

For all terms, we have provided corresponding references for further exploration by interested readers.

1. Mendelian randomization (MR)<sup>1</sup>: An analytical research method that explores causal relationships. Similar to epidemiological methods, causal relationships between exposure/trait (such as disease, and biomarkers) and outcomes (such as disease endpoints) can be explored. In our study, the microbiome (GM) taxa were defined as exposure and age-related macular degeneration (AMD) as the outcome.

2. Instrumental variables (IVs)<sup>2</sup>: In our manuscript, variables related to each GM taxa are included. These variables are not associated with confounders.

3. Pleiotropy<sup>3</sup>: It is the phenomenon by which a single variable influences multiple phenotypes (such as AMD, glaucoma or other diseases). At the same time, it includes horizontal pleiotropy and vertical pleiotropy. Horizontal pleiotropy means that mutations may affect outcomes (such as AMD) through other traits, which should be avoided as much as possible. Vertical pleiotropy means that variables affect other traits through meaningful factors, which is the core of MR and is acceptable<sup>4</sup>.

4. Genome-wide association studies (GWASs)<sup>5</sup>: Linkage disequilibrium allows for exploring the association of variations at the population level.

5. inverse variance weighted (IVW) test<sup>6</sup>: Standard method for MR of summary level data. Calculated using data associated with all IVs and outcomes (such as AMD).

6. weighted median (WM) method<sup>7</sup>: A computational method used to combine multiple variations for cause and effect. This method allows more than half of the instrumental variables to be invalid and can provide consistent causal estimates.

7. MR Egger regression<sup>8</sup>: A method for analyzing causal effects in MR. At the same time, this method can be used to analyze pleiotropy. This method is more robust when the IVs have horizontal pleiotropy.

## Reference

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