# Supplementary File 1

In the present study, we identified single-nucleotide polymorphisms (SNPs) related to thyrotropin receptor antibodies (TRAb) and inflammatory proteins through genome-wide association studies (GWAS), which were subsequently used as instrumental variables (IVs) in Mendelian randomization (MR) analyses. To satisfy the first core assumption of MR that the selected IVs are robustly associated with the exposure, we applied a significance threshold of $P < 1 \times 10^{-5}$ when selecting SNPs. This cutoff was applied to ensure that a sufficient number of valid genetic instruments were included without compromising the strength of their association with the exposure, thus supporting robust MR inference.

Following SNP selection, linkage disequilibrium (LD) clumping was performed to ensure the independence of the instruments. Specifically, SNPs were clumped using an $r^2$ threshold of 0.1 within a 100 kb window, consistent with previously published methodologies [1]. LD clumping was implemented using PLINK software (version 1.9), based on LD estimates from the European population of the 1000 Genomes Project reference panel [2,3]. This procedure retained only the most statistically significant SNP in instances of LD effects among multiple SNPs.

To further reduce bias arising from weak instruments, we calculated the F statistic as ($\beta^2/se^2$) for each SNP as an indicator of instrument strength. SNPs with an F statistic below 10 were considered weak instruments and were excluded, in accordance with established guidelines in MR research [4]. Additionally, SNPs

showing potential direct associations with the outcome ($P < 5 \times 10^{-5}$) were removed to limit violations of the exclusion restriction assumption [5-7]. Finally, Steiger directionality testing was conducted to identify and exclude SNPs that may reflect reverse causality, ensuring that the direction of effect was from exposure to outcome [8].

## References


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