

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

Data analysis https://www.uni-regensburg.de/medizin/epidemiologie-praeventivmedizin/genetische-epidemiologie/software/
METAL (version 2011-03-25): <https://csg.sph.umich.edu/abecasis/metal/download/>
LiftOver (version downloaded in 2019.12.11): <https://genome-store.ucsc.edu/>
ANNOVAR (version 1.2.8): <https://annovar.openbioinformatics.org/en/latest/>
LD score regression (version 1.0.1): <https://github.com/bulik/ldsc>
Genomic SEM (version 0.0.5): <https://github.com/GenomicSEM/GenomicSEM>
FUMA (version 1.4.1): <https://fuma.ctglab.nl/>
MAGMA (version 1.08): <https://ctg.cncr.nl/software/magma>
PLINK2.0 (version 2.00a3.7LM): <https://www.cog-genomics.org/plink/2.0/>
PRS-CS (version as of Nov 3, 2022): <https://github.com/getian107/PRScs>
PRSice-2 (version 2.3.5): <https://choishingwan.github.io/PRSice/>
SMR (version 1.03): <https://yanglab.westlake.edu.cn/software/smr/#Download>
Popcorn (version 1.0): <https://github.com/brielin/Popcorn>
MR-PRESSO (version 1.0): <https://github.com/rondolab/MR-PRESSO>

R "base" (version 4.0.5), "psych" package (version 2.1.9), "stats" package (version 4.0.5), "survival" package (version 3.5.7), "TwoSampleMR" package (version 0.5.6): <https://cran.r-project.org/>

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](#)

Summary statistics of the multivariate and KoGES MetS GWAS are available through GWAS Catalog (<https://www.ebi.ac.uk/gwas/>) under accession IDs GCST90444487–GCST90444489. The PRS weights developed for MetS are available through PGS Catalog (<https://www.pgscatalog.org/>) with publication ID PGP000664 and score ID PGS004928. The individual-level phenotypic and genetic data for UKB (<https://www.ukbiobank.ac.uk/>) and KoGES (<https://is.kdca.go.kr/>) can be accessed through the application. The reference panel for 1kGp3 can be obtained from the following URL: https://mathgen.stats.ox.ac.uk/impute/1000GP_Phase3.html. The NHGRI-EBI GWAS Catalog is available at the following URL: <https://www.ebi.ac.uk/gwas/docs/file-downloads>. The GWAS summary statistics from the following consortia and biobanks are publicly available at the corresponding URL: GIANT (https://portals.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium_data_files), MAGIC (<https://magicinvestigators.org/downloads/>), GLGC (<http://www.lipidgenetics.org/#data-downloads-title>), FinnGen (https://www.finnngen.fi/en/access_results), UKB from Neale lab (<http://www.nealelab.is/uk-biobank>), UKB from Lee lab (<https://www.leelabsg.org/resources>), and PanUKB (<https://pan.ukbb.broadinstitute.org/downloads>). The GWAS summary statistics of the MVP cohort were obtained using an approved dbGaP application (phs001672.v9.p1). The GWAS summary statistics from the MGI cohort are available upon request from <https://precisionhealth.umich.edu/our-research/documents-for-researchers>. The eQTL summary statistics are available from the following URL: GTEx (<https://gtexportal.org/home/downloads/adult-gtex#qtl>), eQTLGen (<https://www.eqtlgen.org/cis-eqtl.html>), BrainMeta v2 (<https://yanglab.westlake.edu.cn/software/smr/#DataResource>), METSIM (<https://mohlke.web.unc.edu/data/1702-2/>), and FUSION (<https://www.ebi.ac.uk/birney-srv/FUSION/>).

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	Sex was determined based on self-reporting. Analyses were conducted by incorporating sex as a covariate.
Reporting on race, ethnicity, or other socially relevant groupings	UK Biobank data includes UK adults, providing self-reported individual race including non-Hispanic Black, Hispanic or Latino, and non-Hispanic White. KoGES data provides self-reported race as Asian.
Population characteristics	We used publicly available (but with restricted access) data such as UK Biobank and KoGES where a detailed demographic information is available at https://www.ukbiobank.ac.uk/ and https://academic.oup.com/ije/article/46/2/e20/2622834 , respectively. The UKB cohort consists of 54.4% of female and mean age of 56.5 (s.d. = 8.1). The KoGES cohort consists of 52.6% of female and mean age of 52.3 (s.d. = 8.9).
Recruitment	NA, we were not involved in participant recruitment and publicly available data were used.
Ethics oversight	The request for UK Biobank data was approved by the National Research Ethics Committee (REC reference 11/NW/0382). The request for KoGES data was approved by Samsung Medical Center Institutional Review Board (SMC 2023-02-084).

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	Detailed sample size for GWAS summary statistics data are available in Methods, Supplementary Note, and Supplementary Table 1. Below are the list of sample size of GWAS summary statistics used for the analyses of the main report and these are the maximum total sample size for the corresponding GWAS. Body mass index (GIANT): 806,834 Fasting glucose (MAGIC): 151,188 High-density lipoprotein (GLGC): 1,244,580 Hypertension (meta-analysis): 508,612
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Triglycerides (GLGC): 1,253,277
 Type 2 diabetes (meta-analysis): 597,437
 Waist circumference (UKB): 385,932

Data exclusions Single-nucleotide polymorphism (SNPs) were excluded based on the quality criteria described in Methods.

Replication Replication is not applicable as we leveraged the largest GWAS summary statistics that are publicly available.

Randomization Randomization to an experimental condition was not applied because this study is not experimental. Analyses were statistically adjusted for age, sex, genetic principal components, genotyping array and batch.

Blinding Blinding is not applicable as the researchers were not involved in participant recruitment and leveraged publicly available GWAS summary statistics which does not contain individual-level data.

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

Methods

- 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

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

Plants

Seed stocks NA

Novel plant genotypes NA

Authentication NA