STROBE-MR checklist of recommended items to address in reports of Mendelian randomization studies[1,2]

Section/item	Item No	Checklist item description	Reported on Page Number/Line Number	Reported on Section/Paragraph
Title and abstract	1	Indicate Mendelian randomization (MR) as the study's design in the title and/or the abstract if that is a main purpose of the study	Page 1/Line 1	Title
Introduction				
Background	2	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	Page 3/Line 50-56	Introduction/Paragraph 3-4
Objectives	3	State specific objectives clearly, including pre-specified causal hypotheses (if any). State that MR is a method that, under specific assumptions, intends to estimate causal effects	Page 3/Line 50-56	Introduction/Paragraph 3-4
Methods				
Study design and data sources	4	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.	Page 3/Line 60-65	Methods/Paragraph 1
		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	Page 4/Line 72-78	Methods/Paragraph 2
		c) Describe measurement, quality control and selection of genetic variants	Page 4/Line 80-93	Methods/Paragraph 3
		d) For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases	Page 4/Line 72-78	Methods/Paragraph 2
		e) Provide details of ethics committee approval and participant informed consent, if relevant	Page 4/Line 76-78	Methods/Paragraph 2
Assumptions	5	Explicitly state the three core IV assumptions for the main analysis (relevance, independence and exclusion restriction) as well assumptions for any additional or sensitivity analysis	Page 3/Line 60-65	Methods/Paragraph 1
Statistical methods: main analysis	6	Describe statistical methods and statistics used		
		a) Describe how quantitative variables were handled in the analyses (i.e., scale, units, model)	Page 4/Line 95-103	Methods/Paragraph 4
		b) Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected	Page 4/Line 80-93	Methods/Paragraph 3

		c) Describe the MR estimator (e.g. two-stage least squares, Wald ratio) and related statistics. Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples	Page 4/Line 95-103	Methods/Paragraph 4
		d) Explain how missing data were addressed	Not applicable.	Not applicable.
		e) If applicable, indicate how multiple testing was addressed	Page 4/Line 95-103	Methods/Paragraph 4
Assessment of assumptions	7	Describe any methods or prior knowledge used to assess the assumptions or justify their validity	Not applicable.	Not applicable.
Sensitivity analyses and additional analyses	8	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)	Page 4/Line 95-103	Methods/Paragraph 4
Software and pre-registration	9	a) Name statistical software and package(s), including version and settings used	Page 4/Line 105-108	Methods/Paragraph 5
		b) State whether the study protocol and details were pre-registered (as well as when and where)	Not applicable.	Not applicable.
Results				
Descriptive data	10	a) Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow diagram	N/A	N/A
		b) Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions)	Supplementary File	Supplementary File
		c) If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies	Not applicable.	Not applicable.
		d) For two-sample MR: i. Provide justification of 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	Supplementary File	Supplementary File
Main results	11	a) Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale	Supplementary File	Supplementary File
		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	Page 5-7/Line 129-144	Table 1-2 and Figure 2
		c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable.	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)	Page 5-7/Line 129-144	Tabel 1-2 and Figrure 2

Assessment of assumptions	12	a) Report the assessment of the validity of the assumptions	Supplementary File	Supplementary File
		b) Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as I^2, Q statistic or E-value)	Supplementary File	Supplementary File
Sensitivity analyses and additional analyses	13	a) Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions	Supplementary File	Supplementary File
		b) Report results from other sensitivity analyses or additional analyses	Supplementary File	Supplementary File
		c) Report any assessment of direction of causal relationship (e.g., bidirectional MR)	Page 6/Line 138-140	Result/Paragraph 3
		d) When relevant, report and compare with estimates from non-MR analyses	Not applicable.	Not applicable.
		e) Consider additional plots to visualize results (e.g., leave-one-out analyses)	Supplementary File	Supplementary File
Discussion				
Key results	14	Summarize key results with reference to study objectives	Page 7/Line 158-168	Discussion/Paragraph 2
Limitations	15	Discuss limitations of the study, taking into account the validity of the IV assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias and any efforts to address them	Page 8/Line 190-192	Discussion/Paragraph 7
Interpretation	16	a) Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies	Page 7/Line 158-159	Discussion/Paragraph 2
		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	Page 7/Line 159-173	Discussion/Paragraph 2-3
		c) Clinical relevance: Discuss whether the results have clinical or public policy relevance, and to what extent they inform effect sizes of possible interventions	Page 7-8/Line 174-189	Discussion/Paragraph 4-5
Generalizability	17	Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure	Page 8/Line 190-192	Discussion/Paragraph 7
Other Information				
Funding	18	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	None	None
Data and data sharing	19	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	N/A	N/A
Conflicts of Interest	20	All authors should declare all potential conflicts of interest	Page 9/Line 215-216	Conflict of intrest

[1] Skrivankova VW, Richmond RC, Woolf BAR, Yarmolinsky J, Davies NM, Swanson SA, *et al.* Strengthening the Reporting of Observational Studies in Epidemiology using Mendelian Randomization (STROBE-MR) Statement. JAMA. 2021;under review.
[2] Skrivankova VW, Richmond RC, Woolf BAR, Davies NM, Swanson SA, VanderWeele TJ, *et al.* Strengthening the Reporting of Observational Studies in Epidemiology using Mendelian Randomisation (STROBE-MR): Explanation and Elaboration. BMJ. 2021;375:n2233.

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*As the checklist was provided upon initial submission, the page number/line number reported may be changed due to copyediting and may not be referable in the published version. In this case, the section/paragraph may be used as an alternative reference.