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Last updated by author(s): Jul 31, 2024

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	The population cohort data had been collected from UK Biobank; the summary-level data used in two-sample MR were collected from previously published GWAS; the RNAseq data were collected from TCGA and GTEx database.No software was involved in data collection.
Data analysis	R version 4.03(LAPACK version 3.11.0) survival 3.7.0 and base 4.0.3 were used to perform Cox proportional harzard regression model and logistic regression model in PheWAS analysis and one-sample MR; TwoSampleMR 0.4.21 and MR-PRESSO 1.0 was used to perform Mendelian randomization study; PRSice-2 2.3.5 was used to calculate polygenetic risk score.All customed codes are available at https://github.com/Luowenjin826/psoriasis_study

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The current analysis was approved by UK Biobank in August 2020 with the ID 103654. The raw UK Biobank data are protected and are not available due to data privacy laws. The UK Biobank data are available through a standard application protocol (https://www.ukbiobank.ac.uk/register-apply/). Summary-level data from publicly available GWAS can be obtained through the IEU OpenGWAS project (https://gwas.mrcieu.ac.uk/) and the GWAS Catalog (https://www.ebi.ac.uk/gwas/). The specific GWAS summary datasets used in PRS calculation and Two-sample MR analyses are listed in Supplementary Data 1. Gene expression RNA-seq data and clinical data from TCGA and GTEx RNA datasets can be accessed via the UCSC XENA database (dataset ID: TcgaTargetGtex_RSEM_Hugo_norm_count, https://xenabrowser.net/datapages/?dataset=TcgaTargetGtex_RSEM_Hugo_norm_count&host=https%3A%2F%2Ftoil.xenahubs.net&removeHub=https%3A%2F%2Fxena.treehouse.gi.ucsc.edu%3A443). The cis-eQTL data can be obtained through the following link: https://www.gtexportal.org/home/snp/[rs_number], where [rs_number] should be replaced with the rs number of each SNP listed in Supplementary Table 18. Source data are provided with this paper.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Our findings could apply to both male and female. We repeated our analyses stratified by sex. Sex (Field ID 31) in the UK Biobank was determined based on self-reporting data via questionnaire.
Reporting on race, ethnicity, or other socially relevant groupings	Race (Field ID 21000) in the UK Biobank was determined based on self-reporting data via questionnaire. In observational PheWAS, race was adjusted. In PRS PheWAS and MR analysis, the populations included were European ancestry.
Population characteristics	Population characteristics are summarized in Table 1.
Recruitment	The UK Biobank is a population-based cohort study of over 500,000 participants aged 37-73 years. Between 2006 and 2010, participants attended one of 22 assessment centers.
Ethics oversight	The National Information Governance Board for Health and Social Care and the National Health Service North West Multicenter Research Ethics Committee (reference 13/NW/0382) approved the UK Biobank ethical application.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	For observational PheWAS we included 476599 participants. For PRS PheWAS and one-sample MR we included 458587 participants. Each GWAS data set included in two-sample MR was derived from large cohort studies. We did not perform any sample size calculations.
Data exclusions	Exclusion criteria were pre-established before the analyses. We excluded participants if they were diagnosed with other autoimmune diseases that might potentially influence the association between psoriasis and cancers. We excluded cancer types with an insufficient number of cases to avoid abnormal HR estimation. We excluded participants who had been diagnosed with any type of cancer at baseline or before the diagnosis of psoriasis to avoid reverse causation. We further excluded participants who were not white European and those who lacked genetic data as the genetic analyses required this information.
Replication	In our study, RLL and WJL independently repeated all analyses once, and the results were further validated by XJC. They all successfully obtained the same conclusions.
Randomization	While genes cannot be randomly allocated, they are inherited in a random fashion (following Mendel's laws of inheritance).
Blinding	Blinding was not relevant to this study because we are not involved in the data collection and utilized pre-existing data from the UK Biobank. In Mendelian randomization, the estimation of the genetic instrument effect (β) relies on the randomization of genotypes during meiosis, which is analogous to blinding.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.