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Analysis

The causal association between psoriasis and 32 types of cancer: a mendelian randomization study

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Abstract

Background Psoriasis is a systemic immune disease associated with the development of various cancers. However, the causal nature of this association remains unclear. This study aims to systematically investigate the potential causal relationship between psoriasis and 32 types of cancer.

Methods We utilized data from two large genomic databases, the UK Biobank and FinnGen, to extract GWAS summary statistics for 32 cancer types as outcomes and psoriasis-related data as exposures. Mendelian randomization (MR) analysis was performed to assess the causal effects of psoriasis on cancer risk. Sensitivity analyses, including heterogeneity and horizontal pleiotropy tests, were conducted to ensure robustness. Additionally, meta-analysis and FDR correction were applied to enhance the reliability of the results.

Results Our findings revealed significant causal relationships between psoriasis and four cancer types: Psoriasis was associated with an increased risk of laryngeal cancer (OR = 1.15, 95% CI: 1.05–1.26). Psoriasis exhibited a protective effect against oral cavity and pharyngeal cancer (OR: 0.91; 95% CI: 0.86–0.97), prostate cancer (OR: 0.97; 95% CI: 0.95–0.99), and malignant non-melanoma cancer (OR: 0.89; 95% CI: 0.82–0.96).

Conclusion Psoriasis may exert bidirectional effects on the development of specific cancers through distinct mechanisms. Specifically, psoriasis may increase the risk of laryngeal cancer while reducing the risk of oral cavity and pharyngeal cancer, prostate cancer, and malignant non-melanoma cancer. These findings provide new insights into the causal relationship between psoriasis and cancer and could inform prevention and treatment strategies for these diseases.

Keywords Psoriasis · Mendelian randomization · Laryngeal cancer · Prostate cancer oral cavity and pharyngeal cancer · Malignant non-melanoma cancer

1 Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by erythematous, scaly plaques, affecting approximately 2–3% of the population [1]. The associated comorbidities impose an additional socioeconomic burden on psoriasis patients [2]. The pathogenesis of psoriasis is closely related to dysregulation of both innate and

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adaptive immune responses in the skin [3]. During disease progression, various immune cells—including CD4+T cells, CD8+T cells, CD3+T cells, and antigen-presenting cells—along with alterations in their microenvironment, play a critical role [4]. Additionally, multiple cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and interferon-gamma (IFN-γ), serve as key regulatory mediators, deeply involved in disease progression [5].

Notably, alterations in the immune microenvironment also play a crucial role in the initiation and progression of various malignancies [6]. Although numerous studies have reported causal associations between psoriasis and individual types of malignancies [7–9], comprehensive investigations examining the systemic association between psoriasis and multiple cancers remain relatively scarce. This limitation underscores the necessity for further research to elucidate the potential mechanisms underlying psoriasis-associated carcinogenesis and its clinical significance.

Systemic therapies (such as methotrexate, cyclosporine, biologics) are pivotal for managing psoriasis symptoms; however, certain agents have been associated with elevated malignancy risks, such as malignant non-melanoma cancer and lymphoma [10, 11]. These risks primarily stem from pharmacological immunosuppression rather than the intrinsic pathophysiology of psoriasis. To disentangle the disease-specific effects from confounding by treatment, our study employs Mendelian randomization (MR) method [12], which leverages genetic variants as instrumental variables to mimic randomized controlled trials. This approach isolates the causal influence of genetic predisposition to psoriasis itself, independent of environmental confounders such as therapeutic interventions [13–15]. Clarifying this distinction is critical for refining cancer surveillance strategies, particularly in untreated populations or early-stage patients where treatment-related biases are minimal.

Psoriasis, as a multifactorial disease with genetic susceptibility, has been associated with specific genetic loci identified through multiple genome-wide association studies (GWAS) [16]. These genetic variants not only offer new insights into the pathogenesis of psoriasis but also provide a foundation for exploring its causal relationship with malignancies. Therefore, this study employs the MR approach to investigate the potential causal associations between psoriasis and 32 types of malignancies, aiming to address the limitations of existing studies while providing new scientific evidence for disease management and cancer surveillance.

2 Methods

In this study, 32 types of cancer were categorized into eight major groups based on system classification: respiratory system cancers, oral cavity and pharyngeal cancers, digestive system cancers, hematologic malignancies, genital system cancers, breast cancer, skin cancers, and other types of cancer. This classification approach facilitates a systematic evaluation of the potential causal relationships between psoriasis and different types of cancer.

2.1 Psoriasis data sources

We utilized psoriasis GWAS data from studies conducted by Tsoi[16] and Chalitsios [17] as the source of instrumental variables (IVs). The selection criteria for single nucleotide polymorphisms (SNPs) as IVs included: $p < 5e{-}8$ and an F-statistic ($beta^2/se^2$) greater than 10, ensuring the strength of the IVs. To enhance the reliability of statistical analysis, we recalculated linkage disequilibrium (LD) for all selected SNPs, applying a threshold of $r^2 < 0.01$. Additionally, LD tools (https://ldlink.nih.gov/?tab=ldtrait) were used to conduct trait association analyses for these SNPs, and SNPs that could potentially introduce confounding bias were excluded. The case definition was restricted to patients diagnosed with psoriasis by a dermatologist. The study sample consisted of 13,229 cases and 21,543 controls.

2.2 Cancer data sources

The 32 types of cancer across eight systems were categorized as follows: respiratory system cancers: larynx, bronchus and lung; oral cavity and pharynx; digestive system cancers: esophagus, small intestine, pancreas, stomach, hepatocellular, hepatic bile duct, and gallbladder and extrahepatic bile ducts; hematologic malignancy: multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, acute lymphoblastic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, and chronic myeloid leukemia; genital system cancers: uterine cervix, uterine

corpus, ovary, vulva, testis, and prostate; breast cancer; skin cancers: malignant melanoma and malignant non-melanoma; other cancers: eye and annexa, kidney, bladder, bone, brain, and thyroid.

The GWAS data for these cancers were obtained from the UK Biobank (Supplementary Table S1) and the FinnGen study (Supplementary Table S2), both of which are large-scale genomic projects encompassing multiple phenotypes and providing extensive human genetic SNP data. Specifically, the UK Biobank data were used as the discovery cohort. Due to incomplete data in a single version of the FinnGen database, we extracted GWAS data for different types of cancer from r8, r9, and r10 to serve as the validation cohort. However, no relevant GWAS data for oral cavity and pharyngeal cancers were found in either the UK Biobank or FinnGen databases. Therefore, we used the study data from Lesseur et al. (IEU: EBI-A-GCST012235) [18] as a substitute. For hepatic bile duct, gallbladder and extrahepatic bile ducts, and malignant non-melanoma, only UK Biobank data were used for statistical analysis.

2.3 Statistical analysis

Given that proxy SNPs cannot fully replace original SNPs, this study did not use proxy SNPs to compensate for the genetic loci lost during the harmonization process. To ensure the independence and robustness of the research results, we established strict SNP screening criteria, retaining only SNP loci with a minor allele frequency (MAF) greater than 1%. Five methods (IVW, weighted median, weighted mode, simple mode, and MR-Egger) [19–22] were employed to assess the causal relationship between psoriasis and 32 types of cancer, with IVW serving as the primary reference method. The odds ratio (OR) was used to quantify the association between a one standard deviation (SD) increase in psoriasis and the corresponding change in cancer risk. To ensure the robustness of the results, Q statistics [23] were used to evaluate heterogeneity in genetic instruments, and the MR-Egger intercept test was performed to detect potential horizontal pleiotropy. When significant heterogeneity was detected ($p < 0.05$), the IVW random-effects model was applied for correction. In cases where horizontal pleiotropy was present, we employed the MR-PRESSO method [24] to remove outlier SNPs and re-estimate the causal effect. Additionally, Steiger filtering [25] was used to evaluate potential reverse causality, ensuring the accuracy of the inferred directionality. To control for multiple comparisons, the false discovery rate (FDR) correction [26] was applied to enhance the reliability and robustness of the findings.

Finally, meta-analysis was conducted using data from the UK Biobank and FinnGen cohorts to assess the causal effects of psoriasis on different cancers from multiple perspectives. If $I^2 > 50\%$, indicating substantial heterogeneity, a random-effects model was applied to combine the results; if $I^2 \leq 50\%$, suggesting minimal heterogeneity, a fixed-effects model was used. For cancers such as oral cavity and pharyngeal cancer, for which only a single dataset was available, the results from that dataset were used as the final analytical basis.

All statistical analyses were performed using R software (version 4.3.3) with the "TwoSampleMR" and "MRPRESSO" packages.

3 Results

3.1 Instrumental variables

In this study, we identified 62 genetic variants significantly associated with psoriasis from previous studies (Supplementary Table S3). Analysis using LD tools revealed that three SNPs (rs8070763, rs3802826, and rs2523461) were associated with human papillomavirus (HPV) infection, thyroid stimulating hormone (TSH) levels, and hepatocellular carcinoma (HCC), respectively (Supplementary Tables S4 and S5). To avoid potential confounding effects introduced by these variants, we excluded these three SNPs in subsequent MR analyses assessing the causal relationships between psoriasis and oral cavity and pharyngeal cancer, thyroid cancer, and hepatocellular cancer.

Table 1 The statistical results of UK Biobank in the initial analysis

Phenotypes	se	pval	$P_{heterogeneity}$	$P_{pleiotropy}$
Respiratory system				
Larynx	0.064	0.012	0.248	0.715
Bronchus and lung	0.023	0.014	0.005	0.240
Oral cavity and pharynx	0.031	0.002	0.705	0.242
Digestive system				
Esophagus	0.033	0.362	0.719	0.314
Small intestine	0.065	0.224	0.914	0.787
Stomach	0.043	0.990	0.572	0.196
Pancreas	0.033	0.280	0.952	0.195
Hepatocellular	0.092	0.025	0.249	0.503
Hepatic bile duct	0.056	0.108	0.001	0.849
Gallbladder and Extrahepatic bile ducts	0.059	0.580	0.838	0.977
Hematologic malignancy				
Multiple myeloma	0.082	0.201	0.488	0.865
Hodgkin lymphoma	0.068	0.024	0.000	0.215
Non-Hodgkin lymphoma	0.041	0.161	0.062	0.278
Acute myelocytic leukemia	0.055	0.680	0.118	0.979
Chronic myelocytic leukemia	0.078	0.821	0.764	0.029
Chronic lymphocytic leukemia	0.057	0.220	0.017	0.964
Genital system				
Ovary	0.030	0.420	0.509	0.583
Uterine cervix	0.060	0.386	0.898	0.241
Uterine corpus	0.027	0.311	0.462	0.294
Vulva	0.088	0.591	0.820	0.957
Testis	0.049	0.375	1.000	0.726
Prostate	0.012	0.828	0.486	0.033
Breast	0.012	0.155	0.013	0.722
Skin cancer				
Malignant melanoma	0.023	0.219	0.039	0.496
Malignant nonmelanoma	0.040	0.002	0.671	0.963
Other				
Eye and annexa	0.070	0.477	0.807	0.605
Kidney	0.028	0.017	0.665	0.228
Bladder	0.022	0.272	0.165	0.398
Bone	0.089	0.852	0.787	0.427
Brain	0.039	0.587	0.628	0.851
Thyroid	0.051	0.020	0.855	0.710

3.2 Cancer risk in the discovery cohort

We analyzed the causal association between psoriasis and cancer using data from the UK Biobank (Table 1 and Supplementary Table S6). In the initial analysis, results for six malignancies (bronchial and lung cancer, hepatic bile duct cancer, Hodgkin lymphoma, chronic lymphocytic leukemia, breast cancer, and malignant melanoma) exhibited heterogeneity. We re-evaluated the statistical results using the IVW random-effects model. Additionally, the analyses of chronic myeloid leukemia and prostate cancer revealed evidence of horizontal pleiotropy. Despite reanalyzing these associations after removing outlier SNPs, significant pleiotropy persisted, suggesting low robustness in the causal inference for these two cancers. As a result, chronic myeloid leukemia and prostate cancer were excluded from further analysis in the discovery cohort. Furthermore, Steiger filtering did not provide evidence of reverse causality in the analyzed associations.

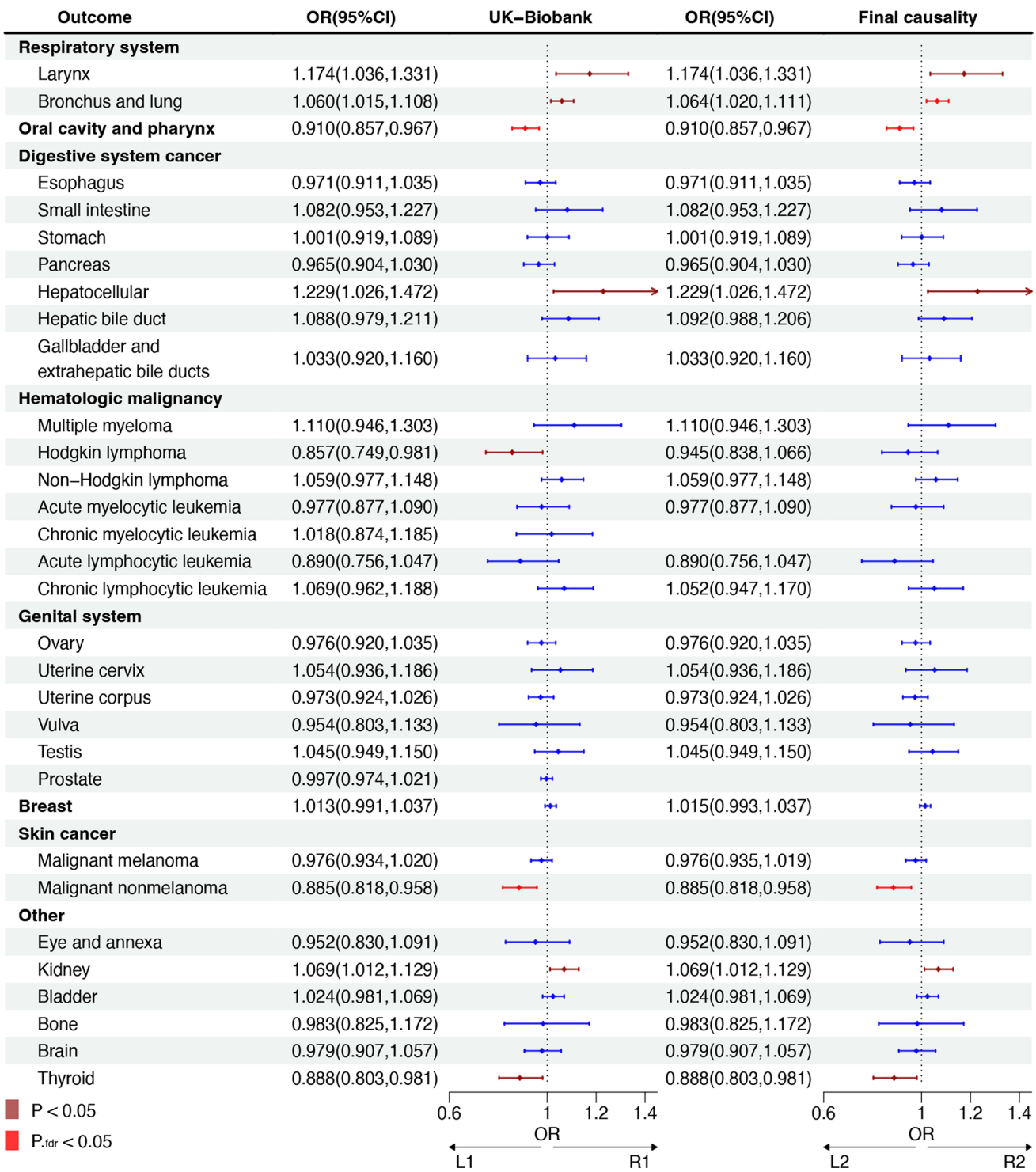

Fig. 1 Forest plot of the causal association between psoriasis and various cancers in the UK Biobank database, including the initial and adjusted ORs values with their corresponding CIs values. OR, odds ratio; CI, confidence interval

The final analysis revealed significant causal associations between psoriasis and seven types of cancer in the UK Biobank study (Fig. 1). Psoriasis showed a positive correlation with four cancers, indicating an increased risk: laryngeal cancer (OR: 1.17; 95% CI: 1.04–1.33), bronchial and lung cancer (OR: 1.06; 95% CI: 1.02–1.11), hepatocellular carcinoma (OR: 1.23; 95% CI: 1.03–1.47), and kidney cancer (OR: 1.07; 95% CI: 1.01–1.13). Conversely, psoriasis showed a negative correlation with three cancers, suggesting a reduced risk: oral cavity and pharyngeal cancer (OR: 0.91; 95% CI: 0.86–0.97),

malignant non-melanoma cancer (OR: 0.89; 95% CI: 0.82–0.96), and thyroid cancer (OR: 0.89; 95% CI: 0.80–0.98). Notably, bronchial and lung cancer, oral cavity and pharyngeal cancer, and malignant non-melanoma cancer remained statistically significant after FDR correction, reinforcing the reliability of the findings.

3.3 Cancer risk in the validation cohort

Due to missing data in the FinnGen database, MR analysis was conducted on summary level GWAS data for 28 different types of malignancies, following the same analytical procedures as before. The final results are presented in Supplementary Table S7. The findings indicate that psoriasis is associated with a protective effect against hepatocellular carcinoma (OR: 0.81; 95% CI: 0.73–0.90), prostate cancer (OR: 0.97; 95% CI: 0.95–0.99), and bladder cancer (OR: 0.95; 95% CI: 0.91–0.99).

3.4 Meta-analysis results

For cancer types with multiple data sources, we conducted a meta-analysis of the MR results, as shown in Fig. 2. The findings indicate that psoriasis promotes the progression of laryngeal cancer (OR: 1.14; 95% CI: 1.04–1.25) (Fig. 3). This result is supported by multiple data sources and is classified as primary evidence. Additionally, the study found that psoriasis has inhibitory effects on the following three types of cancer: oral and pharyngeal cancer (OR: 0.91; 95% CI: 0.86–0.97), prostate cancer (OR: 0.97; 95% CI: 0.95–0.99), and malignant non-melanoma cancer (OR: 0.89; 95% CI: 0.82–0.96). These findings are based on single data sources and are classified as secondary evidence.

4 Discussion

This study systematically evaluated the causal relationships between psoriasis and 32 site-specific cancers using the MR method. Compared to traditional observational studies, this approach based on random allocation of genetic variants, effectively minimized the interference of common confounding factors such as smoking and alcohol consumption [27]. Additionally, rigorous statistical analyses enhanced the reliability of causal inference. The results demonstrated significant causal associations between psoriasis and laryngeal cancer, oral cavity and pharyngeal cancer, prostate cancer, and malignant non-melanoma cancer. Among these, the association with laryngeal cancer showed strong evidence, supported by multiple databases, and its OR was statistically significant in the meta-analysis. The causal associations between psoriasis and oral cavity and pharyngeal cancer, prostate cancer, and malignant non-melanoma cancer were validated based on single databases, resulting in relatively weaker evidence. Nevertheless, the directions of these associations were consistent, and no significant pleiotropy or reverse causality was detected in the sensitivity analyses.

Laryngeal cancer, oral cavity and pharyngeal cancer are classified as head and neck tumors. Our study indicates that psoriasis significantly increases the risk of laryngeal cancer while exhibiting inhibitory effects on oral cavity and pharyngeal cancer. This divergence may be attributed to the heterogeneity of the tumors and their distinct microenvironmental characteristics. Regarding laryngeal cancer, our findings align with the conclusions from meta-analyses by Trafford [28] and Hannuksela-Svahn [29]. The chronic inflammation and immune activation state in psoriasis patients might promote the development of laryngeal cancer by altering cytokine profiles within the tumor microenvironment. Compared with individuals without a history of psoriasis, those with psoriasis face a 1.15-fold increased risk of developing laryngeal cancer. Additionally, Stern et al. [30] also confirmed the association between psoriasis and certain squamous cell carcinomas, supporting our conclusions. Multiple mechanisms are likely involved, including but not limited to immune dysregulation, side effects of biologic therapies, and dietary habits [31–33]. Tyszkiewicz et al. [34] and Wang et al. [35] found that S100 A3 and S10011, important members of the S100 protein family, play a promoting role in the progression of laryngeal cancer. Notably, Eckert et al. [36] confirmed that these two proteins are highly expressed in patients with psoriasis. Given the close association between the S100 protein family and psoriasis, we speculate that the promoting effect of psoriasis on laryngeal cancer may be related to the expression of these two proteins. This hypothesis requires further validation through functional experiments. Unfortunately, in the present study we could not identify specific GWAS datasets for oral cavity and pharyngeal cancer, leading us to use broader data for analysis. This limitation may have affected the precision of our conclusions. For oral cancer, the association with psoriasis may involve unique molecular mechanisms. For example, S100 A7 (psoriasin) is a small calcium-binding protein that is highly expressed in well-differentiated human squamous cell carcinoma of the oral cavity (SCCOC). It can inhibit β-catenin signaling through GSK3β-mediated phosphorylation,

Phenotypes	Data source	OR(95%CI)	Pval
Respiratory system			
Larynx	UKB+FinnGen	1.150(1.050,1.260)	0.003
Bronchus and lung	UKB+FinnGen	1.024(0.951,1.102)	0.534
Oral cavity and pharynx	Lesseur,C	0.910(0.857,0.967)	0.002
Digestive system cancer			
Esophagus	UKB+FinnGen	0.988(0.935,1.043)	0.652
Small intestine	UKB+FinnGen	1.010(0.929,1.097)	0.822
Stomach	UKB+FinnGen	0.977(0.930,1.026)	0.342
Pancreas	UKB+FinnGen	0.986(0.947,1.027)	0.499
Hepatocellular	UKB+FinnGen	0.992(0.661,1.489)	0.970
Hepatic bile duct	UKB	1.092(0.988,1.206)	0.080
Gallbladder and extrahepatic bile ducts	UKB	1.033(0.920,1.160)	0.580
Hematologic malignancy			
Multiple myeloma	UKB+FinnGen	1.013(0.939,1.093)	0.732
Hodgkin lymphoma	UKB+FinnGen	0.938(0.871,1.010)	0.090
Non–Hodgkin lymphoma	UKB+FinnGen	1.015(0.961,1.072)	0.589
Acute myelocytic leukemia	UKB+FinnGen	1.029(0.946,1.120)	0.505
Chronic myelocytic leukemia	FinnGen	0.950(0.752,1.199)	0.664
Acute lymphocytic leukemia	FinnGen	0.890(0.756,1.047)	0.160
Chronic lymphocytic leukemia	UKB+FinnGen	1.013(0.940,1.091)	0.744
Genital system			
Ovary	UKB+FinnGen	0.984(0.945,1.025)	0.430
Uterine cervix	UKB+FinnGen	0.973(0.931,1.017)	0.226
Uterine corpus	UKB+FinnGen	0.964(0.930,1.000)	0.051
Vulva	UKB+FinnGen	0.933(0.824,1.058)	0.280
Testis	UKB+FinnGen	1.047(0.970,1.131)	0.241
Prostate	FinnGen	0.970(0.947,0.993)	0.010
Breast	UKB+FinnGen	1.006(0.990,1.023)	0.467
Skin cancer			
Malignant melanoma	UKB+FinnGen	0.975(0.944,1.007)	0.119
Malignant nonmelanoma	UKB	0.885(0.818,0.958)	0.002
Other			
Eye and adnexa	UKB+FinnGen	0.986(0.889,1.093)	0.786
Kidney	UKB+FinnGen	1.008(0.898,1.131)	0.894
Bladder	UKB+FinnGen	0.986(0.915,1.062)	0.714
Bone	UKB+FinnGen	0.911(0.811,1.024)	0.119
Thyroid	UKB+FinnGen	0.937(0.864,1.016)	0.113

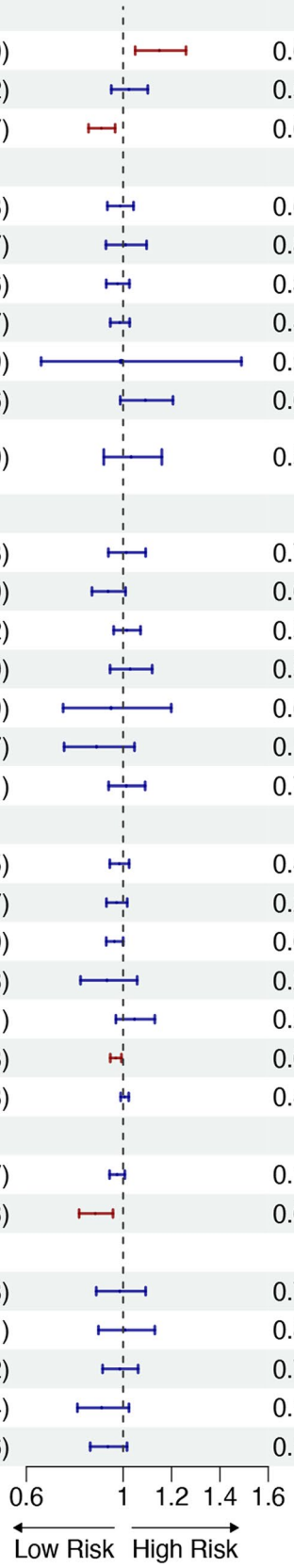

Fig. 2 Forest plot showing the final causal associations between psoriasis and 32 types of cancer

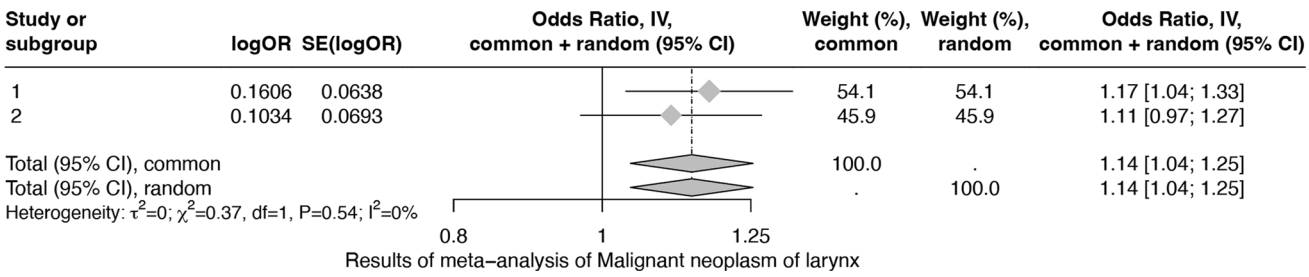

Fig. 3 The meta-analysis results for malignant neoplasm of the larynx, using both fixed-effect and random-effect models

which in turn suppresses the proliferation, invasion, and growth of SCCOC cells [37]. This aligns with our findings, which suggest that psoriasis reduces the risk of oral cancer by 9%. Regarding the relationship between psoriasis and pharyngeal cancer, studies are scarce, and we were unable to locate relevant evidence.

In genital and hematologic cancers, our study found that psoriasis exerts a negative regulatory effect on the risk of prostate cancer and malignant non-melanoma cancer. Specifically, the risk of prostate cancer in psoriasis patients is reduced by 3% (OR = 0.97; 95% CI: 0.95–0.99), while the risk of malignant non-melanoma cancer is reduced by 11% (OR = 0.89; 95% CI: 0.82–0.96). Chronic inflammation associated with psoriasis may alter the activity and proportion of immune cells in the tumor microenvironment, weakening the growth potential of tumors [38]. Proprotein convertase subtilisin/kexin type 9 (PCSK9) levels are significantly higher in psoriasis patients compared to healthy controls [39]. PCSK9 is linked to tumor necrosis factor (TNF) and IL-17, inflammatory cytokines that may enhance tumor cell clearance by modulating immune surveillance functions [40]. Additionally, biologic agents commonly used by psoriasis patients, such as TNF inhibitors, might indirectly reduce cancer risk by modulating pro-inflammatory signaling pathways [41]. Srivastava [42] and Kim et al. [43] have also highlighted the dominant role of the IL-23/Th17 axis in the inflammatory mediators involved in psoriasis. IL-23, secreted by antigen-presenting cells, promotes the proliferation and differentiation of Th17 cells via activation of the STAT3 signaling pathway. IL-17 which is the major effector cytokine downstream of IL-23 exhibits complex bidirectional regulatory effects in the tumor microenvironment [44]. In some cases, IL-17 enhances antigen presentation, thereby promoting the activity of $CD8^+$ T cells and inhibiting tumor growth [45]. The protective effects of psoriasis against prostate cancer and malignant non-melanoma cancer may be closely related to these mechanisms. However, these hypotheses require further validation through functional experiments and prospective studies.

Olveira et al. demonstrated that IL-17, which is closely associated with psoriasis, plays a crucial role in metabolic-associated fatty liver disease. IL-17 accelerates the progression of hepatic fat deposition and fibrosis by enhancing inflammation and insulin resistance, thereby increasing the risk of hepatocellular carcinoma (HCC) [46]. In our study, a positive association between psoriasis and HCC was identified only in the UK Biobank database. In contrast, for kidney cancer, Gantz et al. found no significant association between atopic dermatitis and an increased risk of kidney cancer [47]. This finding aligns with the results observed in our study. We speculate that the following factors may explain this discrepancy: first, the mechanisms underlying different cancers are highly heterogeneous. Second, the effects of inflammatory cytokines in psoriasis patients might be restricted to specific tumor microenvironments. This discovery provides a direction for future research, particularly in further exploring the role of the IL-17 and IL-23/Th17 axis in the development of HCC and kidney cancer. In addition, integrating multi-omics data and conducting functional experiments to clarify the pathways by which psoriasis-associated chronic inflammation influences tumorigenesis will provide new insights into precision therapy strategies.

This study applied a rigorous selection process for psoriasis instrumental variables (SNPs). Each candidate SNP underwent a detailed trait association query to exclude those directly related to the outcomes, thereby minimizing the potential impact of confounding factors and ensuring adequate statistical power. Ultimately, 59 SNPs meeting the criteria were identified. The initial selection of SNPs was based on previously published studies, and subsequent filtering revealed no SNPs associated with known major cancer risk factors, such as smoking, alcohol consumption, or diabetes. To ensure the accuracy and robustness of the results, we conducted stringent sensitivity analyses. For example, in the initial cohort study, chronic myeloid leukemia exhibited strong horizontal pleiotropy. This issue persisted even after certain SNPs were removed, so the disease was excluded from further analysis. Furthermore, to enhance the reliability of the final results, we applied FDR correction to mitigate the risk of false-positive findings caused by multiple testing.

Of course, our study has certain limitations. First, the study relies on large databases such as UK Biobank, which predominantly consist of populations of European ancestry. Differences in genetic backgrounds and environmental

factors may limit the generalizability of the results to other populations. Further studies are needed to verify the applicability and extrapolation of the findings to non-European populations. Second, the functions of some SNPs remain unclear, and undetected horizontal pleiotropy may affect the accuracy of causal inferences. Although participants in the UK Biobank and FinnGen databases are of European descent, regional differences may introduce genomic heterogeneity. This heterogeneity might result in certain conclusions being applicable to UK Biobank but not fully reproducible in FinnGen, highlighting the need to investigate the regional applicability of the findings further. Third, this study did not conduct systematic subgroup analyses, such as stratification based on demographic characteristics like gender and age. For malignancies such as oral cavity and pharynx cancer, stratification according to HPV infection status was also lacking. Given the crucial role of HPV infection status in evaluating the association between psoriasis and the risk of oral cavity and pharynx cancer, the absence of this important stratification variable may to some extent affect the accuracy of the study conclusions. Lastly, due to the inherent limitations of statistical power—particularly when analyzing rare variants or small subgroups—some results may be subject to error. These limitations suggest that future research should include more diverse population samples, incorporate refined subgroup analyses, and integrate multi-omics data to further enhance the robustness and generalizability of the findings.

5 Conclusion

This study employed the MR method to systematically investigate the causal relationships between psoriasis and various cancers, offering a fresh perspective on the role of chronic inflammation in psoriasis in the occurrence and development of cancer. The results indicate a significant positive correlation between psoriasis and laryngeal cancer, while showing a negative correlation with oral cavity and pharyngeal cancer, prostate cancer, and malignant non-melanoma cancer. These findings provide important scientific evidence for the early identification and intervention strategies of psoriasis-related cancers, particularly in establishing a standardized screening mechanism for laryngeal cancer, which holds significant clinical application value.

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Author contributions GYL: Writing-original draft, Conceptualization; JHT: Methodology, Data curation, Investigation,Visualization; XJY: Software; KL: Supervision and editing.All authors reviewed the manuscript.

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Data availability All data analysed in this study can be obtained by a reasonable request to corresponding authors.

Declarations

Ethics approval and consent to participate Our analyses used published studies in public databases or publicly available data. Raw data were not collected for the datasets used, so ethics committee approval was not required.

Consent for publication All authors approved the content and submission.

Competing interests The authors declare no competing interests.

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