Research Article

Jing Wang-Chang, Jia Ma, Han Su, Xiaoqiang Wu, Shunfeng Zhao, Yuan Cai, Ning Feng, Lina Sun, Xin Zhao, Kai Feng, Haoxiao Chang* and Haowen Li*

Multiple sclerosis and type 1 diabetes: a Mendelian randomization study of European ancestry

https://doi.org/10.1515/med-2025-1363
Received February 5, 2025; accepted December 1, 2025; published online December 19, 2025

Abstract

Objectives: Observational studies have indicated that type 1 diabetes (T1D) is prevalent in multiple sclerosis (MS), yet the causality remains unclear. The purpose of this study was to assess the causal association between MS and T1D.

Methods: We employed a Mendelian randomization method using two samples to research the causal association between MS and T1D. The study primarily utilized the inverse variance weighted (IVW) method, and we use three methods (MR Egger, Weighted median, Weighted mode) for auxiliary analysis. To avoid reverse causality, we employed the Steiger Test method to further examine the screened SNPs. Furthermore, sensitivity analysis was conducted to ensure the robustness of the obtained results.

Results: When MS was considered as the exposure variable and T1D as the outcome variable, the results indicated a significant positive correlation (IVW, OR=1.078, 95 % CI: 1.041–1.117; p<0.001). Conversely, when T1D is the exposure in question, the causal relationship with MS remains undetermined. These results were further validated through sensitivity analysis.

Conclusions: The MR analysis results indicate that there is a causal relationship between MS and T1D. We provide compelling genetic evidence to support the causal connection between MS and an increased risk of T1D.

Keywords: multiple sclerosis; type 1 diabetes; Mendelian randomization analysis; genetics

Jing Wang and Jia Ma contributed equally to this work.

***Corresponding authors: Haoxiao Chang and Haowen Li**, China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, No.119 South 4th Ring West Road, Fengtai District, Beijing 100070, China, E-mail: changhaoxiao@iirc.org.cn (H. Chang), heaven_lhw@163.com (H. Li). https://orcid.org/0000-0001-6338-7562 (H. Chang). https://orcid.org/0000-0002-7526-5615 (H. Li)

Jing Wang-Chang, Lina Sun and Xin Zhao, China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China. https://orcid.org/0009-0004-9045-0669 (J. Wang-Chang). https://orcid.org/0009-0009-5954-3396 (L. Sun). https://orcid.org/0009-0007-0692-1141 (X. Zhao)

Jia Ma and Kai Feng, Department of Neurology, Beijing Shunyi Hospital, Beijing, China. https://orcid.org/0009-0003-0358-0506 (J. Ma). https://orcid.org/0000-0002-4251-5729 (K. Feng)

Han Su, First Clinical Medical College, Anhui Medical University, Hefei, Anhui, China. https://orcid.org/0009-0003-6084-6956

Xiaoqiang Wu, Department of Neurosurgery and Neurological Intensive Care Unit, Sixian People's Hospital, Sixian, China. https://orcid.org/0000-0001-7494-6390

Shunfeng Zhao and Ning Feng, Department of Clinical Laboratory, Liaocheng Third People's Hospital, Sub-Regional Centre of China National Clinical Research Center for Neurological Diseases, Liaocheng, China. https://orcid.org/0009-0008-4465-3536 (S. Zhao). https://orcid.org/0009-0009-4867-696X (N. Feng)

Yuan Cai, Division of Neurology, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China. https://orcid.org/0000-0002-7551-2866

Introduction

Multiple sclerosis (MS) is a disease of the immune system that involves inflammation and damage to the protective layer of nerve fibers in the brain and spinal cord, known as demyelination. This autoimmune condition leads to the progressive deterioration of the central nervous system (CNS) [1]. This disease is believed to result from complex interactions between genetic and environmental factors, primarily affecting middle-aged and young adults [2]. It is a recurrent condition without a cure [3]. Comorbidities are common in MS, and chronic comorbidities can lead to delayed diagnosis, increased mortality, and challenges in clinical management and treatment.

Epidemiological studies have found that MS is more prevalent among individuals with autoimmune diseases, including T1D [4]. Although implicating different organs, autoimmune diseases have the shared pathogenesis or are

caused by the shared predisposing factors [5, 6], so comorbidities of autoimmune diseases are common. Previous studies have shown that MS and T1D share immunological and epidemiological characteristics [7]. T1D, a chronic autoimmune disease, is characterized by the destruction of β cells. This ultimately leads to a complete deficiency of insulin [8]. There is evidence to suggest that T1D may directly exacerbate autoimmune dysfunction in MS, suggesting a possible common mechanism in the development of these two diseases [9]. However, the causal relationship between MS and T1D has not been elucidated. In order to examine the genetic causality, we implemented the two sample MR method to scrutinize the plausible causal linkage between MS and T1D.

Mendelian randomization is a statistical approach that harnesses genetic instrumental variables to establish causal links between exposure and outcome [10]. It minimizes bias caused by unmeasured confounding factors and reverse causality [11], providing stronger evidence for causal inference than observational studies [12]. In this study, we implemented the two sample MR method to scrutinize the plausible causal linkage between MS and T1D.

Methods

Study design

This study assessed the Two Sample MR analysis method and Genome-Wide Association Study (GWAS) summary data to estimate the causal effect of exposure on outcomes [13, 14], the objective of this research was to assess the causal association between MS and T1D, its complications. The study is based on three Assumption of Mendelian inheritance [15]: (1) The exposure demonstrates a significant correlation with the selected instrumental variable. (2) No confounding factors are found to be linked to the instrumental variables. (3) The instrumental variables exclusively influence outcomes via exposure and exclude any other mechanisms (Figure 1).

By applying these assumptions and the two sample MR method, this study seeks to provide stronger evidence for the causal relationship between MS and T1D minimizing the bias caused by unmeasured confounding factors and reverse causality.

Data resource

For MS, we utilized a large scale GWAS dataset from the International Multiple Sclerosis Genetics Consortium (IMSGC), comprising of 47,429 cases and 68,374 controls [16]. For T1D, we utilized a GWAS data from the UK-Biobank, comprising of 18,942 cases and 501,638 controls [17]. We used the largest and most comprehensive database that has been analyzed to date (Table 1). To decrease the potential deviation in the analysis of MR caused by population stratification, all the data utilized in this study were obtained from individuals of European descent. Given that the research relied on publicly available GWAS aggregated statistical data and did not involve individual-level data analysis, ethical approval was not sought.

Ethical approval

All data used in this study were obtained from public databases. Formal approval from the Medical Ethics Review Committee was not required as the Medical Research Involving Human Subjects Act does not apply for this study.

Statistical analysis

Selection of instrumental variables (IVs)

Pursuant to the MR analysis principle, for the MS dataset, the sample size is small, to expand the SNP screening range, we set the screening threshold at $P<5 \times 10^{-6}$, for the T1D dataset, we set the screening threshold at $P<5 \times 10^{-8}$. We set the genetic distance to 10,000 kb and excluded SNPs with $R^2<0.001$. From the exposure dataset, we screened out instrumental variables without a linkage effect, and further filtered those significantly associated with outcome ($P<5 \times 10^{-5}$) among the screened instrumental variables. In addition, we employed the Steiger Test method to further examine the screened SNPs, indicating that the selected instrumental variables did not demonstrate a reverse causal relationship and were relatively robust [18]. To ensure the instrumental variables possessed significant statistical significance, we calculated the F statistics for each SNP using the formula $F=R^2 \times (N-2)/(1-R^2)$, $R^2=2 \times EAF \times (1-EAF) \times \beta^2$ (R^2: genetic variance explained by each SNP; N: sample size of the exposed dataset; EAF: the effect allele frequency; β: the estimated effect of SNP), only SNPs with F statistics greater than 10 were included as instrumental variables for analysis [19].

Mendelian randomization analysis

In our research, we primarily use the Inverse Variance Weighted (IVW) method as our main analysis tool, this is the most commonly used MR analysis method, due to its

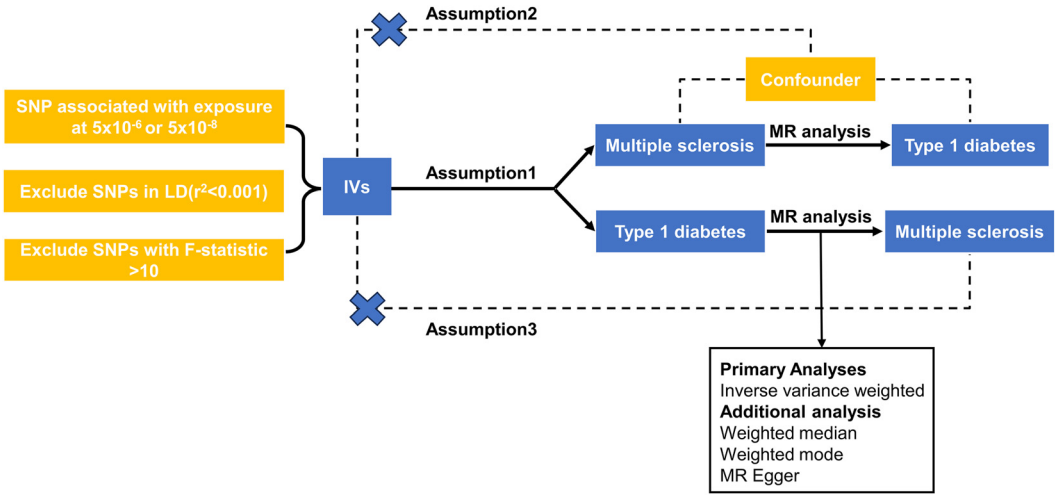

Figure 1: Diagram of the Mendelian randomization study for the association between multiple sclerosis and type 1 diabetes. SNP, single nucleotide polymorphism; IVs, instrumental variables.

Table 1: Exposure and outcome gwas data information.

Traits	Ncase	Ncontrol	Ncases	Year	GWAS id
Multiple sclerosis	47,429	68,374	115,803	2019	Ieu-b-18
Type 1 diabetes	18,942	501,638	520,580	2021	Ebi-a-GCST90014023

simplicity and ease of implementation [20]. It estimates the causal effect by combining the results of multiple genetic variants using the inverse of the variance as a weight. The IVW method does not require an intercept term in the regression model and uses the reciprocal of the outcome variance (standard error's quadratic power) as the weight for fitting [21]. Given the significant heterogeneity among the instrumental variables, we employed the random-effects IVW model as our primary analytical method, as it better accommodates this heterogeneity and provides more robust causal estimates. To enhance the stability of our results, we also employ "MR egger" [22], "Weighted median" [23], and "Weighted mode" as supplementary methods. By combining these approaches, we aim to provide more accurate and reliable estimates of the causal effects associated with genetic variants and their impact on various traits or diseases.

Sensitivity analysis

In sensitivity analysis, to eliminate confounding factors that could introduce bias into the results, we utilized the NHGRI-EBI Catalog (https://www.ebi.ac.uk/gwas/) to meticulously examine each SNP. We excluded those SNPs that were directly associated with the outcome or were suspected of having a potential causal relationship. And then, we employ the MR Egger [22] to assess pleiotropy bias. We utilize MR PRESSO [24] to detect level pleiotropy outliers. Heterogeneity testing is employed to identify disparities between individual instrumental variables. Cochran's Q statistic utilized for calculating heterogeneity [25]. If genetic variance estimates for causal effects exhibit heterogeneity ($p \leq 0.05$), we employ the I^2 metric to measure the portion of SNP variation explained by this divergence [26]. We adopt leave one out test to investigate the influence of individual SNPs on causal relationships and to verify the stability of the results [27]. The statistical analyses were using R (version 4.3.0), and the Two Sample MR software package was utilized to analyze all the collected data. All code used in the analysis has been uploaded to GitHub. We set p value<0.05 as statistically significant.

Results

MS was considered as the exposure variable, while T1D was investigated as the outcome variable, we selected 103 SNPs as instrumental variables, and F statistics are all greater than 10 (Table S1). The MR results revealed that the beta values of the four analysis methods were consistent, the odds ratios (OR) assess was 1.078 (IVW, 95 % CI: 1.041–1.117; $p<0.001$) (Table 2). Sensitivity analysis was also conducted, and heterogeneity testing demonstrated moderate heterogeneity ($Q=196.324$, $p<0.05$). Then, we calculated the I^2 ($I^2=48.045$) (Table S3), which is considered moderate, indicating that heterogeneity is acceptable [26]. MR Egger showed no

pleiotropy (intercept=0.003, p=0.585). When T1D was used as the exposure variable, MS as the outcome variable, we selected 52 SNPs as instrumental variables, and all F statistics were greater than 10 (Table S2). MR results indicated no correlation (IVW, OR=0.994, 95 % CI: 0.947–1.044; p=0.817).

Scatter plot illustrates the correlation between MS and T1D (Figure S1). Leave One Out [27] analyzing each SNP's impact by excluding it revealed that the results remained unchanged (Figure S2, Table S4 and S5). Based on the findings, a significant association between MS and T1D is indicated, this implies that MS elevates the likelihood of developing T1D (Figure 2).

Discussion

This is the first study to Mendelian randomization investigation in Multiple sclerosis and Type 1 diabetes. The current findings from Mendelian randomization research suggest that MS, when considered as an exposure, exhibits a positive causal relationship with T1D. Conversely, when T1D is the exposure in question, the causal relationship with MS remains undetermined.

Previous observational studies have indicated that individuals with MS have a significantly higher risk of developing T1D [9, 28]. In a population-based investigation carried out in Sardinia, it came to light that the frequency of T1D amid MS patients surpasses that of the overall population by fivefold [28].A recent study has identified common genetic characteristics and pathways between T1D and MS through a systems biology approach. Nahid and colleagues analyzed the gene expression profiles of peripheral blood mononuclear cells (PBMCs) and pancreatic β-cells from T1D patients, as well as PBMCs and cerebrospinal fluid (CSF) from MS patients. By integrating the differentially expressed genes with protein-protein interaction data, they constructed an Inquiry-Inquiry Protein-Protein Interaction (QQPPI) network. Further analysis of the QQPPI network revealed that the key genes shared in both T1D and MS diseases include those involved in immune response (IKBKE, NF-κB2, and RAC1), the proteasome (PSMA1), the spliceosome (SRPK1, YBX1, and MYC), and apoptosis (HSP90AB1) [29]. A recent study has further confirmed the shared role of the human leukocyte antigen (HLA) genes, particularly the DRB1 and DQB1 alleles, in the pathogenesis of MS and T1D through meta-analysis and the integration of data from multiple studies [30]. The research findings indicate that certain HLA genetic variants significantly increase the risk of developing both conditions. The perspective of HLA genes acting synergistically in MS and T1D enhances the explanatory power of genetic mechanisms [30]. This phenomenon can be attributed to the presence of DRB1*0405-DQA1*0501-DQB1*0301, DRB1*0301-DQA1*0501-DQB1*0201 haplotypes in this distinctive population, these two haplotypes have been identified as risk factors for both diseases [31]. Genetic variations can only partially explain the concurrent occurrence of MS and T1D, suggesting that other factors are also involved. A recent study has explored in detail the mechanism of enhanced autoimmune response in patients with MS, including abnormal activation of T and B cells, overexpression of inflammatory factors, and disruption of the blood-brain barrier. These immune disorders may increase the risk of T1D in patients with MS [32].

Multiple population-based studies and high-quality clinical investigations involving T1D patients consistently demonstrate an elevated risk of MS development [33, 34]. These results present a fascinating yet perplexing epidemiological phenomenon, which the original researchers described as "together at last" when characterizing the MS-T1D risk association. Notably, despite immunological assertions that HLA patterns of T1D and MS are mutually exclusive [34], rigorous clinical evidence has conclusively

Table 2: The causal association of multiple sclerosis with type 1 diabetes.

Exposure	Outcome	Method	nSNP	Beta	Se	p-Value	OR (95 % CI)
MS	T1D	Inverse variance weighted	103	0.075	0.018	0.000	1.078 (1.041–1.117)
		MR egger	103	0.055	0.041	0.186	1.056 (0.974–1.145)
		Weighted median	103	0.041	0.023	0.070	1.042 (0.997–1.090)
		Weighted mode	103	0.034	0.032	0.291	1.034 (0.972–1.101)
T1D	MS	Inverse variance weighted	52	−0.006	0.025	0.817	0.994 (0.947–1.044)
		MR egger	52	0.000	0.055	0.993	1.000 (0.898–1.113)
		Weighted median	52	−0.004	0.031	0.890	0.996 (0.937–1.058)
		Weighted mode	52	−0.008	0.037	0.825	0.992 (0.922–1.067)

MS, multiple sclerosis; T1D, type 1 diabetes.

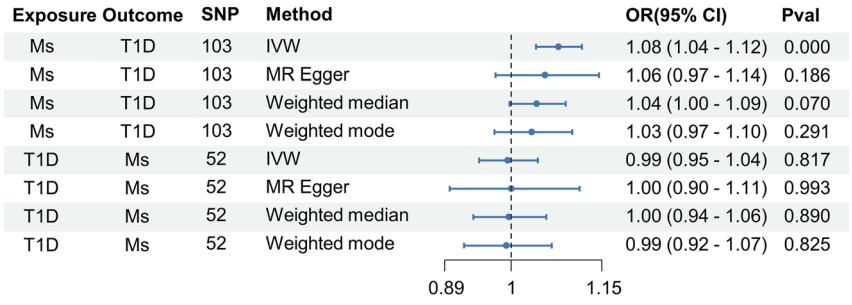

Figure 2: The causal effect estimates from various Mendelian randomization methods. This figure shows the effect of multiple sclerosis on type 1 diabetes. MS, multiple sclerosis; T1D, type 1 diabetes; IVW, inverse variance weighted; OR, odds ratio; CI, confidence interval.

established bidirectional disease risk between these conditions. While our MR analysis indicates a causal relationship between MS and T1D, we emphasize that the genetic evidence specifically supports MS as a causal factor for increased T1D risk. Conversely, when T1D is examined as the exposure, the causal relationship with MS remains statistically undetermined. Given that autoimmune diseases typically arise from complex interactions between genetic predisposition and environmental factors [5], we propose that environmental triggers or other modulators may underlie the observed increased MS risk in T1D patients. Alternatively, future studies may benefit from incorporating more comprehensive and ethnically diverse genomic datasets for MR analyses to further elucidate the underlying genetic relationships.

Uncovering this causal relationship between T1D and MS is crucial for disease prevention and management, ultimately reducing the significant burden of disease. In comparison to observational research, this study possesses significant advantages. GWAS data employed in this research are the largest and most publicly available to date [16, 17]. Rather than solely relying on the IVW method as the main analysis technique, this study also employs various MR analysis methods to enhance the accuracy of our findings. In addition, we prevent potential horizontal pleiotropy in genetic instrumental variables, ensuring the validity of our results. Concurrently, we employ the Steiger Test to detect and screen SNPs to avoid reverse causal relationships [18]. We calculate the F statistics of the SNPs and exclude those with F statistics greater than 10, thus guaranteeing the robustness of the final SNPs included in the analysis. Lastly, we perform multiple sensitivity analyses on our results to guarantee their reliability.

However, this study does possess limitations. Firstly, the GWAS data utilized were sourced from European samples, which raises the question of whether the observed results are applicable to other populations. As such, future studies exploring the causal relationship between MS and T1D using the Mendelian method should consider incorporating samples from diverse ethnic groups, thereby enhancing the breadth and universality of the findings. Secondly, the publicly aggregated GWAS data used in this study prevent subgroup analysis, which may lead to some bias in the results. Finally, we acknowledge that this study lacks experimental validation using an independent cohort.

This study is the first to decipher the causal relationship between MS and T1D, supplementing previous observational studies and providing a reasonable biological explanation. Our findings contribute to enhancing the understanding of the comorbidity mechanism between MS and T1D. Thus, this study significantly contributes to the field of MS and T1D research, offering valuable insights into their potential genetic connections. Concurrently, our research offers a novel foundation for early prevention among T1D patients.

Acknowledgements: We thank the International Multiple Sclerosis Genetics Consortium and the UK Biobank consortium for providing GWAS summary statistics data for our analysis.

Funding information: This study was supported in part by the National Science Foundation of China (82301453) and a grant from the Special Fund for Health Development and Scientific Research of Shunyi District, Beijing, China (Wsjkfzkyzx-2023-y-07).

Author contributions: Conception and study design: HC, HL and JW-C. Drafting of the manuscript: HC, JW-C, and JM. Acquisition of data: JW-C, JM, SZ, KF and NF. Analysis or interpretation of data: JW-C, SZ, YC, LS, XW, HS, and XZ. Critical revision of the manuscript for important intellectual content: HC, HS, and HL. All authors contributed to the article and approved the submitted version.

Conflict of Interests: All authors claimed no competing interests.

Data Availability Statement: The GWAS summary datasets for MS (GWAS ID: ieu-b-18) and T1D (GWAS ID: GCST90014023), are available through the IEU Open GWAS Project (https://gwas.mrcieu.ac.uk/datasets).

References

1. Milo R, Miller A. Revised diagnostic criteria of multiple sclerosis. Autoimmun Rev 2014;13:518–24.
2. Jankowska-Kieltyka M, Roman A, Nalepa I. The air we breathe: air pollution as a prevalent proinflammatory stimulus contributing to neurodegeneration. Front Cell Neurosci 2021;15:647643.
3. Brown C, McKee C, Halassy S, Kojan S, Feinstein D, Chaudhry G. Neural stem cells derived from primitive mesenchymal stem cells reversed disease symptoms and promoted neurogenesis in an experimental autoimmune encephalomyelitis mouse model of multiple sclerosis. Stem Cell Res Ther 2021;12:499.
4. Almeida C, Venade G, Duarte D, Vaz A, Nascimento E. Type 1 diabetes mellitus and multiple sclerosis: an association to consider. Cureus 2022; 14:e30762.
5. Conrad N, Misra S, Verbakel J, Verbeke G, Molenberghs G, Taylor P, et al. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. Lancet (London, England) 2023;401:1878–90.
6. Rose N. Prediction and prevention of autoimmune disease in the 21st century: a review and preview. Am J Epidemiol 2016;183:403–6.
7. Handel A, Handunnetthi L, Ebers G, Ramagopalan S. Type 1 diabetes mellitus and multiple sclerosis: common etiological features. Nat Rev Endocrinol 2009;5:655–64.
8. Gillespie K. Type 1 diabetes: pathogenesis and prevention. CMAJ (Can Med Assoc J): Canadian Medical Association Journal=Journal de l'Association Medicale Canadienne 2006;175:165–70.
9. Tettey P, Simpson S, Taylor B, van der Mei I. The co-occurrence of multiple sclerosis and type 1 diabetes: shared aetiologic features and clinical implication for MS aetiology. J Neurol Sci 2015;348:126–31.
10. Bowden J, Holmes M. Meta-analysis and Mendelian randomization: a review. Res Synth Methods 2019;10:486–96.
11. Grover S, Del Greco MF, Stein C, Ziegler A. Mendelian randomization. Methods Mol Biol 2017;1666:581–628.
12. Sekula P, Del Greco MF, Pattaro C, Köttgen A. Mendelian randomization as an approach to assess causality using observational data. J Am Soc Nephrol: JASN 2016;27:3253–65.
13. Burgess S, Davey Smith G, Davies N, Dudbridge F, Gill D, Glymour M, et al. Guidelines for performing Mendelian randomization investigations: update for summer 2023. Wellcome Open Research 2019;4:186.
14. Leiserson M, Eldridge J, Ramachandran S, Raphael B. Network analysis of GWAS data. Curr Opin Genet Dev 2013;23:602–10.
15. Sanderson E, Glymour M, Holmes M, Kang H, Morrison J, Munafò M, et al. Mendelian randomization. Nat Rev Methods Primers 2022;2:6.
16. Patsopoulos NA, Baranzini SE, Santaniello A, Shoostari P, Cotsapas C, Wong G, et al. Multiple sclerosis genomic map implicates peripheral immune cells and microglia in susceptibility. Science (New York, N.Y.) 2019;365:eaav7188.
17. Chiou J, Geusz R, Okino M, Han J, Miller M, Melton R, et al. Interpreting type 1 diabetes risk with genetics and single-cell epigenomics. Nature 2021;594:398–402.
18. Hemani G, Tilling K, Davey Smith G. Orienting the causal relationship between imprecisely measured traits using GWAS summary data. PLoS Genet 2017;13:e1007081.
19. Burgess S, Thompson S. Avoiding bias from weak instruments in Mendelian randomization studies. Int J Epidemiol 2011;40:755–64.
20. Bowden J, Del Greco MF, Minelli C, Davey Smith G, Sheehan N, Thompson J. A framework for the investigation of pleiotropy in two-sample summary data Mendelian randomization. Stat Med 2017;36:1783–802.
21. Slob E, Burgess S. A comparison of robust Mendelian randomization methods using summary data. Genet Epidemiol 2020;44:313–29.
22. Bowden J, Davey Smith G, Burgess S. Mendelian randomization with invalid instruments: effect estimation and bias detection through egger regression. Int J Epidemiol 2015;44:512–25.
23. Bowden J, Davey Smith G, Haycock P, Burgess S. Consistent estimation in Mendelian randomization with some invalid instruments using a weighted median estimator. Genet Epidemiol 2016;40:304–14.
24. Verbanck M, Chen C, Neale B, Do R. Detection of widespread horizontal pleiotropy in causal relationships inferred from Mendelian randomization between complex traits and diseases. Nat Genet 2018; 50:693–8.
25. Bowden J, Del Greco MF, Minelli C, Zhao Q, Lawlor D, Sheehan N, et al. Improving the accuracy of two-sample summary-data Mendelian randomization: moving beyond the NOME assumption. Int J Epidemiol 2019;48:728–42.
26. <Heterogeneity and subgroup analyses in Cochrane Consumers and Communication Group.pdf>.
27. Wei Z, Yang B, Tang T, Xiao Z, Ye F, Li X, et al. Gut microbiota and risk of five common cancers: a univariable and multivariable Mendelian randomization study. Cancer Med 2023;12:10393–405.
28. Marrosu MG, Cocco E, Lai M, Spinicci G, Pischedda MP, Contu P. Patients with multiple sclerosis and risk of type 1 diabetes mellitus in Sardinia, Italy: a cohort study. Lancet 2002;359:1461–5.
29. Safari-Alighiarloo N, Taghizadeh M, Mohammad Tabatabaei S, Namaki S, Rezaei-Tavirani M. Identification of common key genes and pathways between type 1 diabetes and multiple sclerosis using transcriptome and interactome analysis. Endocrine 2020;68:81–92.
30. Wang J, Jelcic I, Mühlenbruch L, Haunerdinger V, Toussaint NC, Zhao Y, et al. HLA-DR15 molecules jointly shape an autoreactive T cell repertoire in multiple sclerosis. Cell 2020;183:1264–81.e20.
31. Pozzilli V, Grasso E, Tomassini V. Similarities and differences between multiple sclerosis and type 1 diabetes. Diabetes Metabol Res Rev 2022; 38:e3505.
32. van Langelaar J, Rijvers L, Smolders J, van Luijn MM. B and T cells driving multiple sclerosis: identity, mechanisms and potential triggers. Front Immunol 2020;11:760.
33. Dorman JS, Steenkiste AR, Burke JP, Songini M. Type 1 diabetes and multiple sclerosis: together at last. Diabetes Care 2003;26:3192–3.
34. Nielsen NM, Westergaard T, Frisch M, Rostgaard K, Wohlfahrt J, Koch-Henriksen N, et al. Type 1 diabetes and multiple sclerosis: a Danish population-based cohort study. Arch Neurol 2006;63:1001–4.

Supplementary Material: This article contains supplementary material (https://doi.org/10.1515/med-2025-1363).