The impact of PM 2.5 on asthma: A two-sample Mendelian randomization study

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To the Editor:

In recent decades, the relationship between particulate matter (PM) and asthma has been a topic of considerable research interest and debate in the field of environmental health [1, 2]. Mendelian randomization (MR), a methodological approach that leverages genetic variants as instrumental variables to infer causal relationships between exposures and outcomes, has been employed in some studies to explore the potential causal link [3, 4]. In this study, two-sample MR was applied to GWAS summary statistics of PM$_{2.5}$ and asthma using R (version 4.3.2). IVs were chosen based on genome-wide significance thresholds (p < 5×10^{-8}) . The primary analytical approach employed was the Inverse Variance Weighted (IVW) method, while supplementary measures encompassed the Weighted Median Model, MR-Egger, Simple Model, and Weighted Model methods. Additionally, pleiotropy and heterogeneity were evaluated using MR-Egger intercept test and Cochrane’s Q test. A sensitivity analysis was conducted utilizing the leave-one-out method. Results shows eight genome-wide significant single nucleotide polymorphisms (SNPs) associated with PM$_{2.5}$ exposure were extracted as instrumental variables (IVs). Asthma data from three independent GWAS summary statistics were utilized to estimate the causal effect of PM$_{2.5}$ exposure on asthma (ukb-b-11297 [14283 cases, 98300
controls]; ukb-a-255 [10589 cases, 72940 controls]; ukb-d-J10-asthma [1993 cases, 359201 controls]). Our MR results from three databases show that PM$_{2.5}$ was not associated with the risk of Asthma. The Inverse Variance Weighted (IVW) results from the three datasets were combined using a fixed-effect model, revealing no significant evidence of a causal effect of PM on asthma (OR = 0.99, 95% CI: 0.98-1.01) (Figure 1). No heterogeneity or pleiotropy was detected in the results. MR effect of and sensitivity analyses further supported the robustness of our findings (Figure S1). Overall, this study contributes to understanding the complex relationship between PM$_{2.5}$ exposure and asthma, emphasizing the importance of continued research in this area. While our study contributes valuable insights into the PM$_{2.5}$-asthma relationship, several limitations warrant acknowledgment. Foremost among these is the reliance on GWAS data predominantly derived from European populations, which may limit the generalizability of our findings to diverse ethnic and geographical contexts. Future research endeavors should prioritize the inclusion of diverse populations and comprehensive genetic data to enhance the external validity and generalizability of findings. Furthermore, Mendelian randomization (MR) provides a powerful framework for causal inference, it relies on the assumption of instrument validity—that the selected genetic variants are robustly associated with the exposure of interest and are not influenced by confounding factors. While we rigorously assessed the validity of instrumental variables (IVs), potential biases or unmeasured confounders may still exist, which could impact the validity of our causal inference [5].

Figure 1 A: The causal relationship between exposure to PM$_{2.5}$ and Asthma. B: Identification of the causal effects of PM$_{2.5}$ on Asthma by IVW MR method. nSNP, number of SNPs; OR: odds ratio; CI: confidence interval.

1. Bi J, D’Souza RR, Moss S, Senthilkumar N, Russell AG, Scovronick NC, Chang HH, Ebelt S: Acute Effects of Ambient Air Pollution on Asthma by IVW MR method. nSNP, number of SNPs; OR: odds ratio; CI: confidence interval.


