

Supplementary Table S1: Strengthening the reporting of observational studies in epidemiology using MR (STROBE-MR) checklist.

Item	Complete/location
1. Title and Abstract	Title and abstract
Indicate Mendelian randomization (MR) as the study's design in the title and/or the abstract if that is the main purpose of the study.	
Introduction	
2. Background	1. Background, Paragraphs 1-3
Explain the scientific background and rationale for the reported study. What is the exposure? Is a potential causal relationship between exposure and outcome plausible? Justify why MR is a helpful method to address the study question.	
3. Objectives	1. Background, Paragraphs 3
State-specific objectives clearly, including prespecified causal hypotheses (if any). State that MR is a method that, under specific assumptions, intends to estimate causal effects	
4. Study design and data sources	
Present key elements of the study design early in the article. Consider including a table listing sources of data for all phases of the study. For each data source contributing to the analysis, describe the following:	
a) Setting: Describe the study design and the underlying population, if possible. Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, when available.	2. Methods, (section: 2.1 Research framework) and the list of study design is provided in Figure1
b) Participants: Give the eligibility criteria and the sources and methods of selection of participants. Report the sample size and whether any power or sample size calculations were carried out prior to the main analysis	2. Methods (section:2.2 Source of data, and2.3 Selection of instrumental variables) and the detailed information on the GWAS studies and datasets were provided in Supplementary Table S2
c) Describe measurement, quality control and selection of genetic variants	2. Methods (section:2.3 Selection of instrumental variables)
d) For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases	2.Methods, (2.3 Selection of instrumental variables)
e) Provide details of ethics committee approval and participant informed consent, if relevant	not relevant

5. Assumptions	2.Methods, (section : 2.1 Research framework) and the list of study design is provide in Figure1
Explicitly state the three core IV assumptions for the main analysis (relevance, independence and exclusion restriction) as well as assumptions for any additional or sensitivity analysis	
6. Statistical methods main analysis	a, b, c, e) 2. Methods (section:2.4 Statistics, d) not applicable
Describe statistical methods and statistics using	
a) Describe how quantitative variables were handled in the analyses (i.e., scale, units, model)	
b) Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected	
c) Describe the MR estimator (e.g. two-stage least squares, Wald ratio) and related statistics. Detail the included covariates and, in the case of two-sample MR, whether the same covariate set was used for adjustment in the two samples	
d) Explain how missing data were addressed	
e) If applicable, indicate how multiple testing was addressed	
7. Assessment of assumptions	2.Methods, (section: 2.1 Research framework)
Describe any methods or prior knowledge used to assess the assumptions or justify their validity	
8. Sensitivity analyses	2.Methods, (section:2.4 Staistics)
Describe any sensitivity analyses or additional analyses performed (e.g. comparison of effect estimates from different approaches, independent replication, bias analytic techniques, validation of instruments, simulations)	
9. Software and preregistration	a) 2.Methods, (section:2.4 Stastics)
a) Name statistical software and package(s), including version and settings used	
b) State whether the study protocol and details were preregistered (as well as when and where)	Not applicable
Results	
10. Descriptive data	Supplementary Table S2
a) Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider the use of a flow diagram	

b) Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions)	Supplementary Table S3
c) If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies	Not applicable
d) For two-sample MR:	3.Results, (section:3.1Instrumental variable selection3.4 Reverse MR analysis on inflammatory cytokines) and Supplementary Table S3
i. Justify the similarity of the genetic variant-exposure associations between the exposure and outcome samples	
ii. Provide information on the number of individuals who overlap between the exposure and outcome studies	
11. Main results	a) Figure 2,46
a) Report the associations between a genetic variant and exposure and between a genetic variant and outcome, preferably on an interpretable scale	3. Results, (section 3.2 Forward MR analysis of the association of 91 inflammatory cytokines on malignant neoplasm of stomach,3.3 Forward MR analysis of the association of 91 inflammatory cytokines on adenocarcinoma and papillary adenocarcinoma of stomach,3.4 Reverse MR analysis on inflammatory cytokines) , and listed in Figure 2,4-6
b) Report MR estimates of the relationship between exposure and outcome and the measures of uncertainty from the MR analysis on an interpretable scale, such as odds ratio or relative risk per SD difference	
c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful period	Not applicable
d) Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure)	Forest plots were listed in Supplementary Figure S2; scatter plots were listed in Figure 3; Funnel plots were listed in Supplementary Figure S3. a, b) Results, (section : 3.2 Forward MR analysis of the association of 91 inflammatory cytokines on malignant neoplasm of stomach,3.3 Forward MR analysis of the association of 91 inflammatory cytokines on adenocarcinoma and papillary adenocarcinoma of stomach,3.4 Reverse MR analysis on inflammatory cytokines) , and Supplementary Table S4/S5/S6
12. Assessment of assumptions	
a) Report the assessment of the validity of the assumptions	

b) Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as I², Q statistic or E-value)

13. Sensitivity and additional analyses

- a) Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions
- b) Report results from other sensitivity analyses or additional analyses

c) Report any assessment of the direction of a causal relationship (e.g., bidirectional MR)

d) When relevant, report and compare with estimates from non-MR analyses

e) Consider additional plots to visualize results (e.g., leave-one-out analyses)

Discussion

14. Key results

Summarize key results with reference to study objectives

15. Limitations

Discuss the limitations of the study, taking into account the validity of the IV assumptions, other sources of potential bias, and imprecision. Discuss both the direction and magnitude of any potential bias and any efforts to address them

16. Interpretations

- a) Meaning: Give a cautious overall interpretation of results in the context of their limitations and comparison with other studies
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not applicable

Leave-one-out analysis plots were listed in Supplementary Figure S1

4. Discussion, paragraph 1, and 6. Conclusions

5. Innovations and limitations, paragraph 2

a, b, c) 4. Discussion, paragraph 2-4

b) Mechanism: Discuss underlying biological mechanisms that could drive a potential causal relationship between the investigated exposure and the outcome and whether the gene-environment equivalence assumption is reasonable. Use causal language carefully, clarifying that IV estimates may provide causal effects only under certain assumptions

c) Clinical relevance: Discuss whether the results have clinical or public policy relevance and to what extent they inform effect sizes of possible interventions

17. Generalizability

a, b, c) 5. Innovations and limitations, paragraph 1-2

Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure

18. Funding

Financial Support and Sponsorship

Describe sources of funding and the role of funders in the present study and, if applicable, sources of funding for the databases and original study or studies on which the present study is based.

19. Data and data sharing

Availability of data and materials

Provide the data used to perform all analyses or report where and how the data can be accessed, and reference these sources in the article. Provide the statistical code needed to reproduce the results in the article or report whether the code is publicly accessible and, if so, where

20. Conflicts of Interest

Conflicts of Interest

All authors should declare all potential conflicts of interest
