**STROBE-MR checklist of recommended items to address in reports of Mendelian randomization studies**12

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| **Item No.** | **Section** | **Checklist item** | **Page No.** | **Relevant text from manuscript** |
| 1 | **TITLE and ABSTRACT** | 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 | 1 | Novel insights into causal effects of lipid and lipid-lowering targets with autoimmune thyroid disease |
|  | **INTRODUCTION** |  |  |  |
| 2 | **Background** | 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 | 4 | Page 4, lines 67 to 77 describe the background of this study. |
| 3 | **Objectives** | 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 | 4-5 | Page 4, line 85 to page 5, line 92 describe the purpose of the study and why MR is used to conduct the study. |
|  | **METHODS** |  |  |  |
| 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. | 5-6 | Page 5, lines 94 to page 6,line 111, describe the design of the study. |
|  | 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 | 7 | Page 7, lines 141 to 149 describe the data of the disease population involved in the study and the sample size. |
|  | c) | Describe measurement, quality control and selection of genetic variants | 6-7 | From page 6, line 112 to page 7, line 134, the screening process of instrumental variables for circulating lipids and drug targets is described, as well as the use of F statistics to exclude the effects of weak instrumental variables. |
|  | d) | For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases | 7-9 | Page 7, line 150 to page 9, line 188 describe in detail the assessment methods for different exposures and diseases. |
|  | e) | Provide details of ethics committee approval and participant informed consent, if relevant |  | Ineligible |
| 5 | **Assumptions** | 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 | 5 | Page 5, lines 104 to 107 describe the 3 assumptions that this research design meets. |
| 6 | **Statistical methods: main analysis** | Describe statistical methods and statistics used |  |  |
|  | a) | Describe how quantitative variables were handled in the analyses (i.e., scale, units, model) |  | Ineligible |
|  | b) | Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected | 6-7 | From page 6, line 112 to page 7, line 134, the screening process of instrumental variables for circulating lipids and drug targets is described, as well as the use of F statistics to exclude the effects of weak instrumental variables. |
|  | 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 | 7-8 | Page 7, line 150 to page 8, line 171 describe the MR estimator and related statistics. |
|  | d) | Explain how missing data were addressed | 6-7 | Page 6, line 131 to page 7, line 134 describe how to handle missing data. |
|  | e) | If applicable, indicate how multiple testing was addressed | 9 | Page 9, lines 189 to 197, describes how to resolve multiple testing. |
| 7 | **Assessment of assumptions** | Describe any methods or prior knowledge used to assess the assumptions or justify their validity | 5 | Page 5, lines 101 to 102, describes MR analysis using coronary atherosclerotic heart disease as a positive control. |
| 8 | **Sensitivity analyses and additional analyses** | 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 | The sensitivity analysis is described on page 9, lines 189 to 197. |
| 9 | **Software and pre-registration** |  |  |  |
|  | a) | Name statistical software and package(s), including version and settings used |  | This study used R Program (version 4.3.2) to calculate statistical results. |
|  | b) | State whether the study protocol and details were pre-registered (as well as when and where) |  | The study protocol and details were not preregistered. |
|  | **RESULTS** |  |  |  |
| 10 | **Descriptive data** |  |  |  |
|  | a) | Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow diagram | 10 | Page 10, lines 199 to 211 describe the number of IVs included in the study. |
|  | b) | Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions) |  | Supplementary material |
|  | c) | If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies |  | The results did not include meta-analysis content. |
|  | 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 | 6 | Page 6, lines 112 to 129 report similarities in genetic variant exposure associations between the exposure and outcome samples. The Supplementary Material provides information on the number of individuals that overlap between the exposure and outcome studies. |
| 11 | **Main results** |  |  |  |
|  | a) | Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale | 10-11 | Page 10, line 199 to page 11, line 226 describe the associations between genetic variants and exposures and between genetic variants and outcomes. |
|  | 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 | 11-12 | Page 11, line 227 to page 12, line 251 describe the MR estimates and uncertainty measures for the drug target MR results and mediation analysis results. |
|  | c) | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |  | Ineligible |
|  | d) | Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure) |  | Figure2 、Figure3、Table3、Table4 |
| 12 | **Assessment of assumptions** |  |  |  |
|  | a) | Report the assessment of the validity of the assumptions | 8 | Page 8, lines 170 to 171 describe a method for verifying the robustness of the assumptions. |
|  | b) | Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as *I2*, Q statistic or E-value) |  | Table3、Table4 |
| 13 | **Sensitivity analyses and additional analyses** |  |  |  |
|  | a) | Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions | 11、12 | The results of the sensitivity analysis are reported on page 10, lines 216 to 217, and page 11, lines 225 to 226. |
|  | b) | Report results from other sensitivity analyses or additional analyses |  | Table3 |
|  | c) | Report any assessment of direction of causal relationship (e.g., bidirectional MR) |  | Ineligible |
|  | d) | When relevant, report and compare with estimates from non-MR analyses |  | Table3 |
|  | e) | Consider additional plots to visualize results (e.g., leave-one-out analyses) |  | No |
|  | **DISCUSSION** |  |  |  |
| 14 | **Key results** | Summarize key results with reference to study objectives | 12 | Page 12, lines 252 to 260 summarize the key results of the research objectives. |
| 15 | **Limitations** | 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 | 14-15 | The limitations of the study are reported on page 14, lines 304 to page 15 , line309. |
| 16 | **Interpretation** |  |  |  |
|  | a) | Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies | 12-13 | Page 12, line 261 to page 13, line 273 describe and explain the comparison results with other studies. |
|  | 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 | 13-14 | Page 13, line 274 to page 14, line 299 report the potential mechanisms of the study findings. |
|  | c) | Clinical relevance: Discuss whether the results have clinical or public policy relevance, and to what extent they inform effect sizes of possible interventions | 14 | Page 14, lines 300 to 304 report the clinical significance of the study results. |
| 17 | **Generalizability** | Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure | 14-15 | Page 14, lines 300 to page 15，line 309 report the generalizability of the findings. |
|  | **OTHER INFORMATION** |  |  |  |
| 18 | **Funding** | 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 | 2 | Page 2, lines 25 to 28 report the funding sources for this research. |
| 19 | **Data and data sharing** | 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 | 15 | Page 15, lines 321 to 328 reports the data availability for this study. |
| 20 | **Conflicts of Interest** | All authors should declare all potential conflicts of interest | 2 | The authors have no conflict of interest to disclose. |

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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.