nature portfolio

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Last updated by author(s): May 26, 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	No software was used.
Data analysis	We used publicly available software for the data analysis (grf, Metal, Plink, and PRS-CS). R scripts to perform the HTE analysis used in this study are shared in a GitHub repository (https://github.com/tatsuhikonaito/PRS_HTE).

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

Genotype data of the BBJ are available at the NBDC Human Database (research ID: hum0014). The analysis of UKB GWAS data was conducted via the application 47821 number (https://www.ukbiobank.ac.uk/).

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	We conducted sex-stratified analysis to see the differences by sex in our findings. We excluded individuals of ambiguous sex (sex chromosome aneuploidy and inconsistency between self-reported and genetic sex).
Population characteristics	The detailed information of the participants in BBJ is described in the previous literatures [Hirata, M. et al. J. Epidemiol. 27, S9–S21 (2017), and Nagai, A. et al. J. Epidemiol. 27, S2–S8 (2017)]. The detailed information of the participants in UKB is described in the previous literatures [Sudlow, C. et al. PLoS Med. 12, 1–10 (2015), and Bycroft, C. et al. Nature 562, 203–209 (2018)].
Recruitment	The BBJ project collaboratively collected DNA and serum samples from 12 medical institutions in Japan and recruited approximately 200,000 participants with the diagnosis of at least one of 47 diseases, mainly of Japanese ancestry. The UKB project is a population-based prospective cohort that recruited approximately 500,000 people aged between 40 and 69 yr from 2006 to 2010 from across the United Kingdom.
Ethics oversight	All the BBJ individuals provided written informed consent, as approved by the ethical committees of the Institute of Medical Science, University of Tokyo. This study was approved by the ethical committee of Osaka University Graduate School of Medicine.

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	We used all the available UKB individuals who satisfied inclusion criteria to maximize the statistical power of our analysis. We downsampled the control for the BBJ cohort to have the same percentage of diseases as the UKB cohort so that the estimated individual treatment effect for each disease was comparable.
Data exclusions	We excluded individuals of ambiguous sex, outliers of heterozygosity or call rate of high quality markers, and ≤2nd related samples. We also excluded individuals considered to be of non-European and non-Japanese origin for the UKB and BBJ cohort, respectively.
Replication	We did not perform any replication analysis.
Randomization	We randomly down-sampled the control for the BBJ cohort to have the same percentage of diseases as UKB.
Blinding	We did not apply blinding of the samples because no intervention was conducted in our study.

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

Methods

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