nature portfolio

Corresponding author(s): Professor John F Cryan and Dr Gerard Moloney

Last updated by author(s): Mar 6, 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 custom code used in the analysis of the data presented are freely available from https://github.com/thomazbastiaanssen/coffee/
Data analysis	Gen5 1.01.9 MSD Discovery Methodical Mind Software 2 MassLynx 4.2 TargetLynx see MassLynx Xcalibur 2.1 MassARRAY® Assay Design Suite, Agena Bioscience 3 MassARRAY® TYPER, Agena Bioscience 5 IBM SPSS 28 Graphpad Prism 9.4.0 Rstudio GUI 2022.2.2.485 R 4.2.0

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 untargeted metabolomics data generated in this study has been deposited in the MetaboLights database under accession code MTBLS13401 [https://www.ebi.ac.uk/metabolights/MTBLS13401].
The targeted metabolomics data is available at MetaboLights under accession code MTBLS13494, [https://www.ebi.ac.uk/metabolights/MTBLS13494].
The microbiome data generated in this study are available at the European Nucleotide Archive PRJEB108545.
Count data for microbiome (10.5281/zenodo.18661295) are on Zenodo
Participant meta-data has been uploaded to 10.5281/zenodo.18348935

Code Availability
All original code has been deposited at GitHub (https://github.com/thomazbastiaanssen/coffee/) and is publicly available.

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	• In this study, sex was self-reported, and gender was considered a covariate during statistical analysis. • The sex and gender of each participant is stated in the methods section on page 20 and in Table 1 and supplementary Table 15. • Informed consent was obtained from all participants, and this detail is noted on page 19.
Reporting on race, ethnicity, or other socially relevant groupings	Patients were classified as Caucasian or Non-Caucasian, no analysis based on race, ethnicity or other socially relevant grouping was performed.
Population characteristics	Included in methods, results and Table 1 in the manuscript.
Recruitment	Students, staff members and members of the public were recruited through email and social media advertisement and through direct approach of class groups. Additional recruitment took place through newspaper and media outlets. No recruitment of students will take place whereby any of the investigators on the project have material influence over the assessment of academic performance of the particular students.
Ethics oversight	The study protocol was approved by the Clinical Research Ethic Committee of the Cork Teaching Hospitals (Study Identification Number APC115)

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	g*Power was used for power calculations considering an α-error probability (false positive) of 0.05 and a power of 80%. Allowing for attrition, a minimum of 60 volunteers were recruited.
Data exclusions	Outliers have been identified using Grubb's test (α= 0.05) and removed in every set of data except demographic data.
Replication	No replication of data in this study was possible.
Randomization	Described in Methods. Briefly, participants were assigned to groups based on their coffee intake or lack thereof. After the coffee washout period, CDs were block randomized (block of 5, stratified by gender) into either caffeinated or decaffeinated coffee consumption group using a double-blinded, parallel design.
Blinding	Investigators were not blinded to participants groupings.

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

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	ClinicalTrials.gov ID: NCT05927038 and NCT05927103
Study protocol	*Note where the full trial protocol can be accessed OR if not available, explain why.*
Data collection	Participant screening and study visits took place at University College Cork, Ireland. The study started was initiated in October 202, and started in June 2021 due to Covid lockdown. Participant visits were completed in March 2023
Outcomes	The primary outcome measure was a difference in gut microbiota composition between coffee drinkers and non-coffee drinkers at baseline. Secondary outcome measures were gut microbial metabolites and coffee-related metabolites

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.*