

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work we publish. This form is published with all life science papers and is intended to promote consistency and transparency in reporting. All life sciences submissions use this form; while some list items might not apply to an individual manuscript, all fields must be completed for clarity.

For further information on the points included in this form, see [Reporting Life Sciences Research](#). For further information on Nature Research policies, including our [data availability policy](#), see [Authors & Referees](#) and the [Editorial Policy Checklist](#).

► Experimental design

1. Sample size

Describe how sample size was determined.

We used individuals of white, British ancestry in the UK Biobank, for whom we also had data on body mass index (BMI).

2. Data exclusions

Describe any data exclusions.

We excluded individuals flagged as problematic by the UK Biobank quality control documentation: excess heterozygosity, putative sex chromosome aneuploidy, or excess relatives.

3. Replication

Describe whether the experimental findings were reliably reproduced.

We replicated the variance effects of SNPs rs900400 and rs1801282 in data from an external meta-analysis (GIANT).

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Not applicable to a genome-wide association study.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Not applicable to a genome-wide association study.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or the Methods section if additional space is needed).

n/a Confirmed

- | | | |
|-------------------------------------|-------------------------------------|--|
| ☐ | ☒ | The <u>exact</u> sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.) |
| ☒ | ☐ | A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly. |
| ☒ | ☐ | A statement indicating how many times each experiment was replicated |
| ☐ | ☒ | The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section) |
| ☐ | ☒ | A description of any assumptions or corrections, such as an adjustment for multiple comparisons |
| ☐ | ☒ | The test results (e.g. p values) given as exact values whenever possible and with confidence intervals noted |
| ☒ | ☐ | A summary of the descriptive statistics, including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range) |
| ☒ | ☐ | Clearly defined error bars |

See the web collection on [statistics for biologists](#) for further resources and guidance.

► Software

Policy information about [availability of computer code](#)

7. Software

Describe the software used to analyze the data in this study.

HLMM (Heteroskedastic linear mixed model) software. Available under MIT license at <https://github.com/AlexTISYoung/hlmm>

For all studies, we encourage code deposition in a community repository (e.g. GitHub). Authors must make computer code available to editors and reviewers upon request. The *Nature Methods* [guidance for providing algorithms and software for publication](#) may be useful for any submission.

► Materials and reagents

Policy information about [availability of materials](#)

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

Not applicable to a genome-wide association study

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

Not applicable to a genome-wide association study

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

Not applicable to a genome-wide association study

b. Describe the method of cell line authentication used.

Not applicable to a genome-wide association study

c. Report whether the cell lines were tested for mycoplasma contamination.

Not applicable to a genome-wide association study

d. If any of the cell lines used in the paper are listed in the database of commonly misidentified cell lines maintained by [ICLAC](#), provide a scientific rationale for their use.

Not applicable to a genome-wide association study

► Animals and human research participants

Policy information about [studies involving animals](#); when reporting animal research, follow the [ARRIVE guidelines](#)

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

Not applicable to a genome-wide association study

Policy information about [studies involving human research participants](#)

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

General descriptions have been provided by the UK Biobank