeneity, which might be related to the inconsistency of the IVs effect (Table 5). Analysis of horizontal pleiotropy gave a p of greater than 0.05, indicating that there were no horizontal pleiotropy and confounders (Table 6). The forest plot at LOO analysis showed that by progressively eliminating each SNP, the remaining SNP points were all located on the same side, with little variation

Table 5 Heterogeneity test analysis results

| Exposure | ID.outcome | Method | Q | df | P |
|--------------------|------------|---------------------------|---------|-----|----------|
| ebi-a-GCST90038616 | ukb-b-6353 | Inverse variance weighted | 1897.86 | 854 | 4.09E-81 |
| ebi-a-GCST90038616 | ukb-b-6353 | MR Egger | 1897.47 | 853 | 3.05E-81 |

MR: Mendelian randomization.

Table 6 Results of horizontal multiple validity test analysis

| Exposure | ID.outcome | P | Egger_intercept |
|--------------------|------------|-------|-----------------|
| ebi-a-GCST90038616 | ukb-b-6353 | 0.675 | -3.58E-05 |

Table 7 Directional analysis

| ID.exposure | SNP r^2_{exposure} | SNP r^2_{outcome} | Correct_causal_direction | Steiger P |
|--------------------|-----------------------------|----------------------------|--------------------------|-----------|
| ebi-a-GCST90038616 | 0.08872 | 0.004192 | TRUE | P<0.0001 |

SNP: Single nucleotide polymorphism.

in the effect on myopia, suggesting that the results of the MR analyses were reliable and stable. Finally, directional analysis further indicated a unidirectional causal relationship between asthma and myopia (SNP $r^2_{\text{exposure}} > \text{SNP } r^2_{\text{outcome}}$; correct_causal_direction=TRUE; Steiger $P < 0.0001$; Table 7).

DISCUSSION

In recent years, with changes in people's lifestyles and the impact of environmental factors, the incidence of asthma and myopia has been on the rise globally. An increasing number of studies have begun to focus on the potential associations between these two conditions. This study, based on the findings from the NHANES database, demonstrates a close relationship between asthma and myopia. Additionally, we incorporated MR to analyze their causal relationship.

The results from the NHANES database indicate a close relationship between asthma and myopia. When other variables are not considered, asthma, as an exposure factor, shows a significant positive correlation with the occurrence of myopia. This means that the incidence of myopia is significantly higher in the population with asthma compared to those without asthma. After considering multiple covariates (such as race, age, education, PIR), hemoglobin, alcohol consumption, hypertension, and smoking), asthma was still identified as a risk factor for myopia. Asthma had P -values less than 0.05 in three models, indicating a strong association between asthma and myopia, and the effect of asthma on myopia is not significantly interfered with by other covariates. Model 3, which predicts the risk of myopia, has an AUC>0.6, indicating a relatively accurate prediction. These findings suggest that, at the societal level, asthma may be an important risk factor for myopia. This discovery is of great significance for the formulation of public health policies and clinical practice.

Besides epidemiological data, the results of MR analysis also provide robust evidence supporting the causal relationship between asthma and myopia. Following the analysis of the NHANES database, the exposure factor selected was asthma,

and the outcome was myopia. Based on the results from five algorithms, particularly the IVW method, the main discussion focuses on the existence of a causal relationship between asthma and myopia ($P < 0.05$). Additionally, scatter plots, diagnostic forest plots, and funnel plots also demonstrate a positive causal relationship between asthma and myopia, indicating that asthma is a risk factor for myopia and can increase the risk of developing myopia. Subsequently, through a series of sensitivity analyses including Cochran's Q assessment, horizontal pleiotropy evaluation, LOO analysis, and directional testing, the reliability and good stability of the MR results were further explained.

Asthma is a chronic respiratory inflammatory disease primarily driven by a Th2-type immune response, characterized by eosinophilic infiltration of the airway mucosa, elevated levels of pro-inflammatory cytokines (such as IL-4, IL-5, and IL-13), and increased IgE levels^[27]. In recent years, studies have indicated that inflammatory responses play a significant role in the onset and progression of myopia. Elevated inflammation may directly or indirectly promote myopic progression by inducing scleral remodeling^[28]. Furthermore, the dominant role of inflammatory factors in choroidal neovascularization may influence refractive asymmetry in the eye, thereby exacerbating myopia^[29]. In the management of asthma, long-term use of inhaled or oral corticosteroids is a common treatment strategy^[30]. However, these medications may adversely affect ocular development and contribute to myopia progression. Corticosteroids can elevate intraocular pressure by inhibiting trabecular meshwork repair and increasing aqueous humor outflow resistance, potentially impacting ocular health and serving as a risk factor for myopia development. Additionally, due to air quality concerns, asthma patients are often advised to reduce their time outdoors^[31]. This lifestyle adjustment may promote myopia through multiple pathways. First, reduced outdoor activity increases time spent on near-work tasks (such as prolonged reading or electronic device use), which

heightens the accommodative burden on the ciliary muscle and further facilitates myopia progression. Second, limited outdoor exposure leads to insufficient ultraviolet radiation, which is essential for vitamin D synthesis. Adequate vitamin D levels have been shown to help inhibit axial elongation, thereby mitigating myopia onset. This study suggests a potential causal relationship between asthma and myopia, which we hypothesize may be driven collectively by cross-systemic inflammatory effects, medication side effects, and lifestyle modifications. Nevertheless, the interactions among these mechanisms require further investigation. The proposed multi-dimensional mechanism provides a theoretical basis for clinical practices aimed at reducing myopia risk through controlling asthma-related inflammation, optimizing drug therapy, and promoting lifestyle improvements.

Despite the important evidence provided by the NHANES database and MR analysis regarding the association between asthma and myopia, these studies also have certain limitations. First, the sample was derived from a European population, which may introduce racial and geographical representativeness bias. Additionally, the cross-sectional nature of the NHANES data cannot fully capture the temporal sequence between the onset of asthma and myopia. The lack of variables such as time spent outdoors and duration of electronic device use may also act as unmeasured confounders influencing the results. Although the MR analysis underwent sensitivity testing, potential residual confounding and population stratification bias may still exist. Moreover, the proposed mechanisms—such as inflammatory response, medication use, and lifestyle factors—currently lack direct biological evidence. Therefore, future studies should involve longitudinal cohort designs to dynamically monitor asthma patients and collect detailed data to clarify temporal relationships and the influence of confounding factors. Animal models, cell experiments, and randomized controlled trials should also be conducted to validate the underlying mechanisms. Integrating larger-scale and multi-ancestry GWAS data would help optimize MR analyses. Furthermore, subgroup-specific investigations should be carried out to more comprehensively elucidate the relationship between asthma and myopia, thereby providing a basis for targeted prevention and intervention.

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