

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	Access to individuals level data from the 45 cohorts used in this GWAS can be obtained by bona fide scientists through application to the specific data providers, with information about each study listed in detail in the Supplementary Note
Data analysis	Upon publication GWAS summary statistics will be made available at the GWAS catalog (www.ebi.ac.uk/gwas/download/summary-statistics). Analytical methods are described in the Methods section and in more detail in the Supplementary Note. Standard software with available code and algorithms was used, namely: QCGWAS, EasyQC, BOLT-LMM, XWAS, SNPtest, METAL< GCTA, Eagle, SAIGFE, plink and various libraries in R for additional analyses and visualization (coloc, ggplot2). For the biological annotation, we used VEP, MAGMA, SMR (summary based Mendelian Randomisation, HEIDI and LDS-SEG.

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](#)

Upon publication, GWAS summary statistics will be made available at the GWAS Catalog (www.ebi.ac.uk/gwas/downloads/summary-statistics). Access to individual level data from the multiple sources used in this GWAS can be obtained by bona fide scientists through application to each specific data providers, source described in the Supplementary Note.

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender	All analyses were performed in sex combined and sex-specific models. Furthermore we have been careful to distinguish between sex and gender where appropriate.
Population characteristics	Both males and females, if they met the exclusions criteria described.
Recruitment	Recruitment varied over the 45 studies and is described in the supplementary information.
Ethics oversight	Ethics was approved by the University of Oxford, but also for each individual data source locally.

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 sample size was based on the maximum data sample size that could be collected. For Number of children ever born (NEB) N=785,604 (Mlae = 306,980, Female = 478,624). For childlessness (CL) this was N=450,082.
Data exclusions	Individuals were eligible for inclusion if they met the following conditions; a) They were assessed for NEB at least at age 45 for women, age 55 for men; b) Those who have both given birth to a child (parous) and those who have not (nulliparous); c) All relevant covariates (e.g. year of birth) are available for an individual; d) They were successfully genotypes genome-wide (recommended individual genotyping rate > 95%); e) They passed the cohort-specific standard quality controls, e.g. excluding individuals who are genetic outliers in the cohort; f) They were of European ancestry. Data exclusions were specified in advance in the analysis plan pre-deposited in the Open Science Framework website: https://osf.io/b4r4b/ European ancestry samples were chosen due to the availability of large samples and for no biological or substantive reason.
Replication	The study involves large discovery sample with GWAS summary statistics available at the GWAS Catalog upon publication (www.ebi.ac.uk/gwas/downloads/summary-statistics). Partial replication in the FinnGen cohort using data from 37,741 women was used for replication, a binomial sign test was used to assess consistency of the results, and this was strongly significant.
Randomization	Not applicable as no intervention was provided to any participant.
Blinding	Not applicable as no intervention was provided to any participant.

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