

# Enhancing the Rigor of Mendelian Randomization: Methodological Insights from the Study on Obstructive Sleep Apnea and Temporomandibular Disorders [Response to Letter]

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## Dear editor

We are very grateful to receive the letter from Dr. Zhou and his colleagues.<sup>1</sup> In the letter, Dr. Zhou pointed out the flaws of our study:<sup>2</sup>

First, as all of the GWAS data utilized came from the FinnGen database; there may have been some overlap in the samples because the data sources were all from Finnish populations. Based on this, the conclusions of this study may be somewhat biased, which limits the use of the results. We then used the exposure data (OSA: ukb-d-G6\_SLEEPAPNO) that recommended by Zhou to validate and find no significant causal effect of OSA on TMD ( $P=0.074$ ), which suggests that there is some uncertainty in the current results, which needs to be further confirmed by subsequent studies.

Second, some potential confounders, such as body mass index (BMI), smoking status, alcohol consumption, and psychological stress, maybe influence the reliability of results. Under Zhou's supervision, we conducted a Multivariable Mendelian (MVMR) analysis using online data from IEU (OSA: ukb-d-G6\_SLEEPAPNO, BMI: ukb-b-19953, smoking: ukb-b-223, alcohol: ukb-b-5779, stress: ukb-b-17687). When potential confounders were addressed in MVMR analyses, there was no significant change in result ( $P=0.490$ ), indicating that confounders such as smoking, alcohol, and stress had no effect on the results.

Finally, we are grateful to Professor Zhou et al for their invaluable guidance, which we will implement into our future study to improve it even more.

## Disclosure

The authors declare no conflicts of interest in this communication.

## References

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2. Wang YP, Wei HX, Hu YY, Niu YM. Causal relationship between obstructive sleep apnea and temporomandibular disorders: a bidirectional Mendelian randomization analysis. *Nat Sci Sleep*. 2024;16:1045–1052. doi:10.2147/NSS.S476277

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