

Reporting Summary

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Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
- ☐ ☒ An indication of 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 statistics 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
- ☐ ☒ Clearly defined error bars
State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on [statistics for biologists](#) may be useful.

Software and code

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

Data collection

Not applicable

Data analysis

- HOMA-IR to estimate insulin sensitivity (%) and insulin resistance was calculated by using the software HOMA calculator 2 (v2.3.3) available from <http://www.dtu.ox.ac.uk/homacalculator/>
 - Statistical analyses were conducted using the SPSS software (version: 23.0 SPSS, INC).
 - Graphics were drawn using GraphPad Prism software (version 7.0, GraphPad Software, San Diego, CA, USA).
 - Demultiplexing of the sequencing data was performed using LotuS55 (version 1.565), followed by quality control and sequence variants matrix building using the DADA2 pipeline (version 1.6.0) with taxonomic annotation by RDP classifier (version 2.12) with default parameters. Statistical analyses of microbiota composition were performed in R using packages vegan and CoDaSeq. As recommended for microbiota compositional data analysis, the abundance matrix was centre log-ratio (clr) transformed (CoDaSeq:codaseq.clr).

All these information are also mentioned in the methods section of the manuscript

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 upon request. 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 that support the findings of this study are available. All the figures are provided with individual values in order to have a direct access to the raw data. The 16S sequencing datasets generated during the current study are available in the EGA repository (European Genome-Phenome Archive, <https://ega-archive.org/>, accession number EGAS00001003585).

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf](https://www.nature.com/authors/policies/ReportingSummary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The sample size is described in the manuscript as well as the flow-chart (recruitment, selection, subjects included, drop outs). As stated in the manuscript, this study is a pilot proof-of-concept exploratory study, therefore, the study was not powered/designed at this stage to draw definitive conclusions of clinical outcomes. Rather the study was intended as an exploratory trial, the results of which will help design a properly powered study in the future, since several interesting results have been found and are statistically significant.
Data exclusions	As described in the methods, the exclusion criteria were pre-established and have led to the decision to exclude subjects from the dataset, and mentioned as drop-outs of the subjects during the study. Out of the 40 subjects, seven had to be excluded before completion of the study : 1 in the Placebo group, 1 in the Pasteurized group and five in the Alive group, with a total of 3 early termination due to personal reasons (i.e., mainly because of the difficulty to attend the nine scheduled visits at the hospital) and 4 due to untimely use of antibiotics during the study. One additional subject in the Placebo group was excluded from the analysis for protocol violation.
Replication	An experimental replication was not attempted for this study. This study reports the results of a pilot exploratory study. The method to produce Akkermansia has been published in Plovier et al Nature Medicine 2017 and is fully available. Although this is a pilot study a number of 9 to 12 subjects were enrolled.
Randomization	Subjects were allocated to one of the treatment arms following a randomized block design with a block size of 8. The Microsoft Excel randomization function was used to generate the allocation sequence. Subjects and physicians were both blinded to the treatment allocation.
Blinding	All the subjects, the nurses and the physicians were blinded to the treatment allocation. The treatments were provided in a sachet with a numeric code and each subjects samples was also blinded by using a specific code which was not showing any link with the potential treatment.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants

Methods

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

Unique biological materials

Policy information about [availability of materials](#)

Obtaining unique materials

Unique Material consist in the bacterium Akkermansia muciniphila that have been provided to the volunteers. The strain of the bacteria is publicly available http://www.lgcstandards-atcc.org/Products/Collections/Microbiology_Collections/Bacteria.aspx strain code ATCC® BAA-835™ as well as the culture method used (<https://www.nature.com/articles/nm.4236>).

Human research participants

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

Population characteristics

A table described the overall characteristics of the volunteers is provided in the supplementary material. A description of the population is in the methods and described as follows: thirty-two overweight/obese subjects (BMI > 25 kg m⁻²) aged between 18 and 70 years were voluntary enrolled to participate. Eligible participants had been diagnosed with metabolic syndrome following the NCEP ATP III definition (at least three of the five following criteria: fasting glycemia > 100 mg/dl, blood pressure ≥ 130/85 mmHg or antihypertensive treatment, fasting triglyceridemia ≥ 150 mg/dl, HDL cholesterol <40 mg/dl for males, <50 mg/dl for females, and/or waist circumference >102 cm for males, >88 cm for females) and whose insulin sensitivity was <75% evaluated by HOMA-modelling of insulin sensitivity (HOMA Calculator the University of Oxford)

Recruitment

Participants were recruited at the Cliniques Universitaires Saint-Luc located in Brussels, Belgium, based on general advertizing (leaflets and website) and upon discussion with the physicians in charge of the study (3 differents), and blinded to the category of the treatment. Potential self-selection bias or other biases may have been present since all the subjects were interested by the potential effects linked to the bacteria tested (i.e., metabolic effects), however, because both the physicians and the volunteers were blinded to the category of treatments (i.e., placebo versus treatment) and the study was randomized, potential self-selection bias were likely not present and therefore may not impact the overall results.