nature portfolio

Corresponding author(s): Pradeep Natarajan

Last updated by author(s): Feb 13, 2026

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 modified TelSeq implementation used in this study is publicly available at https://github.com/tetnakao/telseq_cram and archived on Zenodo (DOI: 10.5281/zenodo.18395180). The modified NGS-PCA implementation is publicly available at https://github.com/tetnakao/NGS-PCA and archived on Zenodo (DOI: 10.5281/zenodo.18421692).
Data analysis	The code used for the analyses is available on Zenodo (DOI: 10.5281/zenodo.16689623). We used the software listed below: FINEMAP 1.4.2, GCTA version 1.94.2, GWAMA ver. 2.2.2, Hail 0.2, LDSC v1.0.1, LDstore 2.0, MAGMA v1.10, mosdepth v0.3.5, MR-MEGA ver. 0.2, NGS-PCA v.0.0.2 (modified), PLINK 2.00 (Stable beta 7, 16 Jan), PoPS v0.2, R 4.2 (R packages: ggplot2 version 3.5.1, locuszoomr version 0.3.5, metafor version 3.8-1, sf version 1.0-15, qqman version 0.1.9), Regenie v3.4, SaTScan version 10.1.3, TelSeq v0.0.2 (modified).

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 genotypes and phenotypes of UKB and AoU participants are available by application to the UKB (https://www.ukbiobank.ac.uk/register-apply/) and AoU (https://allofus.nih.gov/), respectively. GWAS summary statistics generated in this study are publicly available at Cardiovascular Disease Knowledge Portal (https://cvd.hugeamp.org/) and Zenodo (http://dx.doi.org/10.5281/zenodo.16689623). The previously published GWAS summary statistic for LTL in UKB (Codd et al., Nature Genetics 2021: https://figshare.com/s/caa99dc0f76d62990195; Burren et al., Nature Genetics 2024: https://ftp.ebi.ac.uk/pub/databases/gwas/summary_statistics/GCST90435001-GCST90436000/GCST90435144/GCST90435144.tsv.gz [EUR only]) and meta-analysis with TOPMed and Singapore Chinese Health Study (Chang et al., Nature Communications 2023: https://figshare.com/s/f6de1a56ad7c448c1f4c) are publicly available. The previously published full GWAS summary statistics for LTL in TOPMed are available upon application on dbGap (phs001974).

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	We considered genetically imputed sex in the All of Us Research Program. We excluded participants with discordant sexes between genetically imputed and self-reported sexes in UK Biobank.
Reporting on race, ethnicity, or other socially relevant groupings	We considered genetically imputed ancestry groups throughout this study.
Population characteristics	The All of Us Research Program (AoU) aims to engage a longitudinal cohort of one million or more U.S. participants, with a focus on including populations that have historically been under-represented in biomedical research. Detailed protocol of the AoU cohort and its genomic data have been described previously (N. Engl. J. Med. 381, 668–676 (2019)). The UK Biobank (UKB) is a population-based cohort of >500,000 UK adult residents recruited between 2006 and 2010 and followed prospectively via linkage to national health records. Details of UKB have been described before. (Nature 562, 203–209 (2018)).
Recruitment	AoU recruited adults 18 years and older who have the capacity to consent and reside in the U.S. or a U.S. territory at present are eligible. Informed consent for all participants is conducted in person or through an eConsent platform that includes primary consent, HIPAA Authorization for Research use of EHRs and other external health data, and Consent for Return of Genomic Results. UK Biobank invited approximately 9.2 million individuals whose contact details were obtained from National Health Service (NHS) central registers. 40 to 69 years of age who were living in England, Wales, and Scotland were invited to join the study, and 5.5% participated in the baseline assessment. Recruitment was carried out between 2006 and 2010. Full details of the recruitment process are described before (UK Biobank: Protocol for a large-scale prospective epidemiological resource, 2007, https://www.ukbiobank.ac.uk/media/gnkeyh2q/study-rationale.pdf).
Ethics oversight	The protocol was reviewed by the Institutional Review Board (IRB) of the AoU Research Program. The AoU IRB follows the regulations and guidance of the NIH Office for Human Research Protections for all studies, ensuring that the rights and welfare of research participants are overseen and protected uniformly. Secondary analyses of the UKB data under Application 7089 was approved by the Massachusetts General Hospital IRB.

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	The All of Us Research Program (AoU) version 7 released 245,394 WGS data. In UK Biobank, we used genotyping array for genome-wide association study for common variants (N = 488,188) and used WES for rare variant association study (N = 452,929).
Data exclusions	In All of Us, we excluded flagged samples for sequencing quality by AoU (n = 549), genotyping missingness > 0.01 (n = 395), lacking age

Data exclusions	information (n = 26), and genetically undetermined sex (n = 1,930), to construct a cohort of 242,494 participants included in our analysis, as summarized in Supplementary Fig. 1. In UK Biobank, we excluded samples with consent retraction, excess heterogeneity, sex discordance, or missingness/heterogeneity/outliers in the genotype as summarized in Supplementary Fig. 1.
Replication	We leveraged previous multi-ancestry leukocyte telomere length study in Trans Omics for Precision Medicine (Cell Genom. 2, 100084 (2022)) for replication for some of the findings in this study.
Randomization	NA
Blinding	NA

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.*