Psoriasis: Targets and Therapy

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ORIGINAL RESEARCH

Causal Effect of Plasma Fatty Acid Profiles on Psoriasis Risk: Genetic Evidence from a Mendelian Randomization Study

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Introduction: Emerging evidence indicates that omega-3 fatty acids from fish oil may serve as beneficial dietary supplements for psoriasis management. Clinical observations demonstrate a significant association between psoriasis improvement and increased docosahexaenoic acid (DHA) levels. However, the causal relationship between fatty acids and psoriasis risk requires further investigation.

Methods: Using summary-level genome-wide association study (GWAS) data, we applied univariable (UVMR), reverse, and multivariable (MVMR) Mendelian randomization analyses to assess causal effects of multiple fatty acids—including polyunsaturated (PUFA), saturated (SFA), monounsaturated (MUFA), omega-3/6 fatty acids, DHA, eicosapentaenoate (EPA) and docosapentaenoate (DPA)—on psoriasis risk.

Results: The analysis revealed that higher circulating levels of omega-3 fatty acids were significantly associated with a reduced risk of psoriasis development (UVMR: OR = 0.900, p = 0.022; MVMR: OR = 0.862, p = 0.007). Sensitivity analyses supported the robustness of this causal relationship, with consistent effects across multiple MR methods. Notably, DHA (UVMR: OR = 0.788, p = 0.006; MVMR: OR = 0.856, p = 0.021) drove this inverse association, while EPA and DPA showed marginal contributions.

Conclusion: This study provides valuable insights for targeted nutritional strategies to prevent and manage psoriasis, but further validation is needed.

Keywords: psoriasis, causal inference, fatty acids, Mendelian randomization

Introduction

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by erythematous plaques, epidermal keratinocyte hyperproliferation, leukocyte infiltration, and dysregulated lipid metabolism. With a global prevalence ranging from 0.1% (East Asia) to 1.5% (Western Europe), it imposes significant physical and psychological burdens.[1] Pathogenically, psoriasis involves dysregulated immune mechanisms—notably T-cell and macrophage infiltration into the dermis. Disease progression occurs when antigen-presenting cells and helper T lymphocytes overwhelm epidermal regulatory controls.

Fatty acids critically regulate inflammation and immunity. High saturated fatty acid (SFA) intake exacerbates psoriasis,[2] and patients exhibit elevated monounsaturated/polyunsaturated fatty acids (MUFAs/PUFAs) versus healthy controls.[3] PUFAs—essential for energy production, cellular structure, and human health—demonstrate therapeutic potential in psoriasis. Clinical evidence associates PUFA supplementation with symptom improvement[2] and efficacy in

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other inflammatory dermatoses (eg, atopic dermatitis, acne).[4] Although both are essential PUFAs, omega-6 compounds (eg, linoleic acid) serve as precursors to pro-inflammatory mediators, whereas omega-3 derivatives yield anti-inflammatory and pro-resolving mediators. Cold-water fish oil—rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)—is a promising therapeutic candidate: 12 of 15 clinical trials on fish oil report clinical improvement in psoriasis.[5] Mechanistically, PUFAs modulate immune responses: ultra-long-chain PUFAs exert antiproliferative effects on T cells in vitro,[6] while EPA specifically reduces IL-17A–producing T cells (key drivers of psoriatic inflammation).[7]

However, evidence linking specific fatty acids to psoriasis remains inconclusive. A recent review[8] highlights inconsistent outcomes: while some studies report benefits with omega-3 PUFA (EPA/DHA) supplementation, others show null effects. Mendelian randomization (MR) uses genetic variants linked to an exposure as instrumental variables (IVs) to infer causal effects on outcomes, reducing confounding through random inheritance and eliminating reverse causality as variants predate disease.[9] The literature includes few MR studies[10,11] investigating fatty acid-psoriasis causality, with minimal attention to specific subtypes (eg, EPA and DHA) and predominant use of conventional univariable MR approaches.

To resolve this, we employed MR to systematically evaluate causal relationships between circulating fatty acid profiles—including SFAs, MUFAs, and PUFAs, with specific focus on omega-3/omega-6 PUFAs and their key constituents—and psoriasis risk.

Materials and Methods

Experimental Data

Genome-wide association study (GWAS) summary statistics for fatty acid levels and psoriasis risk were obtained from publicly available datasets. Psoriasis case-control data were derived from a cross-ethnic analysis of European and South Asian populations in the NHGRI-EBI GWAS database, comprising 15,976 cases and 28,194 controls in the European cohort, and 2590 cases and 1720 controls in the South Asian cohort.[12]

Fatty acid metrics (including saturated, monounsaturated, polyunsaturated, omega-3, and omega-6 fatty acids) were obtained from the UK Biobank, where quantification was performed by Nightingale Health in 2020. Additional fatty acid-specific data were obtained from complementary sources. DHA summary data came from a genome-wide association meta-analysis examining 123 circulating metabolic traits across 24,925 European individuals, comprising 13,499 samples with 11,415,610 SNPs.[13] Data for EPA and DPA were derived from one European population study, with EPA data including 7816 samples and 2,545,634 SNPs, and DPA data comprising 7821 samples and 2,545,661 SNPs.[14]

Selection of Instrument Variables

First, we identified significantly associated single nucleotide polymorphisms (SNPs) ($p < 5\times10^{-8}$). Subsequently, we pruned these SNPs to remove those in linkage disequilibrium (LD) ($r^2 < 0.001$ within a 10,000 kb window). Finally, we quantified the strength of the selected genetic variants by computing F-statistics using the following equation:

$$F = (N-2) \times \frac{R^2}{1-R^2}$$

$$R^2 = 2 \times MAF \times (1-MAF) \times \beta^2$$

In the equations above, N represents the sample size of the exposure dataset, R^2 denotes the proportion of variance explained by the SNPs in the exposure dataset, and MAF indicates the minor allele frequency. When MAF is unavailable in the GWAS summary statistics, we used the effect allele frequency (EAF) from the relevant dataset, with the following conversion: if EAF ≤ 0.5, then MAF = EAF; if EAF > 0.5, then MAF = 1 − EAF. Here, β represents the allele effect size, and genetic variants with $F > 10$ were considered strong instrumental variables.[15]

For the outcome analysis, we extracted exposure-associated SNPs from the outcome GWAS data. To ensure valid causal inference, we excluded SNPs showing significant associations with the outcome ($p < 5 \times 10^{-8}$) and replaced missing SNPs with proxy variants in high linkage disequilibrium ($r^2 > 0.8$). Due to the limited sample size for EPA and DPA analyses, we applied a more lenient significance threshold ($p < 1 \times 10^{-8}$) for instrument selection.

Mendelian Randomization Analysis

Univariable Mendelian Randomization Analysis

In MR analyses, valid causal inference requires instrumental variables (IVs) to satisfy three fundamental assumptions:

Relevance Assumption

The genetic variant must exhibit a strong association with the exposure of interest.

Exchangeability Assumption

The genetic variant must not be associated with any known or unknown confounding factors.

Exclusion Restriction Assumption

The genetic variant must influence the outcome exclusively through the exposure, with no alternative biological pathways.

Figure 1 presents a directed acyclic graph (DAG) illustrating the fundamental principles of MR analysis. The diagram depicts the assumed relationships between the genetic variant (G_j), exposure (X), outcome (Y), and unmeasured confounding factors (U). In this graphical representation, solid black arrows indicate permitted causal pathways, while dashed gray arrows denote prohibited associations that would invalidate the genetic variant as an IV.

Following data harmonization between exposure and psoriasis datasets, we performed UVMR analysis using the TwoSampleMR package in R. To comprehensively assess the causal relationship between exposure and outcome, we employed five complementary MR methods: inverse-variance weighted (IVW),[16] serving as our primary analysis; weighted median,[17] providing robust estimates when up to 50% of instruments are invalid; MR-Egger,[18] which accounts for potential pleiotropy; along with simple mode and weighted mode[19] approaches as additional sensitivity analyses.

To assess heterogeneity among individual SNP estimates, we performed Cochran's Q test.[20] When no significant heterogeneity was detected ($p \geq 0.05$), we considered the IVW method as our primary analytical approach. To identify and account for horizontal pleiotropy, we conducted the MR-PRESSO (Mendelian Randomization Pleiotropy RESidual Sum and Outlier) test,[21] which detects outlier variants and provides corrected causal estimates after their removal. A non-significant MR-PRESSO global test ($p > 0.05$) indicated absence of substantial pleiotropic effects. We further performed sensitivity analyses to evaluate the robustness of our findings: Leave-one-out analysis: Sequentially excluding each SNP and re-running IVW estimation to identify influential variants; MR-Egger intercept test: Quantifying directional pleiotropy, where a non-zero intercept ($p < 0.05$) suggests potential bias from unbalanced pleiotropic effects.[22]

Multivariable Mendelian Randomization Analysis

Multivariable Mendelian randomization (MVMR) extends conventional UVMR by enabling simultaneous analysis of multiple exposures. While identifying genetic variants uniquely associated with a single exposure is often challenging, MVMR accommodates variants associated with multiple exposures. Whereas standard MR estimates the total effect of an exposure on an outcome, MVMR isolates the direct effect of each exposure while accounting for others.[23] This approach evaluates the relative contributions of competing exposures, effectively determining which factors drive the observed

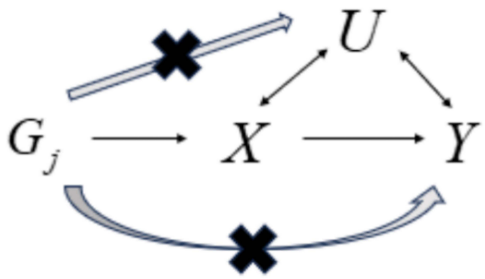

Figure 1 Directed acyclic graph of univariable Mendelian randomization assumptions.

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outcome associations. Conceptually, MVMR can be viewed as establishing a competitive framework among exposures, thereby correcting for potential confounding between interrelated variables.

Figure 2 presents the DAG illustrating the theoretical framework of MVMR analysis and its underlying instrumental variable assumptions. The diagram depicts the hypothesized relationships between: (1) multiple genetic variants (G_1, G_2, G_3), (2) multiple exposures (X_1 and X_2), (3) the outcome (Y), and (4) unmeasured confounding factors (U). Solid arrows indicate permitted causal pathways, while the absence of arrows represents prohibited associations that would violate MVMR assumptions. In brief, MVMR maintains the same core assumptions as UVMR, but extends them to accommodate multiple exposures.

Results

Univariable Mendelian Randomization Analysis

Saturated Fatty Acid Analysis

Initial quality control using MR-PRESSO confirmed the absence of outliers among saturated fatty acid-associated genetic variants ($p > 0.05$). After excluding three outcome-related SNPs (rs58542926, rs102275, and rs632057), we identified 41 valid IVs with strong predictive power (mean F-statistic = 94.29). MR analysis (Figure 3) demonstrated a significant positive association between elevated circulating saturated fatty acids and psoriasis risk (IVW OR = 1.227, 95% CI: 1.082–1.392, $p = 0.001$).

Monounsaturated Fatty Acid Analysis

Similarly, MR-PRESSO analysis revealed no significant outliers for monounsaturated fatty acid variants ($p > 0.05$). Following exclusion of four psoriasis-associated SNPs (rs632057, rs58542926, rs1002687, and rs4564803), we retained 46 valid IVs (mean F-statistic = 84.07). Consistent results across five MR methods confirmed a causal relationship between higher monounsaturated fatty acid levels and increased psoriasis risk, with the primary IVW analysis showing extreme significance (OR = 1.283, 95% CI: 1.132–1.461, $p < 0.001$).

Polyunsaturated Fatty Acid Analysis

In the analysis using polyunsaturated fatty acids as exposure, we identified 48 valid SNPs following quality control procedures. The primary IVW analysis showed a non-significant association with psoriasis risk (OR = 1.098, 95% CI: 0.984–1.224, $p = 0.093$).

Stratified Analysis of Polyunsaturated Fatty Acid Subtypes

Next, for Omega-3 Fatty Acid Analysis, the MR-PRESSO heterogeneity test identified one outlier (rs11242109) which was subsequently removed. Following additional exclusion of five outcome-associated SNPs (rs261290, rs112875651, rs1260326, rs633695, and rs62466318), we selected 35 high-quality IVs with exceptional predictive power (mean F-statistic = 244.49). Our comprehensive MR analysis demonstrated a protective effect of omega-3 fatty acids against psoriasis development, with the IVW method showing statistically significant risk reduction (OR = 0.901, 95% CI: 0.823–0.985, $p = 0.021$).

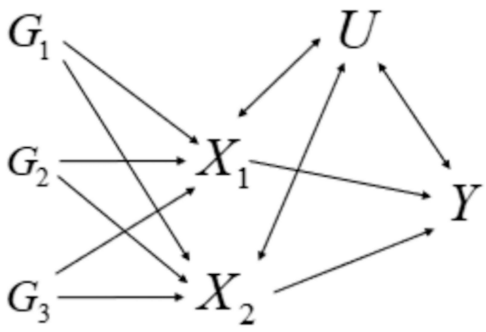

Figure 2 Directed acyclic graph depicting the assumption conditions of multivariable Mendelian randomization.

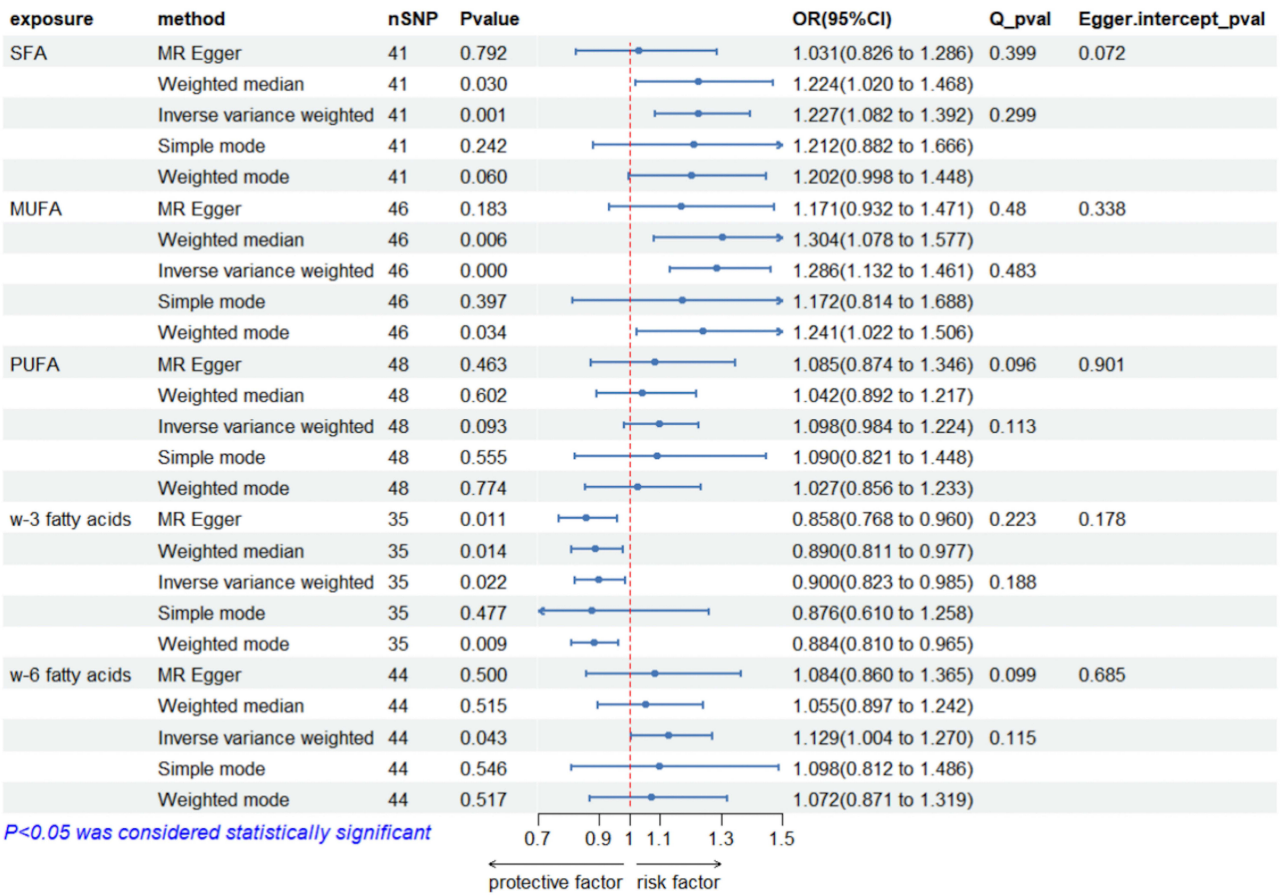

Figure 3 Results of the univariable Mendelian randomization analysis of saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), omega-3 fatty acids, and omega-6 fatty acids in relation to psoriasis.

For omega-6 fatty acids, after excluding invalid variants, 44 SNPs were retained for analysis. Only the IVW method demonstrated a significant positive association with psoriasis (OR = 1.129, 95% CI: 1.004–1.270, p = 0.043), while all other MR methods yielded non-significant results (all p > 0.05).

Across all sets of MR analyses, Cochran's Q test showed no evidence of significant heterogeneity (p > 0.05). The MR-Egger intercept test similarly indicated no substantial pleiotropic effects (intercept p-value > 0.05). These results collectively suggest the absence of horizontal pleiotropy in our analyses.

Stratified Analysis of Omega-3 Fatty Acid Subtypes

Furthermore, our analysis extended to three specific omega-3 fatty acids - DHA, EPA, and DPA - as exposures in the MR framework. The MR-PRESSO heterogeneity test confirmed the absence of outliers in the DHA-associated variants (p > 0.05). Comprehensive analysis across five MR methods consistently demonstrated an inverse relationship between elevated DHA levels and psoriasis risk, with the inverse-variance weighted (IVW) method showing statistically significant protection (OR = 0.789, 95% CI: 0.665–0.933, p = 0.006). This genetic evidence suggests DHA may confer reduced risk of psoriasis development (Figure 4). In contrast, neither EPA (IVW OR = 0.824, 95% CI: 0.372–1.628, p = 0.573) nor DPA (IVW OR = 0.521, 95% CI: 0.130–2.314, p = 0.382) showed significant associations with psoriasis risk. Sensitivity analyses supported the robustness of these findings, with Cochran's Q test indicating no heterogeneity (p = 0.215) and the MR-Egger intercept test showing no evidence of horizontal pleiotropy (intercept p = 0.341), thereby validating IV assumptions.

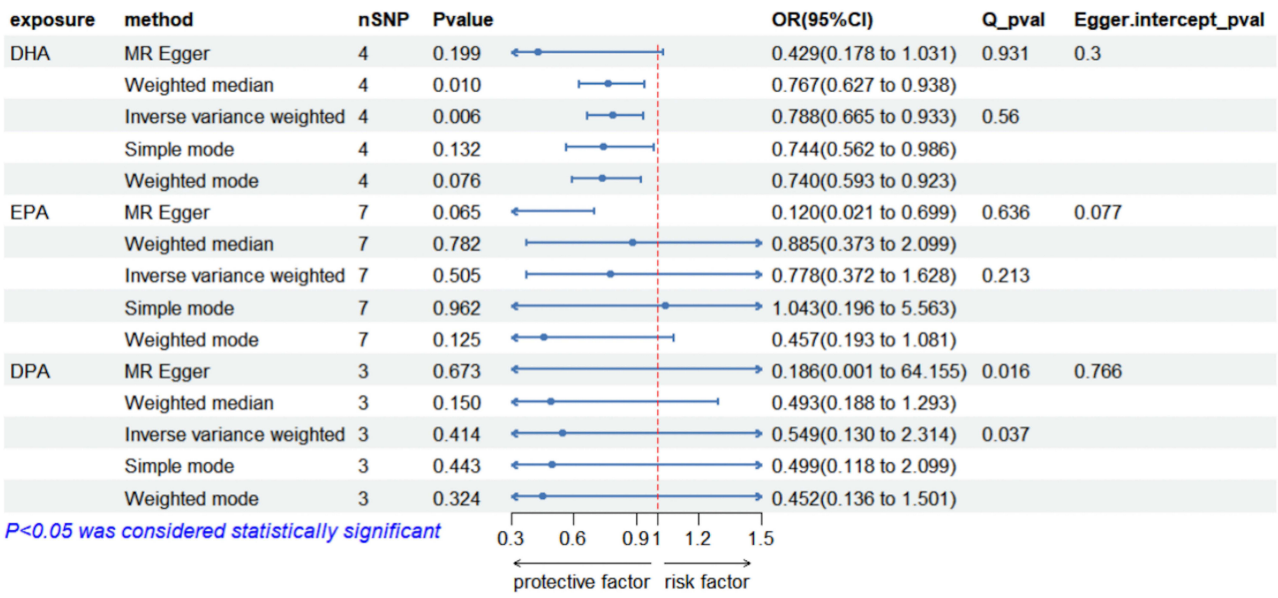

Figure 4 Results of the Mendelian randomization analysis of docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and docosapentaenoic acid (DPA) and psoriasis risk.

Multivariable Mendelian Randomization Analysis

We performed three sets of MVMR-IVW analyses. First, we assessed the joint effect of MUFA, PUFA, and SFA on psoriasis risk and found no causal relationship between any of these fatty acid subtypes after adjusting for the other two (Figure 5).

Second, we assessed the independent causal effect of omega-3 fatty acids on psoriasis risk while accounting for omega-6 fatty acid levels, utilizing 65 genetic variants as IVs. Comparison between the MVMR and UVMR estimates demonstrated consistent protective effects of omega-3 fatty acids across both analytical approaches (UVMR-IVW OR = 0.901, 95% CI: 0.823–0.985, p = 0.021; MVMR-IVW OR = 0.861, 95% CI: 0.774–0.960, p = 0.007) (Figure 5). These results indicate a significant independent causal relationship between higher omega-3 fatty acid levels and reduced psoriasis risk that persists after adjustment for omega-6 fatty acid levels.

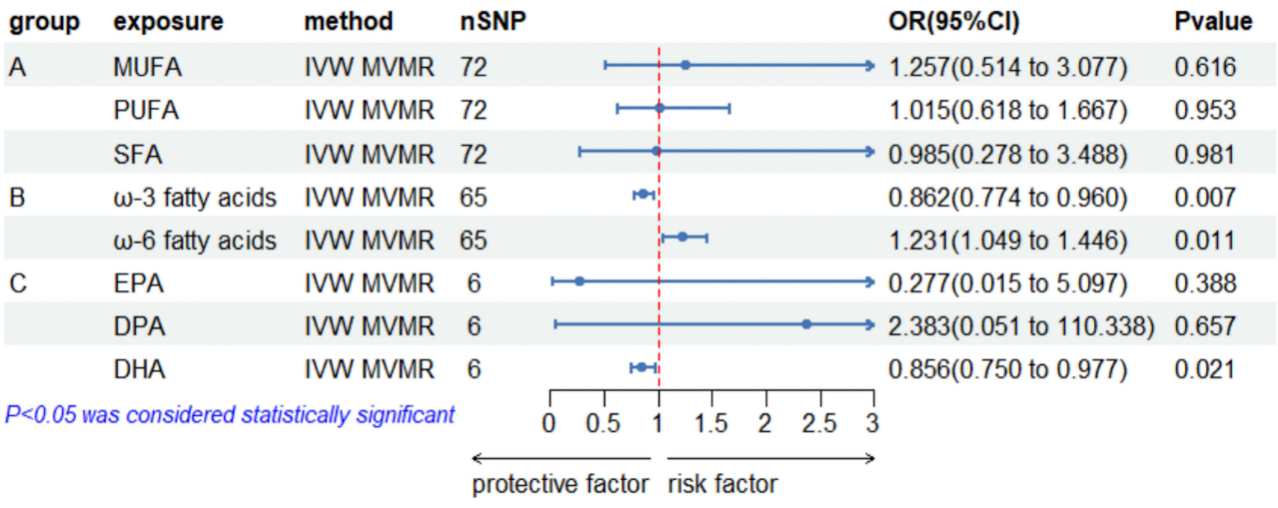

Figure 5 Multivariable Mendelian randomization analysis results examining independent effects of fatty acids on psoriasis risk. (**A**) Analysis for monounsaturated, polyunsaturated, and saturated fatty acids. (**B**) Analysis for competing effects of omega-3 and omega-6 fatty acids. (**C**) Analysis examining specific omega-3 fatty acid subtypes: docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and docosapentaenoic acid (DPA).

outcome	method	nSNP	Pvalue	OR(95%CI)	Q_pval	Egger.intercept_pval
SFA	MR Egger	52	0.488	1.008(0.986 to 1.030)	0.019	0.669
	Weighted median	52	0.128	1.010(0.997 to 1.024)		
	Inverse variance weighted	52	0.479	1.003(0.994 to 1.013)	0.022	
	Simple mode	52	0.792	1.004(0.975 to 1.034)		
	Weighted mode	52	0.075	1.017(0.999 to 1.035)		
MUFA	MR Egger	52	0.203	1.016(0.992 to 1.040)	0.006	0.396
	Weighted median	52	0.045	1.014(1.000 to 1.028)		
	Inverse variance weighted	52	0.235	1.006(0.996 to 1.017)	0.006	
	Simple mode	52	0.315	1.016(0.985 to 1.048)		
	Weighted mode	52	0.015	1.022(1.005 to 1.039)		
PUFA	MR Egger	50	0.352	1.011(0.988 to 1.034)	0.021	0.385
	Weighted median	50	0.497	1.004(0.992 to 1.017)		
	Inverse variance weighted	50	0.727	1.002(0.992 to 1.012)	0.021	
	Simple mode	50	0.746	1.005(0.977 to 1.033)		
	Weighted mode	50	0.334	1.009(0.991 to 1.026)		
w-3 fatty acids	MR Egger	52	0.650	1.005(0.985 to 1.025)	0.183	0.195
	Weighted median	52	0.791	1.002(0.988 to 1.016)		
	Inverse variance weighted	52	0.107	0.993(0.984 to 1.002)	0.169	
	Simple mode	52	0.590	1.008(0.979 to 1.037)		
	Weighted mode	52	0.316	1.010(0.991 to 1.028)		
w-6 fatty acids	MR Egger	50	0.312	1.012(0.989 to 1.035)	0.018	0.329
	Weighted median	50	0.574	1.004(0.991 to 1.017)		
	Inverse variance weighted	50	0.757	1.002(0.992 to 1.012)	0.017	
	Simple mode	50	0.698	1.006(0.978 to 1.034)		
	Weighted mode	50	0.406	1.008(0.990 to 1.027)		

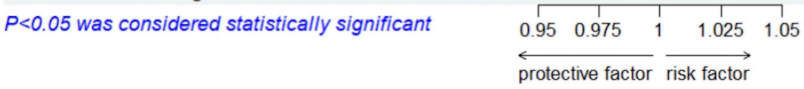

Figure 6 Results of the reverse Mendelian randomization analysis of psoriasis risk and fatty acids levels.

Similarly, we performed MVMR-IVW analysis to estimate the independent causal effect of DHA levels on psoriasis while accounting for EPA and DPA levels. This analysis demonstrated consistent protective effects of DHA against psoriasis risk between univariable and multivariable approaches (UVMR-IVW OR = 0.789, 95% CI: 0.665–0.933, p = 0.006; MVMR-IVW OR = 0.859, 95% CI: 0.750–0.977, p = 0.021).

Reverse Mendelian Randomization Analysis

To assess potential reverse causation, we conducted reverse MR analysis using psoriasis as the exposure and circulating fatty acid levels as outcomes. Employing carefully selected genetic instruments, we found no statistically significant causal effects of psoriasis on any fatty acid subtypes: saturated fatty acids (IVW $\beta = 0.003$, $p = 0.512$), monounsaturated fatty acids (IVW $\beta = 0.006$, $p = 0.238$), polyunsaturated fatty acids (IVW $\beta = 0.002$, $p = 0.682$), omega-3 fatty acids (IVW $\beta = -0.007$, $p = 0.124$), or omega-6 fatty acids (IVW $\beta = 0.002$, $p = 0.692$) (Figure 6). These comprehensive analyses effectively exclude the possibility of reverse causation whereby having psoriasis might alter circulating fatty acid levels.

Furthermore, we also conducted MR analyses to evaluate potential reverse causation by using psoriasis as the exposure and three specific omega-3 fatty acids - DHA, EPA, and DPA - as separate outcomes (Figure 7). The lack of significant causal effects (all $p > 0.05$) suggests that psoriasis does not directly alter circulating levels of DHA, EPA, or DPA, thus there is no reverse causal relationships between DHA, EPA, or DPA and psoriasis risk.

Discussion

In this study, we employed MR to assess the causal relationship between individual fatty acids and psoriasis. Compared to previous MR studies,[10,11] our study offers two key advantages. First, we employed a more comprehensive analytical

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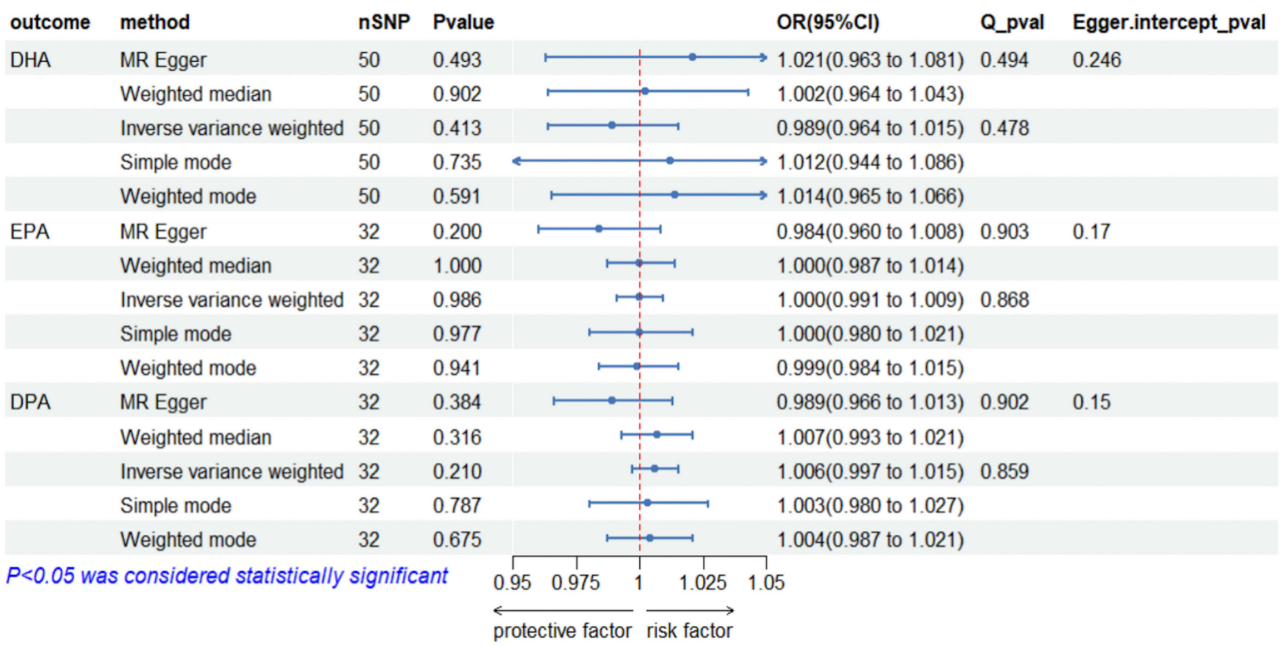

Figure 7 Reverse Mendelian randomization analysis assessing potential reverse causation between psoriasis and specific omega-3 fatty acids: docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and docosapentaenoic acid (DPA).

framework, incorporating UVMR, MVMR, and reverse MR analyses to investigate the relationship between fatty acids and psoriasis risk. Second, we adopted a hierarchical approach—first examining broad fatty acid classes, then specific PUFAs, and finally individual omega-3 subtypes. To our knowledge, no prior MR study has implemented such an extensive strategy to thoroughly assess the causal relationships between fatty acids and psoriasis risk.

This comprehensive analysis showed SFAs and MUFAs had a positive association with psoriasis risk in UVMR, though this effect was not significant in MVMR. While the findings of MUFAs align with a recent MR study[10] suggesting that elevated circulating MUFAs may causally contribute to psoriasis risk, adjustment for other fatty acids —as performed in our MVMR analysis—remains essential, given the potential interplay among these lipids in modulating psoriasis susceptibility. Although Guo et al[24] demonstrated elevated serum SFA levels in psoriasis patients compared to healthy controls using GC-MS—supporting the association between abnormal SFA metabolism and the disease—their cross-sectional study design precludes causal inference. Ultimately, whether SFAs and MUFAs exert a direct causal effect on psoriasis warrants further investigation using complementary causal inference approaches.

Furthermore, our findings demonstrated a strong association between higher levels of omega-3 fatty acids and a reduced risk of psoriasis, suggesting a protective role. Our MVMR analysis further confirmed an independent causal relationship between omega-3 fatty acids and reduced psoriasis risk. This indicates that their protective effect likely persists independently of the detrimental effects associated with omega-6 fatty acids. Omega-3 and omega-6 fatty acids are essential PUFAs that must be obtained from the diet. Although both are crucial for health, they exert opposing effects on inflammation and metabolism: Omega-3 fatty acids are anti-inflammatory and support cardiovascular, brain, and immune health. Conversely, omega-6 fatty acids are pro-inflammatory in excess but remain necessary for skin integrity, hormone production, and cell signaling.[25] An imbalance favoring omega-6 over omega-3 intake promotes chronic low-grade inflammation, contributing to autoimmune and inflammatory diseases like psoriasis.[26,27] Higher omega-3 intake reduces inflammation partly by competing with omega-6 fatty acids for enzymatic pathways.[26] Additionally, the null causal effect observed for total PUFAs in both our UVMR and MVMR analyses suggests opposing associations for these two major PUFA classes, resulting in a net null effect on psoriasis risk due to effect cancellation.

Mechanistically, a recent review[28] indicates that omega-3 fatty acids regulate key epidermal functions, including lipid homeostasis, keratinocyte proliferation, PPAR-mediated barrier function and inflammation control, and cytokine reduction. In the dermis, they modulate keratinocytes, fibroblasts, and immune cells (eg, macrophages) through pathways

involving prostaglandin E, reactive oxygen species (ROS), NRF2, STAT3, AQP3, and HAS2. In contrast, omega-6 PUFAs, particularly linoleic acid (LA) and arachidonic acid (AA) promote inflammation and obesity via eicosanoid signaling, adipocyte differentiation, endocannabinoid-mediated appetite stimulation, and gut microbiome interactions.[29] Taken together, current evidence and our findings suggest that psoriasis patients may benefit from dietary strategies aimed at increasing omega-3 fatty acid intake while reducing omega-6 fatty acid intake.

Notably, one of our MVMR analyses (with EPA, DHA, and DPA as exposures) identified DHA—a key omega-3 fatty acid—as exhibiting a particularly significant protective effect against psoriasis. This supports that DHA contributes the most to the overall impact of omega-3 fatty acids on psoriasis risk. In the literature, several prior studies supported such an association between DHA levels and psoriasis risk or severity. For example, based on 296 Chinese patients with moderate to severe plaque psoriasis, Wang et al[30] performed both cross-sectional and longitudinal studies to investigate the associations between PUFAs and the disease. Their analysis indicated that the higher DHA levels were significantly linked to lower severity scores, particularly in women. This may be due to that DHA is an anti-inflammatory omega-3 fatty acid and may reduce inflammation by suppressing pro-inflammatory cytokines (eg, TNF-α, IL-17) or promoting resolution pathways, therefore having a protective effect on psoriasis severity. Nevertheless, the findings from the longitudinal cohort are inconsistent with the cross-sectional cohort, namely, higher baseline DHA was associated with a lower likelihood of achieving PASI 75 and PASI 90 at 12 weeks. This unexpected finding may stem from the limited sample size or treatment effects. Additionally, the complexity of psoriasis pathogenesis and heterogeneous responses to the intervention could further contribute to the observed inconsistency. Additionally, clinical evidence confirms the elevation of adiponectin with omega-3 fatty acid.[31] Reduced adiponectin in psoriasis[32] attenuates its inhibitory effects on IL-23/IL-17, thereby leading to hBD2-mediated keratinocyte hyperproliferation.

The current study is subject to several limitations. First, the small sample size of several exposure GWAS studies necessitated the use of a more lenient genetic significance threshold, set at 1×10^{-8}. While this threshold allows for the inclusion of more SNPs, it certainly increases the risk of incorporating weak instruments and experiencing horizontal pleiotropy. Additionally, due to the extremely limited sample size of summary GWAS data for specific omega-6 fatty acid subtypes, we were unable to further explore how individual constituents contribute to psoriasis risk—unlike our analysis of omega-3 fatty acids. Further investigation is warranted. Third, like other MR studies, this analysis is susceptible to horizontal pleiotropy, which may compromise the validity of using a genetic variant as an IV. Finally, since all GWAS summary data were derived from European populations, these findings may not generalize to other ethnic groups without further validation.

Conclusion

In summary, these findings of the current study highlight the potential clinical relevance of omega-3 fatty acids, particularly DHA, in psoriasis management. While this study provides evidence supporting DHA supplementation for psoriasis prevention and management, optimal dosage, molecular forms, and delivery methods remain undefined; thus, further clinical studies are warranted.

Data Sharing Statement

The GWAS data of fatty acids and psoriasis were downloaded from the GWAS catalog (https://www.ebi.ac.uk/gwas/) and the Open GWAS project (https://gwas.mrcieu.ac.uk).

Ethics Approval and Consent to Participate

Ethical approval for this study was waived by the IRB of our institute (First Hospital of Jilin University) as no original research data were collected.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author declares that the work 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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