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

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	2	Abstract: We performed a mendelian randomization (MR) study in Europe, using genetic variants associated with relative macronutrient intake among 268,992 participants, and genetic variants with 17 ADs outcomes from two large-scale biobanks including up to 951,301 participants.
	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	Explained in the Introduction section.
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	MR is a popular statistical method to infer causality, when certain assumptions are met
	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.	15	Explained in the "Data sources" of Methods section.
	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	Supplementary Table 1	Supplementary Data 1 provides detailed information on these GWAS studies, including sample size.
	c)	Describe measurement, quality control and selection of genetic variants	16-17	Explained in the "Selection of the genetic IVs" of Method section.
	d)	For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases	15	ICD-9 or ICD-10 was used for the endpoint definition of the above-mentioned ADs diseases.
	e)	Provide details of ethics committee approval and participant informed consent, if relevant	5	The data utilized in this study were sourced from publicly available studies with the consent and ethical approval of relevant participants, ethical

				approval from the institutional review board was not required for this study.
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	4-5	Adherence to three fundamental assumptions is crucial for ensuring the validity of causal estimates in MR studies17,18: First, the genetic variants exhibit a significant association with the exposure. Second, the genetic variants should be independent of confounders. Third, the impact of genetic variants on the outcome is solely mediated through the exposure
6	**Statistical methods: main analysis**	Describe statistical methods and statistics used	16-18	(a)–(e) were described in the Methods section.
	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 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**	Describe any methods or prior knowledge used to assess the assumptions or justify their validity	16-18	It was described in the Methods section.
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)	18	A series of sensitivity analyses were performed to assess the robustness and reliability of the results. The Cochran's Q statistic was calculated to assess heterogeneity among IVs55. MR-Egger regression with intercept terms was utilized to assess the potential presence of horizontal pleiotropy56. In addition to the MR-Egger method, MR-PRESSO global test was utilized as an additional tool for pleiotropy assessment with the “MRPRESSO (version 1.0)” package57. MR-RAPS and weighted median were also conducted to evaluate the robustness of our calculated results. MR-RAPS method could offer robust inferences for MR analysis with multiple weak instruments58. Weighted

				median method could allow up to 50% of the information from variants to violate the MR hypothesis in the presence of horizontal pleiotropy59. Besides, MR Steiger test was performed to estimate the potential reverse causal impact46. We also performed leave-one-out test to detect the influence of a single IV on the overall MR estimate50.
9	**Software and pre-registration**			
	a)	Name statistical software and package(s), including version and settings used	17-20	It was described in the Methods section.
	b)	State whether the study protocol and details were pre-registered (as well as when and where)	No Applicable	This is a secondary analysis based on summary statistics from existing, published studies. The ethical approval and informed consent have been obtained by all original studies.
	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	Supplementary Table 1	
	b)	Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions)	Supplementary Table 1	
	c)	If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies	No 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 Table 1	The population ancestry of the dataset we used all came from Europe and came from independent biobanks
11	**Main results**		5-11	It was described in the Results section.
	a)	Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale		It was described in the Results section.
	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		

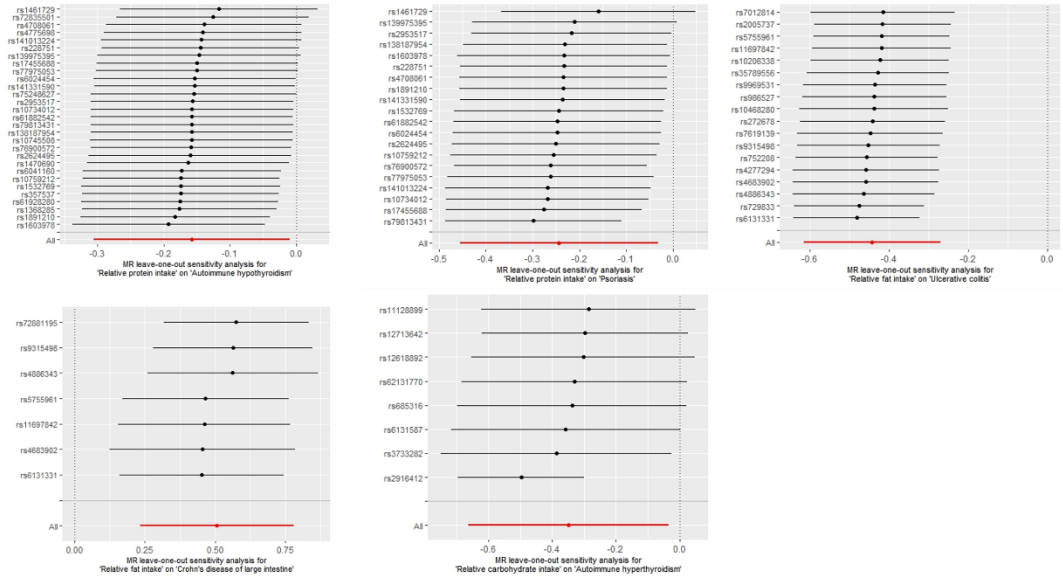
		c)	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	No Applicable	
		d)	Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure)	Fig. 2 and 3	
12	**Assessment of assumptions**			5-11	It was described in the Results section.
		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 I^2, Q statistic or E-value)		
13	**Sensitivity analyses and additional analyses**			5-11	It was described in the Results section.
		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 direction of causal relationship (e.g., bidirectional MR)		
		d)	When relevant, report and compare with estimates from non-MR analyses	No Applicable	
		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	11	It was described in the Discussion section.
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	It was described in the Discussion section.
16	**Interpretation**				
		a)	Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies	13	It was described in the Discussion section.
		b)	Mechanism: Discuss underlying biological mechanisms that could drive a potential causal relationship between the investigated exposure and the	12	It was described in the Discussion section.

		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	13	It was described in the Discussion section.
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	It was described in the Discussion section.
	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	21	This work was supported by National Natural Science Foundation of China (grants 82473628 to Y.J.S.).
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	20	The data utilized in this study were acquired from publicly accessible databases. The code implemented in this research will be made available by the corresponding author upon reasonable request.
20	**Conflicts of Interest**	All authors should declare all potential conflicts of interest	21	There authors report no conflicts of interests.

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.

A



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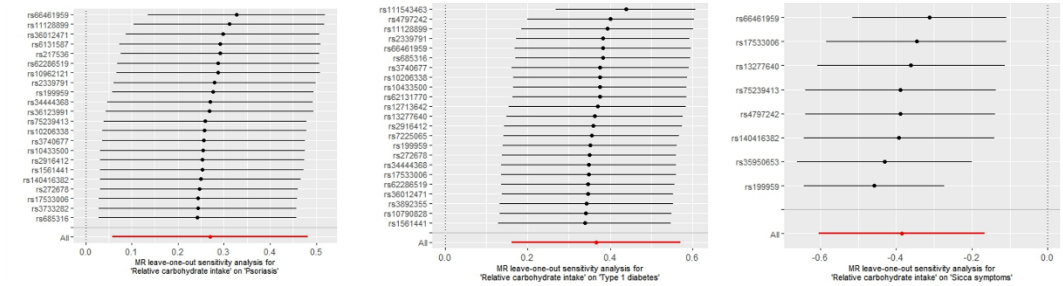

Supplementary Figure 1 | Result of leave-one-out test. A leave-one-out test of autoimmune diseases from the FinnGen biobank**. B** leave-one-out test of autoimmune diseases from the MVP biobank. MVP, Million Veteran Program.