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Genetic information supports a causal relationship between trace elements, inflammatory proteins, and COPD: evidence from a Mendelian randomization analysis

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Objective: Dietary factors and nutritional status may be among the risk factors for Chronic Obstructive Pulmonary Disease (COPD). There exists a certain correlation between trace elements and COPD. Through Mendelian Randomization (MR) analysis, we investigated the causal relationships between trace elements, inflammatory proteins, and COPD.

Methods: We employed MR, multivariable MR (MVMR), and two-step MR (TSMR) approaches to assess the causal links between 15 trace elements and COPD, with 91 inflammatory proteins serving as mediators to further elucidate the tripartite causal relationships.

Results: Trace elements such as Folate (OR = 1.293, 95%CI 1.027–1.628; $p = 0.029$), Vitamin D (OR = 1.331, 95%CI 1.071–1.654; $p = 0.010$), Vitamin B12 (OR = 1.424, 95%CI 1.108–1.828; $p = 0.006$), and Iron (OR = 0.741, 95%CI 0.580–0.946; $p = 0.016$) demonstrated causal relationships with COPD. No causal relationship was observed in reverse MR. After adjusting for BMI, Folate (OR = 1.633, 95%CI 1.098–2.429; $p = 0.015$), Iron (OR = 0.507, 95%CI 0.31–0.778; $p = 0.001$), and Vitamin D (OR = 1.511, 95%CI 1.029–2.217; $p = 0.034$) were identified as independent risk factors for COPD, whereas Vitamin B12 (OR = 1.118, 95%CI 0.751–1.666; $p = 0.581$) was not. Mediation analysis indicated that CDCP1 (5.76%) may play a mediating role between Iron and COPD.

Conclusion: Trace elements such as Folate, Vitamin D, Vitamin B12, and Iron have causal relationships with COPD. After BMI adjustment, Folate, Vitamin D, and Iron emerge as independent risk factors. Furthermore, the inflammatory protein CDCP1 may partially mediate the causal relationship between Iron and COPD, offering a scientific basis for dietary recommendations that could benefit COPD patients. The supplementation of trace elements may be advantageous for individuals suffering from COPD.

KEYWORDS

trace elements, inflammatory proteins, COPD, Mendelian randomization, mediation analysis

1 Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous ailment that is progressively becoming the third leading cause of death globally (1). It is primarily characterized by airway pathologies (bronchitis, bronchiolitis) and/or alveolar abnormalities (emphysema) leading to chronic respiratory symptoms (dyspnea, cough, expectoration) and a persistent, progressive limitation of airflow (2). Studies have revealed that nearly half of COPD patients experience weight loss (3) and diminished appetite (4), often resulting in an intake of trace elements significantly below the recommended dietary allowances (5). Observational studies have identified that malnutrition and weight loss are prevalent among COPD outpatient attendees (6), and nutritional supplementation can enhance the quality of life for these patients (7). Trace elements play a protective role in lung function, potentially decelerating the rate of pulmonary decline (8). They also influence the diffusing capacity of the lungs and the strength of the respiratory muscles (9). Deficiencies in trace elements are common in COPD and may influence the progression of the disease (10). Dietary interventions and targeted supplementation of single or multiple trace elements could be beneficial for patients with COPD (11).

Dietary factors and nutritional status may be among the risk factors for COPD. Alterations in dietary habits can modulate the impact of adverse environmental exposures on the lungs (12). For instance, excessive consumption of processed red meat has been associated with an increased risk of developing COPD (13), whereas a high dietary fiber intake is inversely related to the risk of COPD (14). Malnutrition can heighten the risk of mortality in patients with COPD (15), underscoring the pivotal role that nutrition plays in respiratory diseases (16). Relevant studies have identified that diet can influence the development of COPD through three primary mechanisms, with the most significant being the modulation of inflammation (17). Inflammatory responses are correlated with various diseases (18–20), and the intake of trace elements can alleviate the inflammatory reactions associated with COPD (21). Metal ions such as iron and copper in trace elements are crucial to the presence of pulmonary inflammation and oxidative stress in COPD (22), potentially leading to diminished activity of macrophages (23). Exposure to environments like iron factories increases the risk of COPD (24), whereas improving environmental risks can decrease it (25). Inhibiting ferroptosis may alleviate emphysema and airway inflammation (26). There is a correlation between copper and pulmonary inflammation (27). Zinc can mitigate the progression of COPD induced by harmful gasses and offers protective benefits to lung tissue (28). There is also a correlation between zinc and the pathogenesis of COPD (29). Supplementing with vitamins A and K may reduce the risk of emphysema (30), with vitamin K potentially improving the condition (31). Carotene is correlated with lung function (32) and may enhance pulmonary health (33). Vitamin D is associated with respiratory diseases (34), and vitamin E can reduce the risk of COPD (35). Thus, trace elements may be significant influencing factors for patients with COPD (36).

Although observational studies and systematic reviews have established a connection between trace elements, nutritional status (37–41), and COPD, suggesting that malnutrition and deficiencies in trace elements can adversely affect COPD patients, the precise causal relationships and underlying mechanisms remain unclear. Mendelian randomization (MR) is a potential method for causal inference, used to estimate the causal effects of exposure factors on outcomes while controlling for confounding factors and avoiding reverse causation (42). Therefore, we aim to utilize MR analysis to elucidate the causal relationships between trace elements, inflammatory factors, and COPD, thereby providing scientifically sound dietary recommendations for COPD patients.

2 Methods

2.1 Study design

This study employs MR analysis, focusing on 15 trace elements, including Copper, Calcium, Folate, Iron, Vitamin D, and Vitamin B6, as the primary exposures, with COPD as the outcome. To further explore the mechanisms underlying the causal relationship between trace elements and COPD, we consider 91 inflammatory proteins as potential mediators to determine whether these proteins play a significant mediating role in the causal pathway between trace elements and COPD. This research adheres to the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology using Mendelian Randomization (STROBE-MR) Statement (43).

Our MR analysis is structured into three distinct phases. Initially, we employ a two-sample MR approach to investigate whether a causal relationship exists between trace elements and COPD, and to ascertain the presence of any reverse causality, thereby determining the feasibility of further mediation analysis. Subsequently, after adjusting for BMI, we conduct MVMR to identify which trace elements independently contribute to risk. Lastly, we utilize TSMR to examine whether the causal effects are mediated by any of the 91 inflammatory proteins, thus performing mediation analysis and elucidating the proportion of the mediation effect (Figure 1).

2.2 Data sources

The genetic information for the 15 trace elements is sourced from the GWAS database,[1] all pertaining to European populations. The data for the 91 inflammatory proteins are derived from a 2023 study involving 14,824 Europeans (44), cataloged under the identifiers GCST90274758 to GCST90274848. The COPD data is obtained from the tenth round of analysis by the FinnGen database (45),[2] also concerning European populations. Additionally, the genetic information for BMI is acquired from the GWAS database and is likewise representative of European demographics (Table 1).

2.3 Instrumental variable selection

The selection of instrumental variables must satisfy several assumptions (46): the instrumental variables should be closely associated with trace elements, independent of confounding factors in the exposure-outcome relationship, and must influence COPD solely through the trace elements (47). To ensure their relevance (48), we conduct an association analysis on the 15 trace elements using a

1 https://gwas.mrcieu.ac.uk/

2 https://www.finngen.fi/en

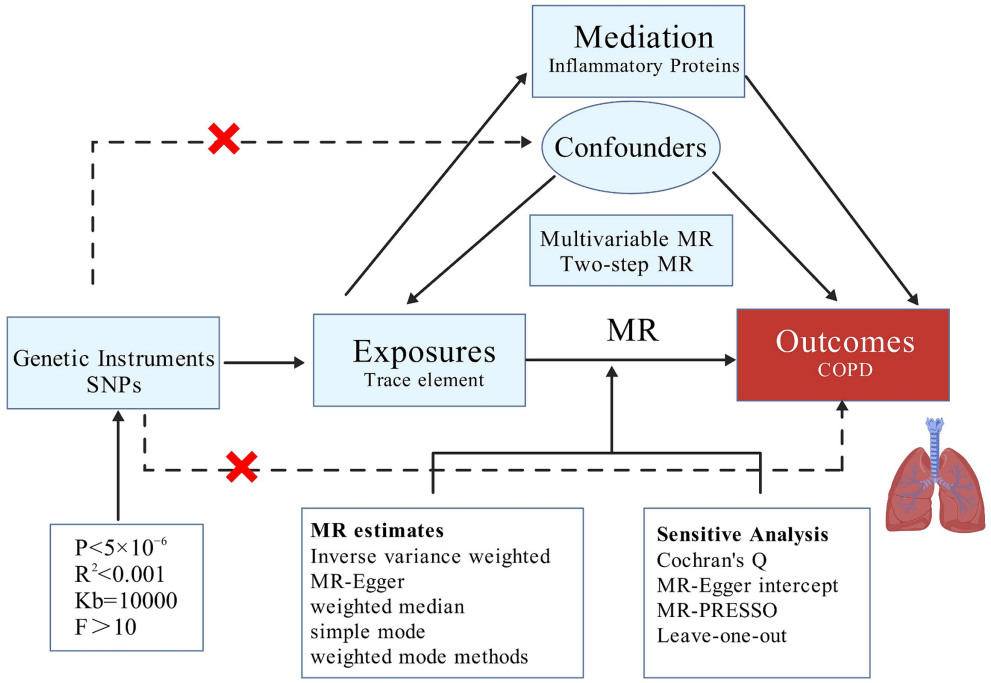

FIGURE 1
Research ideas.

TABLE 1 Genetic information data sources.

Name	Number	Samples	SNP
Copper	ieu-a-1073	2,603	2,543,646
Calcium	ukb-b-8951	64,979	9,851,867
Carotene	ukb-b-16202	64,979	9,851,867
Folate	ukb-b-11349	64,979	9,851,867
Iron	ukb-b-20447	64,979	9,851,867
Magnesium	ukb-b-7372	64,979	9,851,867
Potassium	ukb-b-17881	64,979	9,851,867
Selenium	ieu-a-1077	2,603	2,543,617
Vitamin A	ukb-b-9596	460,351	9,851,867
Vitamin B12	ukb-b-19524	64,979	9,851,867
Vitamin B6	ukb-b-7864	64,979	9,851,867
Vitamin C	ukb-b-19390	64,979	9,851,867
Vitamin D	ukb-b-18593	64,979	9,851,867
Vitamin E	ukb-b-6888	64,979	9,851,867
Zinc	ieu-a-1079	2,603	2,543,646
COPD	finngen_R10_J10_COPD	358,369	1,048,576
BMI	ieu-a-1089	120,286	8,654,252

significance threshold of $p < 5 \times 10^{-6}$. Subsequently, we eliminate any single nucleotide polymorphisms (SNPs) exhibiting linkage disequilibrium by applying criteria of $R^2 < 0.001$ and Kb = 10,000 (49). We then calculate the F-statistic for the selected SNPs to exclude weak instrumental variables, considering an *F*-value greater than 10 as indicative of the absence of weak instrumental variables (50, 51).

2.4 Statistical analysis

We employed five methods to assess causality: Inverse Variance Weighted (IVW), MR-Egger, Weighted Median, Simple Mode, and Weighted Mode, with IVW serving as the primary method (47, 52). A *p*-value less than 0.05 indicates a causal relationship (53), while the other four methods serve as supplementary approaches (54). To evaluate the robustness of our results, we conducted sensitivity analysis using the "leave-one-out" technique (55). Additionally, we employed Cochran's Q test, MR-Egger intercept test, and MR-PRESSO to test for pleiotropy and heterogeneity (56, 57), with a *p*-value greater than 0.05 indicating the absence of both (58, 59). Using the TSMR approach, we first calculated the total effect (β0) of trace elements on COPD, the effect of trace elements on inflammatory proteins (β1), and the effect of inflammatory proteins on COPD (β2). The mediating effect was computed as β1*β2, and the direct effect as the total effect minus the mediating effect. The proportion mediated was calculated as (β1 × β2)/β0 (60). All analyses were conducted using the R language (version 4.3.3). The specific package employed was TwoSampleMR (version 0.6.0).

3 Results

3.1 Causal relationship between 15 trace elements and COPD

Through the judicious selection of instrumental variables, we conducted an associative analysis, eliminated linkage disequilibrium and weak instrumental variables, and identified 188 SNPs across 15 trace elements, with the smallest F-statistic being 20.86

and the largest 84.68. Univariate MR analysis supports a causal relationship between trace elements such as Folate, Vitamin D, Vitamin B12, and Iron, and COPD. The results of the IVW analysis indicate a positive correlation between Folate (OR = 1.293, 95% CI 1.027–1.628; $p = 0.029$), Vitamin D (OR = 1.331, 95% CI 1.071–1.654; $p = 0.010$), and Vitamin B12 (OR = 1.424, 95% CI 1.108–1.828; $p = 0.006$) with COPD, while Iron shows a negative correlation (OR = 0.741, 95% CI 0.580–0.946; $p = 0.016$). Concurrently, reverse MR analysis revealed no reverse causality between Folate, Vitamin D, Vitamin B12, and Iron with COPD ($p > 0.05$).

To evaluate the robustness of our analytical results, we employed Cochran's Q test, the MR-Egger intercept test, and MR-PRESSO to examine pleiotropy and heterogeneity. No evidence of pleiotropy or heterogeneity was detected ($p > 0.05$). The leave-one-out analysis indicated that the exclusion of any single SNP would not significantly affect the estimation of causal relationships, suggesting that the results of the MR analysis are robust (Table 2; Figure 2).

3.2 Multivariate MR analysis

According to the results of the univariate MR analysis, a causal relationship exists between Folate, Vitamin D, Vitamin B12, and Iron with COPD. By adjusting for the influence of Body Mass Index (BMI),

TABLE 2 MR and sensitivity analyses of trace elements and COPD.

Exposure	Method	snp	Beta	Se	p	Pleiotropy test		Heterogeneity test	
						MR-PRESSO	MR-Egger intercept	IVW Q	MR-Egger Q
Folate	IVW	12	0.257	0.117	0.029	0.412	−0.012 ($p = 0.247$)	12.522 ($p = 0.326$)	10.879 ($p = 0.367$)
Vitamin D	IVW	13	0.286	0.111	0.010	0.974	0.011 ($p = 0.510$)	4.625 ($p = 0.969$)	4.161 ($p = 0.965$)
Vitamin B12	IVW	8	0.353	0.128	0.006	0.536	0.002 ($p = 0.885$)	6.161 ($p = 0.521$)	6.137 ($p = 0.408$)
Iron	IVW	11	−0.300	0.125	0.016	0.924	0.001 ($p = 0.908$)	4.497 ($p = 0.922$)	4.482 ($p = 0.877$)

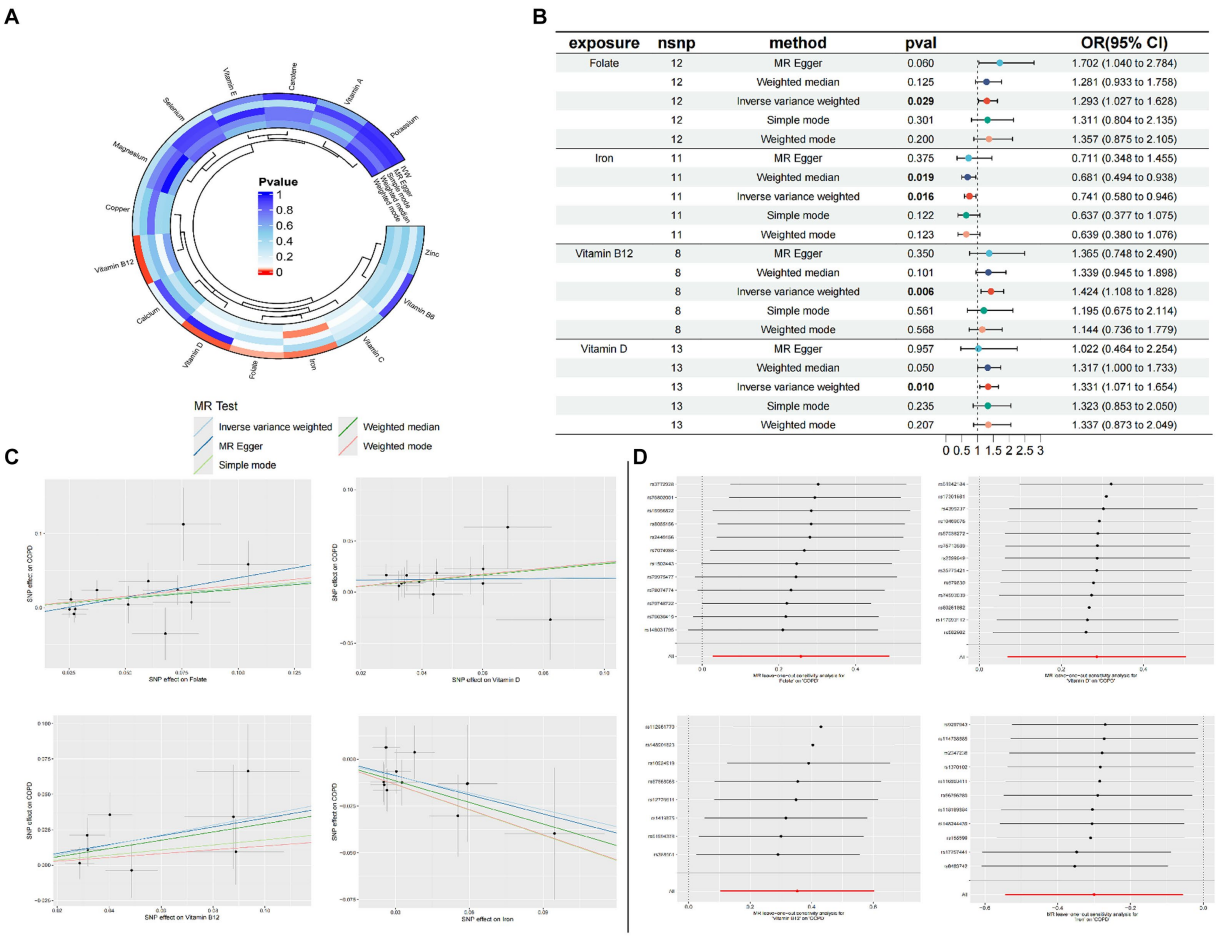

FIGURE 2
Circle plots of the five Mendelian randomization methods ($p < 0.05$) **(A)**; Forest plot of MR Analysis of trace elements and COPD **(B)**; MR scatter plot of trace elements and COPD **(C)**; Result of leave-one-out sensitivity analysis of trace elements and COPD **(D)**.

we conducted a MVMR analysis with these four trace elements and BMI. We discovered that the causal relationships with COPD persist for Folate (OR = 1.633, 95% CI 1.098–2.429; $p = 0.015$), Iron (OR = 0.507, 95% CI 0.31–0.778; $p = 0.001$), and Vitamin D (OR = 1.511, 95% CI 1.029–2.217; $p = 0.034$), indicating that Folate, Vitamin D, and Iron are independent risk factors for COPD. However, Vitamin B12 (OR = 1.118, 95% CI 0.751–1.666; $p = 0.581$) is not an independent risk factor for COPD (Table 3).

3.3 TSMR and mediation analyses

We conducted a TSMR analysis, selecting 91 inflammatory proteins as instrumental variables. After analyzing associations, removing linkage disequilibrium, and excluding weak instrumental variables, we obtained 2,973 SNPs with the smallest F-statistic being 19.51 and the largest 1472.73. The univariate MR analysis of these 91 inflammatory proteins with COPD revealed positive causal relationships for CXCL10 (OR = 1.093, 95% CI 1.034–1.155; $p = 0.001$), EN-RAGE (OR = 1.117, 95% CI 1.041–1.198; $p = 0.002$), CD6 (OR = 1.064, 95% CI 1.022–1.107; $p = 0.002$), STAMPB (OR = 1.104, 95% CI 1.012–1.205; $p = 0.025$), and CXCL6 (OR = 1.062, 95% CI 1.015–1.112; $p = 0.008$). Conversely, negative causal relationships were observed for CD40 (OR = 0.948, 95% CI 0.903–0.997; $p = 0.038$) and CDCP1 (OR = 0.940, 95% CI 0.899–0.982; $p = 0.006$). Tests for pleiotropy and heterogeneity were conducted ($p > 0.05$), with consistent OR directions, and the leave-one-out analysis confirmed the robustness of the MR results (Table 4).

In further MR analyses of four trace elements and inflammatory proteins, we found positive correlations between Iron and CDCP1 (OR = 1.321, 95% CI 1.026–1.702; $p = 0.031$), as well as Iron and CXCL10 (OR = 1.389, 95% CI 1.070–1.803; $p = 0.013$). Conversely, negative correlations were observed between Folate and EN-RAGE (OR = 0.750, 95% CI 0.583–0.964; $p = 0.025$), and between Vitamin D (OR = 0.724, 95% CI 0.563–0.930; $p = 0.011$) and EN-RAGE (Table 5).

In our final mediation analysis, we elucidated the causal effect proportions of four trace elements on COPD, mediated by seven inflammatory proteins. It was discovered that only CDCP1 mediated the impact of iron on COPD, with a mediation effect of −0.282, a direct effect of −0.017, and a mediation proportion of 5.76%. Regrettably, the other mediation effects were not established (Figure 3).

4 Discussion

This study provides genetic evidence supporting the causal relationships between trace elements such as Folate, Vitamin D, Vitamin B12, and Iron, and COPD in univariate MR analysis. After adjusting for BMI, further MVMR analysis revealed that Folate, Vitamin D, and Iron are independent risk factors for COPD. Finally, through TSMR and mediation analysis, CDCP1 is suggested to partially mediate the causal relationship between Iron and COPD. Our findings offer insights into dietary management and trace element supplementation for patients with COPD.

Malnutrition and trace element deficiencies are integral components of the rehabilitation process for patients with COPD, exhibiting a profound connection (61). Compared to healthy controls, COPD patients exhibit significantly reduced levels of Folate, presenting a novel therapeutic target for the treatment of COPD (62). Folate possesses antioxidative properties (63) and the capability to ameliorate endoplasmic reticulum stress (64), correlating positively with pulmonary function in COPD patients (65), thereby enhancing lung function (66)

TABLE 3 MVMR and sensitivity analysis of trace elements and COPD.

Exposure	Outcome	Beta	Se	*p*	OR	95%CI	*Q*	Egger intercept	Ple	Het
Folate	COPD	0.491	0.202	0.015	1.633	1.098–2.429	41.396	−0.001	0.649	0.497
Vitamin D		0.418	0.195	0.034	1.511	1.029–2.217				
Vitamin B12		0.112	0.203	0.581	1.118	0.751–1.666				
Iron		−0.678	0.218	0.001	0.507	0.331–0.778				
BMI		−0.023	0.059	0.692	0.976	0.869–1.097				

Ple, Pleiotropy Test; Het, Heterogeneity Test.

TABLE 4 MR and sensitivity analyses of inflammatory proteins and COPD.

Exposure	Method	snp	Beta	Se	*p*	Pleiotropy Test		Heterogeneity Test	
						MR-PRESSO	MR-Egger intercept	IVW Q	MR-Egger Q
CXCL10	IVW	33	0.089	0.028	0.001	0.650	−0.001 ($p = 0.759$)	28.273 ($p = 0.655$)	29.177 ($p = 0.611$)
EN-RAGE	IVW	23	0.111	0.036	0.002	0.288	−0.009 ($p = 0.228$)	26.450 ($p = 0.232$)	24.643 ($p = 0.262$)
CD6	IVW	25	0.062	0.020	0.002	0.764	−0.001 ($p = 0.729$)	20.113 ($p = 0.690$)	19.990 ($p = 0.642$)
CD40	IVW	23	−0.052	0.025	0.038	0.286	0.006 ($p = 0.232$)	20.664 ($p = 0.224$)	24.876 ($p = 0.252$)
CDCP1	IVW	36	−0.062	0.022	0.006	0.442	0.001 ($p = 0.703$)	36.182 ($p = 0.413$)	36.025 ($p = 0.373$)
STAMPB	IVW	20	0.099	0.045	0.025	0.282	−0.005 ($p = 0.643$)	22.473 ($p = 0.261$)	22.199 ($p = 0.223$)
CXCL6	IVW	22	0.061	0.023	0.008	0.604	0.004 ($p = 0.367$)	20.111 ($p = 0.514$)	19.261 ($p = 0.504$)

TABLE 5 MR and sensitivity analysis of trace elements and inflammatory proteins.

Exposure	Outcome	Method	snp	Beta	Se	*p*	Pleiotropy test		Heterogeneity test	
							MR-PRESSO	MR-Egger intercept	IVW Q	MR-Egger Q
Folate	EN-RAGE	IVW	13	−0.287	0.128	0.025	0.436	0.001 ($p = 0.954$)	12.387 ($p = 0.415$)	12.384 ($p = 0.335$)
Vitamin D	EN-RAGE	IVW	13	−0.322	0.127	0.011	0.936	−0.002 ($p = 0.882$)	5.738 ($p = 0.928$)	5.715 ($p = 0.891$)
Iron	CDCP1	IVW	12	0.278	0.129	0.031	0.697	−0.012 ($p = 0.394$)	8.208 ($p = 0.694$)	7.418 ($p = 0.685$)
Iron	CXCL10	IVW	12	0.328	0.133	0.013	0.575	−0.005 ($p = 0.688$)	9.596 ($p = 0.566$)	9.426 ($p = 0.492$)

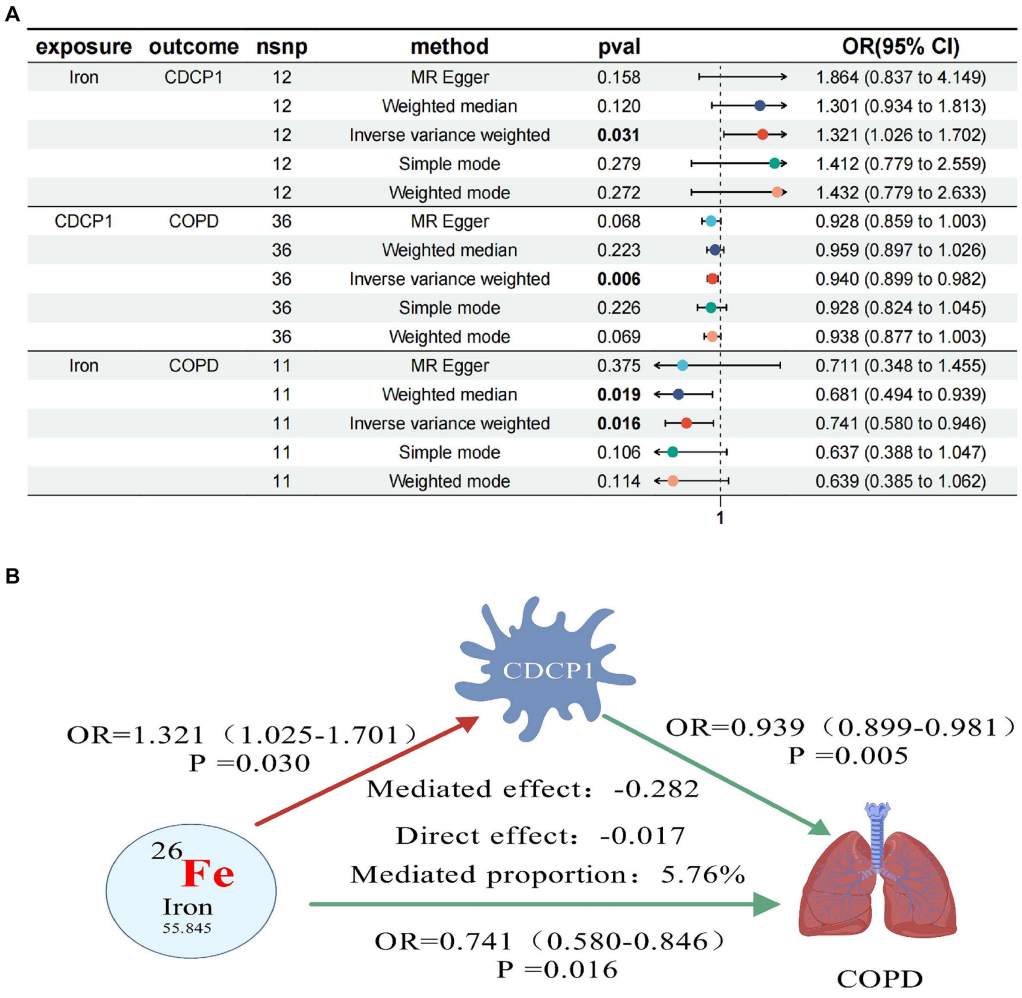

FIGURE 3
Forest plots of trace elements iron, CDCP1 and COPD **(A)**; CDCP1 mediates causal relationship between trace element iron and COPD (red is a risk factor, green is a protective factor) **(B)**.

and alleviating respiratory distress (67). A reduction in Folate intake may lead to restricted airflow (68), whereas increasing Folate intake could potentially benefit pulmonary function (69). Folate may confer protective effects against acute lung injury by mitigating inflammatory responses (70). Serum Folate levels are positively correlated with lung function in elderly males (71) and are also associated with pulmonary function in children with asthma (72). However, supplementation with Folate does not influence changes in FEV1 (67), nor has a significant correlation been observed between serum Folate levels and lung function in females (65). These results present contradictions, and our MR analysis serves as a complement to observational studies and systematic reviews. Vitamin D plays a crucial role in both innate and adaptive immunity (73) and acts as a significant regulator in defending against pulmonary infectionss (74). It may also contribute to reducing mortality from respiratory diseases. Additionally (75), supplementation with Vitamin D alone can enhance lung function (5). Prospective studies have identified a correlation between lower Vitamin D levels and accelerated decline in lung function (76). Systematic reviews have concluded that Vitamin D supplementation can reduce the risk of respiratory infections (34) and enhance resistance to such infections (77). In COPD patients, the response to Vitamin D supplementation is diminished compared to healthy controls (78), and supplementation does not affect the muscular

response to resistance training in COPD patients treated with Vitamin D_3 (79). While some studies suggest that Vitamin D supplementation does not reduce the exacerbation rate of COPD (80), it is inversely related to inflammatory signaling in COPD (81). A deficiency in Vitamin D receptors may increase pulmonary inflammation (82), and Vitamin D may inhibit COPD-related pulmonary emphysema by maintaining the homeostasis and functionality of alveolar macrophages (83). Despite some contradictions in research concerning Vitamin D and COPD (84), our analyses using MR and MVMR have established a causal relationship between Vitamin D and COPD.

Vitamin B12, as a supplement in the rehabilitation of COPD patients, can regulate the secretion of NT-proBNP (85), exerting a positive effect on patients with advanced COPD (86). However, the intake of Vitamin B12 is not associated with the risk of frailty in COPD. After adjusting for BMI, our multivariate MR analysis indicates that Vitamin B12 is not an independent risk factor for COPD (87). Iron regulation is significantly associated with respiratory diseases (88). Dysregulation of iron homeostasis is a critical mechanism in lung injury (89). Iron-induced cell death can lead to airway remodeling and emphysema (90), exacerbating inflammation and oxidative stress (91). Targeting iron-induced cell death may ameliorate respiratory diseases (92) and alleviate the progression of COPD (93). Iron is related to the genetic susceptibility of COPD (94, 95), and COPD patients may experience non-anemic iron deficiency (96), which is associated with inflammatory responses (97), skeletal muscle disorders (98), hypoxemia, and reduced exercise tolerance (99). Clinical studies have shown that iron supplementation can improve the exercise endurance and quality of life of COPD patients (100, 101). Non-anemic iron deficiency can impair the response of COPD patients to pulmonary rehabilitation, resulting in lower aerobic capacity (102). Iron deficiency is linked to more severe pulmonary vascular diseases (103). Dysregulation of iron homeostasis in the lungs and cellular iron accumulation are factors in the development of COPD (104). Ferroptosis, an iron-dependent form of cell death, plays a role in the pathogenesis of COPD (105) and can ameliorate cigarette smoke-induced inflammation and emphysema (106). CXCL10 is a potential biomarker for impaired lung development (107), capable of modulating pulmonary inflammation (108) and the lung microenvironment (109). There is a correlation between EN-RAGE and COPD (110). CD6 serves as a therapeutic target in cancer immunotherapy (111), while CD40 is associated with the severity of COPD and the degree of pulmonary function alteration (112). Additionally, a correlation exists between CXCL6 and mortality in IPF (113). CDCP1, which may be involved in cell adhesion and matrix binding, could serve as a biomarker for lung cancer detection (114) and is somewhat associated with COVID-19 (115). Our research suggests that iron may mediate the effects on COPD through its influence on the inflammatory protein CDCP1, necessitating further exploration of the relationship between inflammatory responses, trace elements, and COPD.

This study, through MR analysis, investigates the causal relationships between trace elements, inflammatory proteins, and COPD, aiming to provide scientifically sound dietary recommendations for COPD patients and further suggest that supplementation with trace elements may be beneficial for COPD. This research has certain limitations; primarily, the study population is confined to Europeans, which may restrict the generalizability of the findings. Secondly, there is a need for a deeper exploration of the mechanisms linking trace elements, inflammatory proteins, and COPD, as the mediating effects observed were not significant, necessitating further.

5 Conclusion

In conclusion, our research demonstrates a causal relationship between genetically predicted trace elements such as Folate, Vitamin D, Vitamin B12, and Iron, and COPD. After adjusting for BMI, Folate, Vitamin D, and Iron emerge as independent risk factors for COPD. Furthermore, the inflammatory protein CDCP1 may play a partial mediating role in the causal relationship between Iron and COPD. Our findings can better inform scientifically sound dietary recommendations for patients, suggesting that supplementation with trace elements may be beneficial for those suffering from COPD.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

ZC: Conceptualization, Visualization, Writing – original draft, Writing – review & editing. SZ: Data curation, Methodology, Writing – original draft, Writing – review & editing. TW: Data curation, Investigation, Writing – original draft, Writing – review & editing. FS: Data curation, Writing – original draft, Writing – review & editing. HD: Data curation, Writing – original draft, Writing – review & editing. SH: Conceptualization, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing. LS: Conceptualization, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1430606/full#supplementary-material

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