

Reporting Summary

Nature Research 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 Research policies, see [Authors & Referees](#) 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 from questionnaires, clinical visits and laboratory data was entered using comma delimited files, excel spreadsheets and microsoft access. CGM and accelerometer data was imported from text files into the analysis pipeline. Microbiome data was analyzed using the open source software described in the Methods.

Data analysis

Analyses were carried out using version 3.4.2 R Core Team, or with Python 3.0 using the open source libraries mentioned in the Methods. Dietary analysis was undertaken using FETA software <http://www.srl.cam.ac.uk/epic/epicffq/>. Microsoft Excel 365 (version 1904) was used to process spreadsheets. All open source software used in the analysis is reported in the Methods.

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [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 list of figures that have associated raw data
- A description of any restrictions on data availability

Metagenomes are deposited in EBI ENA under accession number PRJEB39223. The non-metagenomic data used for analysis in this study are held by the department of Twin Research at King's College London. The data can be released to bona fide researchers using our normal procedures overseen by the Wellcome Trust and its guidelines as part of our core funding. We receive around 100 requests per year for our datasets and have a meeting 3 times per month with independent members to assess proposals. The application is at <https://twinsuk.ac.uk/resources-for-researchers/access-our-data/>. This means that the data need to be anonymized and conform to GDPR standards.

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](https://www.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	1002 individuals were recruited for the UK cohort (allowing for 80% power to detect correlations $r=0.15$ with $p<0.0001$ to allow adjustment for 500 test), 100 for the US cohort to enable replication of the larger effects (80% for $r=0.28$ with $p<0.05$), the final sample size excludes individuals who dropped out (didn't finish the clinic visit)
Data exclusions	Pre-established exclusion criteria were T2D. Exclusion and inclusion criteria available in "Berry, S.E., Valdes, A.M., Drew, D.A. et al. Human postprandial responses to food and potential for precision nutrition. Nat Med 26, 964–973 (2020)."
Replication	the US cohort has been used as replication for findings in the larger UK cohort
Randomization	There were 3 different test meal protocols. Meal order in each test meal protocol was randomised using Microsoft Access for each participant, using a 2-block randomisation and 1 non-randomised block. For additional details on the test meal protocols please see: https://protocolexchange.researchsquare.com/article/pex-802/v1
Blinding	Participants were blinded to the nutrient composition of test meals. Test meals were labelled with a barcode and randomization code. Laboratory analysis was performed on blinded coded samples.

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
☒	☐ Animals and other organisms
☐	☒ Human research participants
☐	☒ Clinical data

Methods

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

Human research participants

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

Population characteristics	Study participants were healthy individuals aged between 18-65 years and able to provide written informed consent. In total, 1002 individuals were recruited for the UK cohort (279 males and 723 females, average age 45.58 years and std 11.88 years) and 100 for the US validation cohort (32 males and 68 females, average age 41.33 years and std 12.82 years).
Recruitment	Participants enrolled already in the TwinsUK cohort were recruited as part of studies which are included in the cohort's annual newsletter and also mentioned on our website: http://www.twinsuk.ac.uk/ Non-twins were recruited via independent recruitment agencies, project specific website and online advertising including the use of social media platforms and social media. The study specifically aimed to recruit from the Twins UK cohort to enable genetic contributions to be estimated and ~30% of participants were recruited from outside of this cohort. The Twins UK cohort characteristics is representative of the UK population and we do not report any selection bias.
Ethics oversight	Ethical approval for the study was obtained in the UK from the Research Ethics Committee (REC approval 18/LO/0663) and Integrated Research Application System (IRAS 236407) and in the US from the Institutional Review Board (Partners Healthcare IRB 2018P002078). The trial was registered on ClinicalTrials.gov (registration number: NCT03479866) and was run in accordance with the Declaration of Helsinki and Good Clinical Practice. Study procedures were only carried out after having received written informed consent from each participant.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	NCT03479866
Study protocol	https://clinicaltrials.gov/ct2/show/record/NCT03479866
Data collection	Data was collected at St Thomas' Hospital, London and Massachusetts General Hospital, Boston between June 2018 and May 2019
Outcomes	Gut microbiome profile, triglyceride blood concentration, glucose blood concentration, record of sleep pattern using a wearable device (i.e. fitness watch), record of physical activity using a wearable device (i.e. fitness watch)