nature portfolio

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Last updated by author(s): Mar 25, 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	All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc) and R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). The SAS and R code for our study is available on GitHub at https://github.com/Xuan891101/UKB_iso_lone_LE_analysis
Data analysis	All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc) and R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). The SAS and R code for our study is available on GitHub at https://github.com/Xuan891101/UKB_iso_lone_LE_analysis

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 UK Biobank data used in this study are accessible in a public, open-access repository (https://www.ukbiobank.ac.uk/). The data are available for approved researchers following a formal application and review process. This study was conducted under approved project number 29256.

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 performed the analysis stratified by sex because the mortality rates were different in man and women.
Reporting on race, ethnicity, or other socially relevant groupings	Because over 95% participants were Whites, we category race/ethnicity group as Whites and Non-Whites.
Population characteristics	UK Biobank recruited 500,000 people aged between 40 and 70 who agreed to have their health followed. Detailed information on this cohort is available elsewhere: https://bmjopen.bmj.com/content/6/3/e009161
Recruitment	The UK Biobank participants were recruited between 2006 and 2010 from across the UK. UK Biobank is not a representative population with about 95% participants are Whites.
Ethics oversight	All participants provided written informed consent. This study was approved by the North West Multi-Centre Research Ethics Committee and the Tulane University Biomedical Committee Institutional Review Board.

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	In the present study, a total of 277,489 participants were eligible, after excluding 35,704 participants with incomplete data on loneliness or SI, 189,160 participants with prevalent 7 chronic diseases at baseline. This study used data from the UK Biobank, a large prospective cohort. The sample size was determined by the availability of eligible participants with complete data. No formal power calculation was performed a priori. Among the 189,160participants included, 16,356 deaths occurred during follow-up. This number of events provided adequate statistical power.
Data exclusions	We exlude 35,704 participants with incomplete data on loneliness or social isolation, and 189,160 participants with prevalent cardiovascular disease, diabetes, cancer, neurodegenerative disease, chronic respiratory disease, depression, or anxiety at baseline.
Replication	All analyses were conducted using R with fully documented code. Key results were independently verified by the second author using the same analytical scripts. All reported findings were successfully reproduced using the same data extraction criteria and analytical methods.
Randomization	This study was based on a prospective population-based cohort. Participants were not randomized to any intervention; exposure status was determined based on pre-existing characteristics.
Blinding	Investigators were not involved in the original data collection process. Given the observational nature of the study, traditional blinding procedures were not applicable.

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.