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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 (Microsoft Office 365 2019). CGM and accelerometer data was imported from text files into the analysis pipeline.
Data analysis	Analyses were carried out using version 3.4.2 R Core Team ,the “mets” (Multivariate Event Times) package in R, and the DADA2 pipeline

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

The data used for analyzing this study are held by the department of Twin Research at Kings 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 three times a month with independent members to assess proposals Application is via https://twinsuk.ac.uk/resources-for-researchers/access-our-data/. This means that the data needs to be anonymized and conform to GDPR standards. Specifically for this paper, all the variables used in the models can be requested as well as the summary outcome measures for each person. The 16S microbiome data used here will be uploaded onto the EBI site with unlimited access.

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	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. At the analysis level, exclusions were performed wherever c-peptide, glucose, triglyceride measures were missing for the any of the postprandial responses.
Replication	the US cohort has been used as replication for findings in the larger UK cohort. Prediction models for triglyceride and glucose were successfully replicated but not so for c-peptide
Randomization	given the single arm nature of the study, randomization was not applicable
Blinding	there was no control or placebo arm therefore blinding was 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
☒	☐ 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
Recruitment	Particpants enrolled already in the TwinsUK cohort were recruited as part of studies which are included in the cohort's annual newsletter and also mentioned onour 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
Ethics oversight	Ethics was granted by the London - Hampstead Research Ethics Committee (REC approval18/LO/0663) and by the Partners Healthcare IRB (2018P002078)

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
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)