SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Meal plan used in the study for meat diet

- The energy level of the average diet was set at 2400 kcal per day. Adjustments will be made to accommodate individual requirements according to energy intake strata.

Background information

- In the VERDI study we want to investigate the effects on cardiometabolic risk factors of a lacto-ovo-vegetarian diet vs. a diet with meat in quantities corresponding to average meat intake in the Swedish population. You will, during two four-week-periods, follow a meal plan adapted to your calorie requirements so that you do not lose weight during the trial. It is important that you follow the meal plan.

Lunch and dinner

- During two four-week-periods, you will be provided with frozen, ready-made dishes for lunch and dinner. You are advised to consume the entire meal. In addition, you are given an individual meal plan which you should strictly follow.

Meal plan

- You will eat breakfast, snacks, and side dishes according to the meal plan adjusted to meet your energy requirements.
- The meal plan includes a number of alternatives for breakfast, snacks, and side dishes.
- The side dishes consist mainly of bread with toppings and can be consumed along with the main dish for lunch and dinner or between meals.

Please note

- It is important that you complete the daily food diary. In the food diary you record which alternative you have chosen for breakfast, snack, and side dish. Please note any deviations from the meal plan.
- It is important that you follow the meal plan, but you are allowed to deviate from it one day each week. You must still eat the ready-made frozen dishes during this day.

Each day choose **one** of the five breakfast alternatives below. Try to vary your choice from day to day.

- Fill in the food diary and check the alternative you have chosen.
- You do not have to eat the breakfast at any particular time, and you do not have to eat the entire breakfast at one time.

1. Yoghurt with oat cereal, sunflower seeds and apple sauce. Sandwich with butter, ham, and cheese.

Food item	*Quantity*	*Alternative*
Yoghurt (0.5% fat)	2.5 dl	Sour milk (0.5% fat)
Oat cereal	2 dl	Bran flakes, rye cereal
Sunflower seeds	1.5 tbsp	Pumpkin seeds, nuts
Applesauce	2 tbsp	Banana, raisins, jam
Whole grain rye bread	1-1.5 slices (50 g)	Rye crisp bread (3 slices)
Butter (Bregott mellan)	3 tsp	
Ham	2.5 slices (or 5-6 thin slices)	
Bell pepper	2 slices	Tomato, cucumber

2. Oat porridge with raisins and milk. Sandwich with butter, ham and cheese

Food item	*Quantity*	*Alternative*
Rolled oats + water	1 dl + 2 dl	Rye flakes, Buckwheat flakes
Milk (1.5% fat)	2.5 dl	
Raisins	2.5 tbsp	Banana, jam
White bread	1-2 slices (50 g)	Wheat crisp bread (3 slices)
Butter (Bregott mellan)	4 tsp	
Ham	2.5 slices (or 5-6 thin slices)	
Cucumber	4 slices	Bell pepper, tomato

3. Sandwich with butter, ham, eggs and bell pepper. Banana.

Food item	*Quantity*	*Alternative*
White bread	2 large slices (or 3 small)	Wheat crisp bread (3 slices)
Butter (Bregott mellan)	2 tsp	
Ham	2.5 slices (or 5-6 thin slices)	
Eggs	1	Boiled, fried, scrambled
Cheese (17% fat)	2 slices	
Bell pepper	2 slices	Cucumber, tomato
Banana	1 piece	

4. Sandwichs with butter, ham, cheese and tomato. Fruit yoghurt.

Food item	*Quantity*	*Alternative*
Whole grain rye bread	2 slices (80 g)	Rye crisp bread (4 slices)
Butter (Bregott mellan)	4 tsp	
Ham	2.5 slices (or 5-6 thin slices)	
Cheese (17% fat)	1.5 slices	
Tomato	2-3 slices	Cucumber, bell pepper
Fruit yoghurt (0.5%)	2.5 dl	Yoghurt + jam or raisins

5. Yoghurt with muesli and banana. Wheat crisp bread with butter, ham and bell pepper.

Food item	*Quantity*	*Alternative*
Yoghurt (0.5% fat)	2.5 dl	Filmjölk (0.5% fat)
Muesli with fruit and nuts	0,75 dl	
Banana	1	
Wheat crisp bread	2 slices	1 slice white bread
Butter (Bregott mellan)	4 tsp	
Ham	2.5 slices (or 5-6 thin slices)	
Bell pepper	2 slices	Cucumber, tomato

Food items

- *Whole grain rye bread* refers to breads such as Lingongrova, Gott och gräddat, Frökusar, Skördelycka.
- *White bread* refers to breads such as formfranska, bergis, rost/toast.
- *Muesli with fruit and nuts* refers to cereal such as Familjemuesli, F-muesli.
- *Oat cereal (Havrefras)* refers to cereal such as havrefras, Havrekuddar, Havreringar, rågfras, rågkuddar, rågringar

Every day choose **two** of the six light meal/snack alternatives below. Preferably vary your choice from day to day.

- Complete the food diary and check the alternative you have chosen.
- You do not have to eat the light meals/snacks at any particular time, and you can eat them at the same time or separately.

1. Yoghurt with raisins and sunflower seeds. Fruit

Food item	*Quantity*	*Alternative*
Yoghurt (0.5% fat)	2 dl	Sour milk (0.5%)
Raisins	3 tbsp	Banana, jam
Sunflower seeds	1.5 tbsp	Pumpkin seeds, nuts
Fruit (apple)	1 piece	Pear, orange, nectarine

2. Sandwich with cottage cheese and avocado. Fruit

Food item	*Quantity*	*Alternative*
White bread	2 slices	Wheat crisp bread (4 slices)
Cottage cheese (4% fat)	2 tbsp	Quark, cream cheese (4%)
Avocado	0.25	
Fruit (apple)	1 piece	Pear, orange, nectarine

3. Cheese sandwich. Fruit

Food item	*Quantity*	*Alternative*
Whole grain rye bread	2 slices	Rye crisp bread (4 slices)
Butter (Bregott mellan)	2 tsp	
Cheese (17% fat)	1.5 slices	
Fruit (apple)	1 piece	Pear, orange, nectarine

4. Wasa-sandwich and yoghurt drink. Fruit

Food item	*Quantity*	*Alternative*
Wasa-sandwich	1 piece	Crispbread (2 slices) + Cream cheese 2 tbsp

Yoghurt drink	2.5 dl	Fruit yoghurt (2 dl)
Fruit (apple)	1 piece	Pear, orange, nectarine

5. Rusks with cheese and marmalade and fruit		
Food item	*Quantity*	*Alternative*
Whole grain rusks	1.5 – 2 pieces	
Butter (Bregott mellan)	2 tsp	
Cheese (17%)	2 slices	
Marmalade	1 tbsp	
Fruit (apple)	1 piece	Pear, orange, nectarine

6. Rusks with peanut butter and fruit		
Food item	*Quantity*	*Alternative*
Wheat rusks	2 pieces	
Peanut butter	4 tsp	
Fruit (apple)	1 piece	Pear, orange, nectarine

- The side dishes consist of bread with topping and can be served along with the ready-made lunch or dinner dish or at any time during the day.
- Each day, choose **one** of the five alternatives. Preferably vary your choice from day to day.
- Fill in the food diary and check the alternative you have chosen.

1.	
Crisp bread (Wasa husman)	2 slices
Margarine (Bregott mellan)	1 tsp

2.	
Crisp bread (Finn crisp)	3 slices
Hummus	2 tbsp

3.	
Whole grain rye bread (rågkusar)	0.5 rågkuse
Light mayonnaise (35% fat)	2 tsp

4.	
Crisp bread (Wasa sport)	2 slices
Avocado	0.25 piece

5.	
Whole grain rusks	2 pieces
Peanut butter	1.5 tsp

Analysis of cardiometabolic risk factors, gut microbiota, and plasma metabolome

Anthropometric measurements and assessment of quality of life

A digital automatic sphygmomanometer (OMRON M6 AC, OMRON HEALTHCARE Co., Ltd. Kyoto, Japan) was used to measure blood pressure and heart rate. Blood pressure was measured in the right arm after five minutes of seated rest. Body height in centimeters was measured at baseline. Body weight in kilograms was measured at the four monitoring visits with the participants dressed in light clothing without shoes. BMI was calculated as body weight in kilograms divided by height in meters squared. At all monitoring visits, quality of life was assessed with the EuroQoL five-dimension questionnaire (EQ5D), which assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, with results presented on a visual analogue scale.

Blood sampling and biochemical analyses

Venous blood samples were collected at the four monitoring visits in evacuated plastic tubes (VACUETTE® TUBE, Greiner Bio-One GmbH, Kremsmunster, Austria). Upon collection, the tubes were gently inverted 10 times and placed on ice. Samples were centrifuged in a cooling system at 1560 x g for 10 min at -40°C and stored at -80°C in aliquots for analysis.

Analyses of samples were conducted at the Clinical Chemistry Laboratory, Örebro University Hospital. Total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured by a dry chemistry method using a membrane and colorimetric detection in a Vitros 5.1 FS chemistry system (Ortho Clinical Diagnostics and Johnson & Johnson, Stockholm, Sweden). High-sensitivity CRP (hs-CRP), apolipoprotein A1 (ApoA1), and apolipoprotein B (ApoB) were measured with two-site sandwich assays on a Siemens ADVIA 1800 Chemistry System (Siemens Healthcare, Upplands Väsby, Sweden). A six-point calibration curve and pooled samples for quality control were also assayed to confirm accurate measurement according to SS-EN ISO/IEC 15 189, STAFS 2011:33 and STAFS 2010:10 (SWEDAC). The HbA_{1c} was measured by the gold standard method on a Tosho G8 High Performance Liquid Chromatography instrument (Tosho Bioscience, Tessenderlo, Belgium).

We used a sandwich ELISA assay kit (Mercodia, Uppsala, Sweden) for quantitative measure of plasma oxidized LDL-C levels. The assay uses the specific murine monoclonal antibody mAb-4E6 directed against the oxidized antigenic determinants on the oxidized ApoB molecule, as described by Holvoet et al. Fresh-frozen plasma (25 μL) was diluted in two steps to a final dilution of 1/6561 and combined with 100 μL of assay buffer and 25 μL of each calibrator. Control and diluted samples were added to appropriate wells on the plate. Plates were incubated in a plate shaker (700–900 rpm) for 2 hours at 20^{o}C and washed six times with 700 μL wash buffer per well using an automatic plate washer. The plates were inverted and tapped against absorbent tissue, and 100 μL of enzyme conjugate was added to each well. Following a second incubation for 1 h on a plate shaker, the plates were washed, and 200 μL of substrate tetramethylbenzidine was added. Finally, the plates were incubated for 15 min on the bench, 50 μL of a solution to stop the reaction was added, and the optical density was measured spectrophotometrically at 450 nm. Two commercially available controls were included on each plate (n=3) for internal quality control. The intra-assay coefficient of variation for oxidized LDL-C concentration was <10% for 95.7% of samples.

16S rRNA gene sequencing for gut microbiome

Fecal samples were collected in sterile stool tubes on the day prior to each baseline/follow-up visit and stored at Örebro biobank at -80°C until extraction. DNA was extracted from each sample by repeated bead-beating and was subjected to 16S rRNA gene sequencing in an Illumina Miseq instrument (Illumina, San Diego, California, USA) using the 515F and 806R primers and the V2 kit (2 × 250 bp paired-end reads) (Illumina).

Illumina reads were merged using Usearch v. 11 64-bit allowing for up to 30 mismatches in the alignment of the paired-end reads, while discarding reads with a merged length greater than 270 bp and fewer than 230 bp. The merged reads were quality-filtered based on expected errors, removing reads above the threshold of 1.0. The merged reads were converted to zero-radius operational taxonomic units (ZOTU) by compiling the sequences into sets of unique reads and performing error-correction using the UNOISE3 algorithm, discarding sequences with fewer than four reads. The ZOTUs were assigned taxonomy using DADA2's assign Taxonomy (minBoot = 80) and were assigned species, using the properly formatted version of the Silva v. 132 database. A phylogenetic tree of the sequence attributed to each ZOTU was created by aligning the reads using MAFFT v. 7.407 and FastTree v. 2.1.10. The process produced 3,126 ZOTUs after removing dropouts, comprising 8,344,360 reads from 102 samples. The OTU-table was subjected to filtering based on abundance, and ZOTUs below 0.002% of total reads in the table were discarded,[13] resulting in 1,264 amplicon sequence variants in 102 samples (8,253,321 reads). Data were rarefied to the minimum sample sequence depth (56,103 reads) to reduce the effect of sequencing depth.

Measurement of fecal short chain fatty acids and branched chain fatty acids

Fecal concentrations of the short chain fatty acids (SCFA) acetate, propionate, and butyrate and branched chain fatty acids (BCFA) isobutyrate and isovalerate, as well as succinate and lactate, were determined using gas chromatograph-mass spectrometry (Agilent Technologies) as previously described. In brief, 100 mg of frozen fecal material was transferred to a 16 x 125 mm glass tube fitted with a screw cap, and a volume of 100 µL of internal standard stock solution [(1-13C)acetate, (2H6)propionate 1 M, (13C4)butyrate 0.5 M, (1-13C1)isobutyrate, and (1-13C)isovalerate 0.1 M] was added. Prior to extraction, samples were freeze-dried at -50^{o}C for 3 h. After acidification with 50 µL of 37% HCl, the organic acids were extracted twice in 2 mL of diethyl ether. A 500 µL aliquot of the extracted sample was mixed with 50 µL of N-tert-butyldimethylsilyl-N-methyltrifluoracetamide (Sigma) at 20^{o}C. One µl of the derived material was injected into a gas chromatograph (Agilent Technologies 7890 A) coupled to a mass spectrometer detector (Agilent Technologies 5975 C). Temperature was increased in a linear gradient consisting of initial temperature of 65^{o}C for 6 min, increase to 260 ^{o}C at 15^{o}C min^{-1}, and increase to and held at 280^{o}C for 5 min. The injector and transfer line temperatures were 250^{o}C. Quantitation was completed in ion-monitoring acquisition mode by comparison to labelled internal standards, with the m/z ratios 117 (acetic acid), 131 (propionic acid), 145 (butyric acid), 146 (isobutyric acid), 159 (isovaleric acid), 121 [(2H2)- and (1-13C)acetate], 136 [(2H5)propionate], 146 [(1-13C1)isobutyrate], 149 [(13C4) butyrate], 160 [(1-13C)isovalerate].

Plasma metabolome analysis

Plasma samples were de-proteinized using ultracentrifugation and analyzed by high performance liquid chromatography-quadrupole time-of-flight mass spectrometry (HPLC-qTOF-MS/MS, Agilent qTOF 6520) (Agilent Technologies). Reverse-phase chromatography was applied using an ACQUITY UPLC HSS T3 Column (130Å, 1.8 µm, 2.1 mm×100 mm (Waters) in positive (ESI+) and negative electrospray ionization (ESI-) modes.

The mobile phase delivered at 400 µL/min consisted of eluent A (MilliQ purified water) (Millipore) and eluent B (methanol, methanol CHROMASOLV™ LC-MS Ultra) (Honeywell

Riedel-de Haen), both containing 0.04% (vol:vol) formic acid. The ESI source was operated under the following conditions: gas (nitrogen) temperature 175℃ and dry gas flow 10 L/min, nebulizer pressure 45 PSI, capillary voltage 3500 V, fragmenter 125 V, and a skimmer of 65V. For data acquisition, a 2-GHz extended dynamic range mode was used, with the instrument set to acquire data over the m/z range 50–1700. Data were collected in centroid mode at an acquisition rate of 1.67 spectra/s with an abundance threshold of 200 counts. Continuous mass axis calibration was performed in an infusion solution throughout the runs by monitoring reference ions m/z 121.050873 and m/z 922.009798 for positive mode and m/z 112.988900 and 966.000725 for negative mode.

Plasma samples were analyzed in two batches. Within-individual samples were analyzed in the same batch, with full within-batch randomization. The stability and functionality of the system were monitored throughout the instrumental analyses using pooled plasma samples as quality control. Data acquisition used MassHunter Acquisition software (Agilent Technologies).

Raw data acquired in each analytical batch were converted to mzXL format, and deconvolution was performed with the open source R package "XCMS." Key parameters of XCMS including peak detection, alignment, and correspondence were optimized using the R package "IPO" to increase the reliability and stability of processed metabolomics data. The number of obtained metabolite features (mass spectral peak, a molecular entity with a unique mass-to-charge ratio and retention time as measured by LC-MS instrument) with ESI+ and ESI- was 1645 and 1363, respectively. The within- and between- batch measurement errors due to shifts in retention time, mass-to-charge ratio (m/z), and intensity of metabolite features between analytical runs were corrected using R package "batchCorr." After correction, metabolite features passing the quality control tests (CV<0.3) in both batches were considered qualified features and were subjected to statistical analysis. In total, 840 and 982 features from the ESI+ and ESI- were retained after stringent normalization procedures.

Plasma trimethylamine N-oxide (TMAO), choline, carnitine, and acetyl-carnitine were measured by liquid chromatography tandem mass spectrometry (LC-MS/MS) analyzed on an Exion UHPLC coupled to a QTRAP 6500+ MS/MS system, both from AB Sciex LLC (Framingham, USA). Plasma (50 μL) was thoroughly mixed with methanol (150 μL) and internal standard solution (50 μL) containing d9-TMAO, d11-choline, and d9-carnitine was centrifuged at 15 000 x g at 5°C for 10 min and supernatants collected on vials for analysis. Calibration curves were obtained from a stock solution containing all compounds. The separation used a Waters BEH Amide column (100 x2.1 mm, 1.7 μm) at 35°C with flow of 0.75 mL/min. The gradient was 0% B 0–1.3 min to 80% B at 4.5 min (B was 10mM ammonium formate in acetonitrile and A 10 mM ammonium formate in water, pH 3, injection volume 0.3 μL). The analytes were detected using positive electrospray ionization. Transitions were TMAO 76.1–>58.2, choline 105.1–>61, L-carnitine 163.1–>116.9, acetyl-carnitine 204.1–>85.1.

Statistical analysis

All analyses were performed in R v. 3.5.1. (R Foundation for Statistical Computing, Vienna, Austria).

Packages	Purpose	References and open source tutorials
XCMS	Metabolomics data processing	https://bioconductor.org/packages/release/bioc/vignettes/xcms/inst/doc/xcms.html
IPO	XCMS parameters optimization	https://bioconductor.org/packages/release/bioc/vignettes/IPO/inst/doc/IPO.html

mixOmics	Supervised modelling	http://mixomics.org/
batchCorr	Metabolomics data normalization	https://www.ncbi.nlm.nih.gov/pubmed/27746707
MUVR	Supervised modelling	https://academic.oup.com/bioinformatics/article/35/6/972/5085367
vegan	Microbiota data analyses	http://cc.oulu.fi/~jarioksa/opetus/metodi/vegantutor.pdf
ggplot2	Results visualization and interpretation	https://cran.r-project.org/web/packages/ggplot2/ggplot2.pdf
phyloseq	Microbiome census data analysis	https://joey711.github.io/phyloseq/
Picante	Microbiota diversity calculation	https://cran.r-project.org/web/packages/picante/vignettes/picante-intro.pdf
Hmisc	Descriptive statistics	http://math.furman.edu/~dcs/courses/math47/R/library/Hmisc/html/Overview.html
lme4	Generalized linear mixed model	https://github.com/lme4/lme4/

Descriptive statistics of anthropometric measurements and clinical markers

Normality of distribution of the variables and residuals was visualized using a histogram and tested using the Shapiro-Wilks test. Missing values were imputed in an intention-to-treat analysis using the last observation carried forward method for the participants (n=2) who were randomized but did not receive intervention and for the participants that dropped out after the first intervention (n=2). A two-sided *P* value <0.05 was considered significant.

To investigate whether a VD could alter cardiovascular risk factor in IHD patients, the number of participants exhibiting guideline target values of clinical markers before and after intervention was calculated. Cut-off values of clinical markers routinely measured after a cardiac event were defined based on European Guidelines on cardiovascular disease prevention in clinical practice: LDL-C <1.8 mmol/L, systolic blood pressure <130 mmHg or diastolic blood pressure <80 mmHg, and BMI <25 kg/m^2.

Descriptive statistics of gut microbiota

The graphic representations and statistical analyses of microbiota were performed using phyloseq v. 1.26 and ggplot2 v. 3. To investigate bacterial richness and phylogenetic diversity within samples, Faith's Phylogentic Diversity and richness were calculated using Picante v. 1.7, and pairwise comparisons of the diets were implemented using a paired Wilcoxon test. To compare gut bacterial patterns of subjects consuming the same and different diets, Bray-Curtis dissimilarity, Weighted UniFrac, and Unweighted UniFrac were calculated using Vegan v. 2.5-4. Principal Coordinates Analysis (PcoA) and a permutation ANOVA (Adonis) was performed to assess differences in the microbiome associated with the diets. A differential abundance analysis of the OTUs was conducted on a subset of the OTUs existing in more than 20 samples using a pairwise paired Wilcoxon test.

Multilevel-predictive modelling for gut microbiota and plasma metabolome

To identify microbial taxa and plasma metabolites discriminating the VD from the MD, random-forest-modeling-based multilevel data analyses (ML-RF) were applied using the R package 'MUVR' for the pair-wise comparison of the ZOTUs or metabolites in subjects consuming the VD and MD. A multilevel analysis deals with dependent data structures and has been successfully used to exploit the differences specific to diet in cross-over human nutrition intervention studies. In this ML-RF algorithm, random forest is applied on the within-subject variation matrix, i.e. the relative abundance of microbial genera observed in the two interventions as independent variables. The model is further incorporated into repeated double cross-validation with unbiased variable selection to reduce statistical overfitting, improve prediction accuracy, and to identify the most informative features of treatments. Permutation analysis was performed to test overall model validity and degree of overfitting by calculating the cumulative probability of actual model misclassification within a t-distributed H0 population (n=100).

We applied generalized linear mixed modelling to compare VD vs. MD with respect to each of the selected discriminative ZOTUs and metabolites using the R package 'lme4.' Fixed factors included diet, sequence of intervention allocation, and baseline values as covariates and subject as random factor. This analysis was also applied on fecal concentrations of SCFAs. Within-treatment effects were similarly investigated with respect to relative abundance of microbial taxa at baseline and following intervention.

Baseline gut microbiota and plasma metabolites associated with response to diet with respect to clinical outcomes

We investigated whether gut microbiota configuration or plasma metabolome at baseline was associated with the effects a VD on metabolic risk factors including oxidized LDL-C, LDL-C, TC, and BMI. Random forest modelling (R package 'MUVR') was used to identify a panel of baseline microbial genera and plasma metabolites that discriminated subjects who showed lower metabolic risk factors after VD than seen with MD (responders) from those in whom VD did not reduce improve metabolic risk factors compared to MD (non-responders).

Energy-adjusted meal plans

The meal plan was personally adapted according to individual energy requirements and was energy- and macronutrient balanced. A research dietitian calculated the energy requirement for each subject by multiplying the Basal Metabolic Rate (BMR) with the Physical Activity Level (PAL). Henry´s energy equation was used to calculate the BMR and the PAL values according to Nordic Nutrition Recommendations based on data of physical activity stated by participants at the first study visit.

Table S1. Details of ready-made meat meals.

Week	Day	Meal	Dish	Weight (g)	Energy (kcal)	Protein (g)	Fat (g)	Carbohydrates (g)	Fiber (g)	Saturated fatty acids (g)
1.	1. Mon	Lunch	Dafgårds – Chicken Quiche	240	592.8	22.32	38.4	38.4	2.88	23.28
		Dinner	Dafgårds - Meatballs & Red Peppers	400	480	24	24	36	12	10.8
		Total			1072.8	46.32	62.4	74.4	14.88	34.08
	2. Tue	Lunch	Dafgårds - Spaghetti Bolognese	400	480	24.4	16.4	64	5.6	7.6
		Dinner	Dafgårds – Cheese and Ham Quiche	240	602.4	21.36	40.8	36	1.68	24
		Total			1082.4	45.76	57.2	100	7.28	31.6
	3. Wed	Lunch	Dafgårds – Beef Stew	400	364	20	13.2	35.6	4.8	5.2
		Dinner	Dafgårds – Kebab	400	672	20.4	44	56	7.2	16
		Total			1036	40.4	57.2	91.6	12	21.2
	4. Thur	Lunch	Dafgårds – Greek Beef	380	456	18.24	23.94	41.8	6.84	9.5
		Dinner	Dafgårds – Hash	380	646	14.44	37.62	60.8	4.94	11.78
		Total			1102	32.68	61.56	102.6	11.78	21.28
	5. Fri	Lunch	Dafgårds – Oven roasted chicken	420	504	30.66	13.02	63	4.2	5.88
		Dinner	Dafgårds – Taco plate	390	565.5	19.11	26.52	58.5	3.9	12.09
		Total			1069.5	49.77	39.54	121.5	8.1	17.97
	6. Sat	Lunch	Dafgårds – Fried Falun sausage	400	504	10.4	38.4	48	3.2	13.2
		Dinner	Dafgårds – Fried Pork Loin	420	558.6	22.68	26.04	54.6	7.14	8.82
		Total			1062.6	33.08	64.44	102.6	10.34	22.02
	7. Sun	Lunch	Dafgårds – Chicken Lasagna	420	504	29.4	13.86	67.2	2.52	8.4
		Dinner	Dafgårds – Angus burger	380	558.6	17.1	36.86	38	4.56	14.82
		Total			1062.6	46.5	50.72	105.2	7.08	23.22
2.	8. Mon	Lunch	Dafgårds – Farmer burger	400	640	20.4	38	52	6.8	11.2
		Dinner	Dafgårds - Spaghetti Bolognese	400	480	24.4	16.4	64	5.6	7.6

		Total			1120	44.8	54.4	116	12.4	18.8
	9. Tue	Lunch	Dafgårds - Greek Beef	380	456	18.24	23.94	41.8	6.84	9.5
		Dinner	Dafgårds – Chicken schnitzel	390	624	23.4	29.25	66.3	7.02	7.02
		Total			1080	41.64	53.19	108.1	13.86	16.52
	10. Wed	Lunch	Dafgårds - Cheese and Ham Quiche	240	602.4	21.36	40.8	36	1.68	24
		Dinner	Dafgårds - Meatballs & Red Peppers	400	480	24	24	36	12	10.8
		Total			1082.4	45.36	64.8	72	13.68	34.8
	11. Thur	Lunch	Dafgårds - Fried Falun sausage	400	504	10.4	38.4	48	3.2	13.2
		Dinner	Dafgårds - Chicken Quiche	240	592.8	22.32	38.4	38.4	2.88	23.28
		Total			1096.8	32.72	76.8	86.4	6.08	36.48
	12. Fri	Lunch	Dafgårds - Beef Stew	400	364	20	13.2	35.6	4.8	5.2
		Dinner	Dafgårds – Italian style veal burgers	400	660	24.4	32.4	64	6.4	9.2
		Total			1024	44.4	45.6	99.6	11.2	14.4
	13. Sat	Lunch	Dafgårds - Oven roasted chicken	420	504	30.66	13.02	63	4.2	5.88
		Dinner	Dafgårds – Taco plate	390	565.5	19.11	26.52	58.5	3.9	12.09
		Total			1069.5	49.77	39.54	121.5	8.1	17.97
	14. Sun	Lunch	Dafgårds - Cabbage pudding	400	352	13.6	22.8	37.6	6	5.6
		Dinner	Dafgårds – Kebab	400	672	20.4	44	56	7.2	16
		Total			1024	34	66.8	93.6	13.2	21.6
3.	15. Mon	Lunch	Dafgårds – Angus burger	380	558.6	17.1	36.86	38	4.56	14.82
		Dinner	Dafgårds - Chicken Lasagna	420	504	29.4	13.86	67.2	2.52	8.4
		Total			1062.6	46.5	50.72	105.2	7.08	23.22
	16. Tue	Lunch	Dafgårds - Farmer burger	400	640	20.4	38	52	6.8	11.2
		Dinner	Dafgårds – Pork stew	380	418	20.14	9.88	57	3.04	4.56
		Total			1058	40.54	47.88	109	9.84	15.76
	17. Wed	Lunch	Dafgårds - Fried Pork Loin	420	558.6	22.68	26.04	54.6	7.14	8.82
		Dinner	Dafgårds - Oven roasted chicken	420	504	30.66	13.02	63	4.2	5.88
		Total			1062.6	53.34	39.06	117.6	11.34	14.7
	18. Thur	Lunch	Dafgårds - Cabbage pudding	400	352	13.6	22.8	37.6	6	5.6

		Dinner	Dafgårds - Italian style veal burgers	400	660	24.4	32.4	64	6.4	9.2
		Total			1012	38	55.2	101.6	12.4	14.8
	19. Fri	Lunch	Dafgårds - Hash	380	646	14.44	37.62	60.8	4.94	11.78
		Dinner	Dafgårds - Greek Beef	380	456	18.24	23.94	41.8	6.84	9.5
		Total			1102	32.68	61.56	102.6	11.78	21.28
	20. Sat	Lunch	Dafgårds – Kebab	400	672	20.4	44	56	7.2	16
		Dinner	Dafgårds - Meatballs & Red Peppers	400	480	24	24	36	12	10.8
		Total			1152	44.4	68	92	19.2	26.8
	21. Sun	Lunch	Dafgårds - Spaghetti Bolognese	400	480	24.4	16.4	64	5.6	7.6
		Dinner	Dafgårds - Chicken schnitzel	390	624	23.4	29.25	66.3	7.02	7.02
		Total			1104	47.8	45.65	130.3	12.62	14.62
4.	22. Mon	Lunch	Dafgårds - Chicken Quiche	240	592.8	22.32	38.4	38.4	2.88	23.28
		Dinner	Dafgårds - Angus burger	380	558.6	17.1	36.86	38	4.56	14.82
		Total			1151.4	39.4	75.26	76.4	7.44	38.1
	23. Tue	Lunch	Dafgårds - Cabbage pudding	400	352	13.6	22.8	37.6	6	5.6
		Dinner	Dafgårds - Italian style veal burgers	400	660	24.4	32.4	64	6.4	9.2
		Total			1012	38	55.2	101.6	12.4	14.8
	24. Wed	Lunch	Dafgårds - Cheese and Ham Quiche	240	602.4	21.36	40.8	36	1.68	24
		Dinner	Dafgårds – Pork Stew	380	418	20.14	9.88	57	3.04	4.56
		Total			1020.4	41.5	50.68	93	4.72	28.56
	25. Thur	Lunch	Dafgårds - Beef Stew	400	364	20	13.2	35.6	4.8	5.2
		Dinner	Dafgårds - Hash	380	646	14.44	37.62	60.8	4.94	11.78
		Total			1010	34.44	50.82	96.4	9.74	16.98
	26. Fri	Lunch	Dafgårds - Fried Falun sausage	400	504	10.4	38.4	48	3.2	13.2
		Dinner	Dafgårds - Chicken schnitzel	390	624	23.4	29.25	66.3	7.02	7.02
		Total			1128	33.8	67.65	114.3	10.22	20.22
	27. Sat	Lunch	Dafgårds - Farmer burger	400	640	20.4	38	52	6.8	11.2
		Dinner	Dafgårds - Chicken Lasagna	420	504	29.4	13.86	67.2	2.52	8.4
		Total			1144	49.8	51.86	119.2	9.32	19.6

	28. Sun	Lunch	Dafgårds - Taco plate	390	565.5	19.11	26.52	58.5	3.9	12.09
		Dinner	Dafgårds - Fried Pork Loin	420	558.6	22.68	26.04	54.6	7.14	8.82
		Total			1124.1	41.79	52.56	113.1	11.04	20.91
			Mean/meal		1076	41.43	53.68	106.52	10.7	22.2

Kcal=kilocalorie

Table S2. Details of ready-made vegetarian meals.

Week	Day	Meal	Dish	Weight (g)	Energy (kcal)	Protein (g)	Fat (g)	Carbohydrates (g)	Fiber (g)	Saturated fatty acids (g)
1.	1. Mon	Lunch	Dafgårds - Pea/Sun-dried tomato steak with pasta	400	576	20.4	24	66	7.6	4
		Dinner	Dafgårds - Cheese & Broccoli pie	220	484	19.8	28.6	37.4	2.64	14.52
		Total			1060	40.2	52.6	103.4	10.24	18.52
	2. Tue	Lunch	Dafgårds - Asparagus pie	240	561.6	19.2	38.4	36	2.64	23.04
		Dinner	Dafgårds – Broccoli balls with quinoa and pepper sauce	400	448	27.2	15.2	45.6	10.4	5.6
		Total			1009.6	46.4	53.6	81.6	13.04	28.64
	3. Wed	Lunch	Dafgårds – Vegetable pie with wholegrain crust	220	440	14.96	21.56	41.8	7.04	9.9
		Dinner	Dafgårds - Falafel	400	560	20.4	25.2	64	11.2	3.6
		Total			1000	35.36	46.76	105.8	18.24	13.5
	4. Thur	Lunch	Dafgårds - Pea/Sun-dried tomato steak with pasta	420	508.2	19.32	16.8	65.52	7.14	4.62
		Dinner	Dafgårds - Indian lentil Stew	400	516	23.2	20.4	56	11.6	11.2
		Total			1024.2	42.52	37.2	121.52	18.74	15.82
	5. Fri	Lunch	Dafgårds - Cheese & Broccoli pie	220	484	19.8	28.6	37.4	2.64	14.52
		Dinner	Dafgårds – Veggie burger	400	516	19.2	26.4	48	9.6	4.4
		Total			1000	39	55	85.4	12.24	18.92
	6. Sat	Lunch	Dafgårds - Kale steak	380	338.2	13.68	6.84	53.2	9.12	0.76
		Dinner	Dafgårds - Asparagus pie	240	561.6	19.2	38.4	36	2.64	23.04
		Total			899.8	32.88	45.24	89.2	11.76	23.8
	7. Sun	Lunch	Dafgårds – Broccoli balls with quinoa and pepper sauce	400	448	27.2	15.2	45.6	10.4	5.6
		Dinner	Dafgårds - Mexican bean steak	390	534.3	14.04	24.96	66.3	4.68	8.97
		Total			982.3	41.24	40.16	111.9	15.08	14.57
2.	8. Mon	Lunch	Dafgårds - Cheese & Broccoli pie	220	484	19.8	28.6	37.4	2.64	14.52
		Dinner	Dafgårds - Falafel	400	560	20.4	25.2	64	11.2	3.6
		Total			1044	40.2	53.8	101.4	13.84	18.12

	9. Tue	Lunch	Dafgårds – Vegetable pie with wholegrain crust	220	440	14.96	21.56	41.8	7.04	9.9
		Dinner	Dafgårds - Pea/Sun-dried tomato steak with pasta	400	576	20.4	24	66	7.6	4
		Total			1016	35.36	45.56	107.8	14.64	13.9
	10. Wed	Lunch	Dafgårds – Broccoli balls with quinoa and pepper sauce	400	448	27.2	15.2	45.6	10.4	5.6
		Dinner	Dafgårds - Mexican bean steak	390	534.3	14.04	24.96	66.3	4.68	8.97
		Total			982.3	41.24	40.16	111.9	15.08	14.57
	11. Thur	Lunch	Dafgårds - Indian lentil Stew	400	516	23.2	20.4	56	11.6	11.2
		Dinner	Dafgårds – Veggie burger	400	516	19.2	26.4	48	9.6	4.4
		Total			1032	42.4	46.8	104	21.2	15.6
	12. Fri	Lunch	Dafgårds - Kale steak	380	338.2	13.68	6.84	53.2	9.12	0.76
		Dinner	Dafgårds - Asparagus pie	240	561.6	19.2	38.4	36	2.64	23.04
		Total			899.8	32.88	45.24	89.2	11.76	23.8
	13. Sat	Lunch	Dafgårds – Sun-dried tomato/pea steak with vegetables	420	508.2	19.32	16.8	65.52	7.14	4.62
		Dinner	Dafgårds - Mexican bean steak	390	534.3	14.04	24.96	66.3	4.68	8.97
		Total			1042.5	33.36	41.76	131.82	11.82	13.59
	14. Sun	Lunch	Dafgårds - Falafel	400	560	20.4	25.2	64	11.2	3.6
		Dinner	Dafgårds - Indian lentil Stew	400	516	23.2	20.4	56	11.6	11.2
		Total			1076	43.6	45.6	120	22.8	14.8
3.	15. Mon	Lunch	Dafgårds - Pea/Sun-dried tomato steak with pasta	400	576	20.4	24	66	7.6	4
		Dinner	Dafgårds - Kale steak	380	338.2	13.68	6.84	53.2	9.12	0.76
		Total			914.2	34.08	30.84	119.2	16.72	4.76
	16. Tue	Lunch	Dafgårds - Asparagus pie	240	561.6	19.2	38.4	36	2.64	23.04
		Dinner	Dafgårds – Broccoli balls with quinoa and pepper sauce	400	448	27.2	15.2	45.6	10.4	5.6
		Total			1009.6	46.4	53.6	81.6	13.04	28.64
	17. Wed	Lunch	Dafgårds - Sun-dried tomato/pea steak with vegetables	420	508.2	19.32	16.8	65.52	7.14	4.62
		Dinner	Dafgårds - Falafel	400	560	20.4	25.2	64	11.2	3.6

		Total			1068.2	39.72	42	129.52	18.34	8.22
	18. Thur	Lunch	Dafgårds – Veggie burger	400	516	19.2	26.4	48	9.6	4.4
		Dinner	Dafgårds - Cheese & Broccoli pie	220	484	19.8	28.6	37.4	2.64	14.52
		Total			1000	39	55	85.4	12.24	18.92
	19. Fri	Lunch	Dafgårds - Asparagus pie	240	561.6	19.2	38.4	36	2.64	23.04
		Dinner	Dafgårds - Indian lentil Stew	400	516	23.2	20.4	56	11.6	11.2
		Total			1077.6	42.4	58.8	92	14.24	34.24
	20. Sat	Lunch	Dafgårds - Kale steak	380	338.2	13.68	6.84	53.2	9.12	0.76
		Dinner	Dafgårds - Pea/Sun-dried tomato steak with pasta	400	576	20.4	24	66	7.6	4
		Total			914.2	34.08	30.84	119.2	16.72	4.76
	21. Sun	Lunch	Dafgårds – Vegetable pie with wholegrain crust	220	440	14.96	21.56	41.8	7.04	9.9
		Dinner	Dafgårds - Mexican bean steak	390	534.3	14.04	24.96	66.3	4.68	8.97
		Total			974.3	29	46.52	108.1	11.72	18.87
4.	22. Mon	Lunch	Dafgårds - Veggieburger	400	516	19.2	26.4	48	9.6	4.4
		Dinner	Dafgårds - Sun-dried tomato/pea steak with vegetables	420	508.2	19.32	16.8	65.52	7.14	4.62
		Total			1024.2	38.52	43.2	113.52	16.74	9.02
	23. Tus	Lunch	Dafgårds - Falafel	400	560	20.4	25.2	64	11.2	3.6
		Dinner	Dafgårds – Vegetable pie with wholegrain crust	220	440	14.96	21.56	41.8	7.04	9.9
		Total			1000	35.36	46.76	105.8	18.24	13.5
	24. Wed	Lunch	Dafgårds - Pea/Sun-dried tomato steak with pasta	400	576	20.4	24	66	7.6	4
		Dinner	Dafgårds - Kale steak	380	338.2	13.68	6.84	53.2	9.12	0.76
		Total			914.2	34.08	30.84	119.2	16.72	4.76
	25. Thur	Lunch	Dafgårds – Broccoli balls with quinoa and pepper sauce	400	448	27.2	15.2	45.6	10.4	5.6
		Dinner	Dafgårds - Asparagus pie	240	561.6	19.2	38.4	36	2.64	23.04
		Total			1009.6	46.4	53.6	81.6	13.04	28.64
	26. Fri	Lunch	Dafgårds - Cheese & Broccoli pie	220	484	19.8	28.6	37.4	2.64	14.52

		Dinner	Dafgårds – Veggie burger	400	516	19.2	26.4	48	9.6	4.4
		Total			1000	39	55	85.4	12.24	18.92
	27. Sat	Lunch	Dafgårds - Sun-dried tomato/pea steak with vegetables	420	508.2	19.32	16.8	65.52	7.14	4.62
		Dinner	Dafgårds - Indian lentil Stew	400	516	23.2	20.4	56	11.6	11.2
		Total			1024.2	42.52	37.2	121.52	18.74	15.82
	28. Sun	Lunch	Dafgårds – Vegetable pie with wholegrain crust	220	440	14.96	21.56	41.8	7.04	9.9
		Dinner	Dafgårds - Mexican bean steak	390	534.3	14.04	24.96	66.3	4.68	8.97
		Total			974.3	29	46.52	108.1	11.72	18.87
			Mean/meal		999	38.5	45.7	104.8	15	17

Kcal=kilocalorie

Table S3. Dietary intake before and during the two intervention periods, VD (vegetarian diet) and MD (meat diet), based on 3-day weighed food records+.

	Pre VD		*VD*		*Pre MD*		*MD*	
	Pooled data (n=31)	Original data (n=20)	Pooled data (n=31)	Original data (n=18)	Pooled data (n=31)	Original data (n=18)	Pooled data (n=31)	Original data (n=20)
	mean	median [IQR]	mean	median [IQR]	mean	median [IQR]	mean	median [IQR]
Energy (kcal)	2147	2097 [1929-2360]	2168	2079 [1797-2515]	2373	2266 [2104-2630]	2267	2286 [2042-2567]
Protein (g)	85*	86 [72-101]	78*	79 [65-86]	92**	92 *** [79-99]	80**	81*** [73-88]
Carbohydrates (g)	229	216 [192-294]	247	249 [197-294]	259	253 [201-285]	266	251 [209-293]
Fat (g)	89	89 [73-101]	89	83 [68-102]	96	92 [86-107]	90	85 [71-102]
Saturated fat (g)	36	35 [28-44]	36	35 [27-43]	39	38 [30-49]	34	33 [29-41]
Fiber (g)	24	24 [19-28]	31****	30 [26-37]	26	27 [22-31]	28****	29 [25-33]

♦ Pre VD/MD: Reported dietary intake before VD or MD intervention period (at baseline or end of washout) ♦ VD/MD: Reported dietary intake of VD/MD ♦

♦ IQR: Interquartile range ♦ Pooled data: Multiple imputation was used for missing values ♦ Wilcoxon Rank Sum test was used for all comparisons ♦ p <0.05 was considered significant ♦

** Borderline significant difference in pooled data (Imputation number/p-values: 1/0.006, 2/0.04, 3/0.01, 4/0.03, 5/0.07) of protein intake of Pre VD and VD*
*** Significant difference in pooled data (Imputation number/p-values: 1/P=0.000, 2/P=0.000, 3/P=0.000, 4/P=0.001, 5/P=0.000) of protein intake between Pre MD and MD. *** Significant difference in original data (p=0.046) of protein intake between Pre MD and MD.*
***** Significant difference in pooled data (Imputation number/p-values: 1/P=0.008, 2/P=0.02, 3/P=0.02, 4/P=0.002, 5/P=0.01) between fiber intake of VD and MD.*
+three-day weighed food information was collected four times during the study: during the week before baseline, the last week of VD, the last week of the washout period, and the last week of MD. 58% (18/31) completed all four registrations. Food records with daily total energy intake:basal metabolic rate <1 were considered as underreported and excluded from the analysis. n of original data refers to the number subjects completing the food record and that remain following exclusion.

Table S4. Adherence to the intervention diets.

	VD		*MD*	
	Pooled data (n=31)	Original data (n=28)	Pooled data (n=31)	Original data (n=27)
	mean %	median % [IQR]	mean %	median % [IQR]
Breakfast	94	100 [96-100]	92	100 [96-100]
Lunch	97	100 [96-100]	98	100 [96-100]
Dinner	94	98 [93-100]	96	96 [95-100]
Side dish	79	92 [73-99]	68	89 [30-100]
Snack (light meals)	67*	76 [43-94]	57*	50 [40-94]
Overall adherence	86**	88 [83-98]	83**	88 [77-96]

♦ Pooled data: Multiple imputation was used for missing values ♦ Wilcoxon signed rank sum test was used for analysis ♦

**Significant difference in overall adherence of the pooled data (Imputation number/P-values: 1/P=0.01, 2/P=0.02, 3/P=0.01, 4/P=0.02, 5/P=0.01) in snacks of VD and MD.*

***Borderline significant difference in overall adherence (Imputation number/p-values: 1/P=0.05, 2/P=0.03, 3/P=0.03, 4/P=0.04, 5/P=0.1) between VD and MD.*

VD (vegetarian diet) and MD (meat diet), in mean percentage (%) adherence the prescribed diet, calculated from the self-reported study diaries. To assess the adherence to the intervention diets, the participants were asked to conduct a compliance diary every day during the two intervention periods.

Table S5. Participants exhibiting guideline target values of clinical markers/dietary intervention.

	Pre VD (n=31)	Post VD (n=31)	Pre MD (n=31)	Post MD (n=31)	Post VD vs. Post MD
LDL-C <1.8 mmol/L, n (%)	22 (71.0)	27 (87.1)	22 (71.0)	24 (77.4)	-3 (9.7)
BMI <25 kg/m2, n (%)	4 (12.9)	6 (19.4)	5 (16.1)	4 (12.9)	-2 (6.5)
Diastolic Bp <80 mmHg, n (%)	9 (29.0)	8 (25.8)	7 (22.6)	6 (19.4)	-2 (6.5)
Systolic Bp <130 mmHg, n (%)	11 (35.5)	14 (45.2)	9 (29.0)	12 (38.7)	-2 (6.5)

BMI, Body-mass index; Bp, Blood pressure; LDL-C, Low-density lipoprotein cholesterol; MD, meat diet; VD, vegetarian diet.

Table S6. Assessed quality of life relative to dietary intervention.

	Pre VD n=31	Post VD n=31	Pre MD n=31	Post MD n=31	Post VD vs. Post MD
Eq5d, VAS	81.38 (77.25–85.53)	80.84 (76.21–85.47)	80.58 (76.63–84.53)	80.45 (75.55–85.35)	-0.37 (-3.74–2.99)
Mobility					
-No problems, n (%)	27 (87)	27 (87)	28 (90)	27 (87)	0 (0)
-Some problems, n (%)	4 (13)	4 (13)	3 (10)	4 (13)	0 (0)
-Extreme problems, n (%)	0 (0)	0(0)	0 (0)	0 (0)	0 (0)
Self-care					
-No problems, n (%)	31 (100)	31(100)	31 (100)	31(100)	0 (0)
-Some problems, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
-Extreme problems, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Usual-activities					
-No problems, n (%)	30 (97)	31 (100)	31(100)	31(100)	0 (0)
-Some problems, n (%)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)
-Extreme problems, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pain/discomfort					
-No problems, n (%)	17 (55)	17 (55)	16 (52)	17 (55)	0 (0)
-Some problems, n (%)	14 (45)	14 (45)	14 (45)	14 (45)	0 (0)
-Extreme problems, n (%)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)
Anxiety/depression					
-No problems, n (%)	24 (77)	26 (84)	24 (77)	25 (81)	1 (3.2)
-Some problems, n (%)	7 (23)	5 (16)	7 (23)	6 (19)	-1 (-3.2)
-Extreme problems, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Eq5d, the EuroQoL five-dimension questionnaire; VAS, visual analog scale.

Table S7. Effect of dietary intervention on clinical parameters according to on-treatment analysis.

	Pre VD	Post VD	Pre MD	Post MD	Post VD vs Post MD#	p$^{\#}$
Oxidized LDL-C, U/L	41.7 (37.1-46.0)	37.0 (33.6-40.3)**	42.1 (37.7-46.6)	40.2 (35.8-44.6)	-3.16 (-5.53--0.78)	0.02
TC, mg/dL	133.4 (123.0-143.6)	121.4 (113.7-129.2)***	135.1 (127.6-145.0)	127.6 (117.9-136.9)*	-6.2 (-10.1--1.9)	0.005
LDL-C, mg/dL	61.9 (54.5-68.1)	53.4 (48.3-58.8)***	63.8 (57.6-70.4)	58.4 (51.8-65.0)*	-5.0 (-8.5--1.2)	0.008
HDL-C, mg/dL	46.4 [41.8-51.8]	43.3 [38.7-48.3]**	48.3 [43.7-53.4]	44.9 [39.8-50.3]	-1.2 [-3.1-0.4]	0.2
TG, mg/dL	85.0 [73.5-96.5]	90.3 [80.6-100.9]	85.0 [73.5-97.4]	85.0 [74.4-96.5]	5.3 [-2.7-13.3]	0.2
Apo B, g/L	0.64 (0.59-0.70)	0.58 (0.53-0.62)***	0.66 (0.61-0.71)	0.60 (0.55-0.65)**	-0.026 (-0.05--0.001)	0.04
Apo A1, g/L	1.40 (1.33-1.47)	1.39 (1.31-1.46)	1.42 (1.35-1.49)	1.41 (1.34-1.49)	-0.023 (-0.058-0.012)	0.2
Apo B/ApoA1 ratio	0.45 [0.42-0.49]	0.41 [0.38-0.45]**	0.46 [0.42-0.5]	0.42 [0.38-0.46]***	-0.025 [-0.07-0.03]	0.3
HbA$_{1c}$, mmol/mol	38.0 [36.9-39.2]	38.2 [36.9-39.6]	38.1 [36.9-39.3]	38.2 [37.0-39.5]	0.0001 [-0.022-0.022]	0.9
Weight, kg	82.6 (78.2-86.9)	82.1 (77.7-86.6)	83.2 (78.7-87.7)	82.8 (78.2-87.3)	-0.7 (-1.24--0.15)	0.01
Hs-crp, mg/L	0.69 [0.48-0.99]	0.69 [0.45-1.05]	0.77 [0.57-1.04]	0.76 [0.51-1.14]	-0.10 [-0.48-0.27]	0.4
Systolic Bp, mmHg	134 (127-141)	131 (125-137)	138 (130-145)	134 (127-141)	-3.1 (-6.5-0.3)	0.07
Diastolic Bp, mmHg	85 (81-89)	85 (82-88)	87 (83-90)	87 (83-91)	-1.5 (-4.6-1.6)	0.3
Hr, bpm	62.5 [59.4-65.7]	62.6 [60.1-65.2]	63.8 [60.4-67.5]	63.6 [60.0-67.4]	-0.01 [-0.05-0.03]	0.5

Data are presented as mean (95% C.I) or as geometric mean [95 % C.I]. Within-group change p-value was calculated with paired t-test. *P<0.05,**P<0.01,***P<0.001.

#Differences in clinical parameters between vegetarian diet (VD) and meat diet (MD) were examined using linear mixed-effects models adjusted for sequence of randomisation and period of interventions. Apo: Apolipoprotein, Bp; Blood pressure, Bpm; beats per minute, HbA_{1c}; Glycated haemoglobin; HDL-C; High-density lipoprotein cholesterol, Hr; Heart rate, Hs-CRP; High-sensitive c-reactive protein, Kg; Kilograms, LDL-C; Low-density lipoprotein cholesterol, mmHg; millimetres of mercury, MD: meat diet; TC; Total cholesterol, TG; Triglycerides; VD: vegetarian diet. To convert cholesterol markers to millimoles per liter, multiply by 0.02586. To convert triglycerides to millimoles per liter, multiply by 0.01.

Table S8. Gut bacteria genera post-dietary intervention.

Phylum	Class	Family	Genus	Post-MD*	Post-VD*	SEM	p
Firmicutes	**Clostridia**	**Lachnospiraceae**	**Shuttleworthia #**	**0.56**	**7.02**	**1.24**	**0.00**
Firmicutes	**Clostridia**	**Ruminococcaceae**	**DTU089#**	**15.41**	**7.17**	**1.99**	**0.00**
Firmicutes	**Clostridia**	**Ruminococcaceae**	**Ruminiclostridium_5#**	**390.12**	**200.71**	**38.41**	**0.00**
Firmicutes	**Clostridia**	**Clostridiaceae_1**	**Clostridium_sensu_stricto_1#**	**567.77**	**353.04**	**106.86**	**0.00**
Firmicutes	**Clostridia**	**Ruminococcaceae**	**Negativibacillus#**	**24.94**	**13.05**	**3.85**	**0.00**
Firmicutes	**Clostridia**	**Ruminococcaceae**	**Anaerofilum#**	**4.33**	**2.01**	**0.68**	**0.01**
Proteobacteria	**Gammaproteobacteria**	**Burkholderiaceae**	**Parasutterella#**	**46.45**	**33.73**	**4.43**	**0.03**
Firmicutes	**Clostridia**	**Ruminococcaceae**	**Oscillospira#**	**16.38**	**11.52**	**2.38**	**0.04**
Firmicutes	**Clostridia**	**Lachnospiraceae**	**Fusicatenibacter#**	**743.99**	**898.35**	**90.56**	**0.04**
Cyanobacteria	**Melainabacteria**	**NA**	**NA#**	**19.44**	**8.29**	**4.43**	**0.04**
Bacteroidetes	**Bacteroidia**	**Tannerellaceae**	**Parabacteroides#**	**309.61**	**216.68**	**33.51**	**0.05**
Verrucomicrobia	**Verrucomicrobiae**	**Akkermansiaceae**	**Akkermansia#**	**426.26**	**811.53**	**203.63**	**0.04**
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_FCS020_group#	98.89	85.22	6.00	0.06
Actinobacteria	Coriobacteriia	Eggerthellaceae	Adlercreutzia#	25.77	17.66	2.90	0.06
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	NA#	13.85	7.14	3.82	0.06
Firmicutes	Clostridia	Clostridiales_vadinBB60_group	NA#	25.56	16.79	4.71	0.07
Bacteroidetes	Bacteroidia	NA	NA#	0.98	2.15	0.43	0.07
Actinobacteria	Coriobacteriia	Eggerthellaceae	DNF00809#	4.53	7.36	1.11	0.08
Tenericutes	Mollicutes	NA	NA#	15.37	9.09	3.36	0.08
Firmicutes	Clostridia	Ruminococcaceae	Butyricicoccus#	179.12	220.22	27.20	0.08
Actinobacteria	Coriobacteriia	Eggerthellaceae	Senegalimassilia#	39.67	29.54	5.61	0.08
Tenericutes	Mollicutes	NA	NA#	23.83	60.39	16.18	0.08
Euryarchaeota	Methanobacteria	Methanobacteriaceae	Methanobrevibacter#	110.14	162.22	34.79	0.09
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-005#	834.72	677.37	98.87	0.09
Firmicutes	Clostridia	Peptostreptococcaceae	Intestinibacter#	338.76	239.26	49.91	0.09
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_UCG-010#	24.47	20.36	2.63	0.10

Firmicutes	Negativicutes	Veillonellaceae	Dialister#	618.60	468.50	82.27	0.10
Firmicutes	Bacilli	Lactobacillaceae	Lactobacillus#	33.00	93.27	29.36	0.10
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-007#	6.70	5.09	1.11	0.14
Firmicutes	Clostridia	Lachnospiraceae	Marvinbryantia#	121.84	185.73	33.03	0.15
Firmicutes	Clostridia	Ruminococcaceae	Angelakisella#	12.38	9.88	1.69	0.17
Firmicutes	Clostridia	Family_XIII	Family_XIII_UCG-001#	20.74	15.66	2.97	0.17
Bacteroidetes	Bacteroidia	Rikenellaceae	Alistipes#	566.34	484.11	58.10	0.20
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_NK4A214_group#	301.27	382.87	66.64	0.27
Proteobacteria	Gammaproteobacteria	Enterobacteriaceae	Escherichia/Shigella#	125.64	292.68	106.65	0.28
Actinobacteria	Coriobacteriia	Eggerthellaceae	Eggerthella#	7.20	1.60	4.47	0.29
Firmicutes	Clostridia	Lachnospiraceae	Butyrivibrio#	321.91	107.98	140.78	0.29
Firmicutes	Clostridia	Ruminococcaceae	Hydrogenoanaerobacterium#	3.32	3.89	1.14	0.39
Firmicutes	Clostridia	Lachnospiraceae	UC5-1-2E3#	8.12	5.97	2.13	0.40
Firmicutes	Clostridia	Lachnospiraceae	GCA-900066755#	1.89	1.56	0.51	0.57
Bacteroidetes	Bacteroidia	Marinifilaceae	Butyricimonas#	24.58	26.22	5.23	0.76
Firmicutes	Clostridia	Ruminococcaceae	NA#	776.35	746.43	79.88	0.78
Firmicutes	Clostridia	Lachnospiraceae	Coprococcus_1#	181.22	188.32	23.13	0.79
Firmicutes	Clostridia	Family_XIII	NA#	2.23	2.04	0.62	0.83
Firmicutes	Clostridia	Lachnospiraceae	Roseburia#	480.41	499.21	78.37	0.87
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcus_2#	1233.61	1217.96	142.38	0.89
Firmicutes	Clostridia	Lachnospiraceae	Lachnospira	546.75	800.77	108.00	0.11
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-013	121.20	167.57	25.67	0.11
Firmicutes	Clostridia	Lachnospiraceae	Tyzzerella	2.83	1.71	0.65	0.13
Actinobacteria	Coriobacteriia	NA	NA	16.33	12.24	3.04	0.13
Firmicutes	Clostridia	Peptostreptococcaceae	Romboutsia	318.28	200.60	53.86	0.14
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-009	7.12	4.67	1.50	0.14
Bacteroidetes	Bacteroidia	Prevotellaceae	Prevotella_9	1344.78	2184.64	675.17	0.15

Firmicutes	Clostridia	Peptococcaceae	NA	2.29	3.58	0.61	0.15
Proteobacteria	Gammaproteobacteria	Pasteurellaceae	Haemophilus	93.83	65.94	27.52	0.15
Actinobacteria	Coriobacteriia	Eggerthellaceae	NA	95.20	80.95	11.11	0.15
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_UCG-008	31.22	25.32	5.06	0.16
Firmicutes	Clostridia	Family_XIII	Family_XIII_AD3011_group	54.59	44.70	10.09	0.16
Firmicutes	Clostridia	Ruminococcaceae	Candidatus_Soleaferrea	6.82	4.08	1.39	0.18
Proteobacteria	Gammaproteobacteria	Burkholderiaceae	Sutterella	119.28	100.68	13.34	0.18
Firmicutes	Clostridia	Lachnospiraceae	CAG-56	129.53	108.30	16.04	0.19
Actinobacteria	Coriobacteriia	Coriobacteriales_Incertae_Sedis	NA	9.06	5.99	1.60	0.19
Proteobacteria	Deltaproteobacteria	Desulfovibrionaceae	Bilophila	27.30	23.77	4.71	0.21
Firmicutes	Clostridia	Lachnospiraceae	Coprococcus_3	224.07	187.07	27.56	0.22
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-003	89.41	108.96	13.98	0.22
Firmicutes	Clostridia	Lachnospiraceae	Howardella	12.54	10.49	2.67	0.24
Firmicutes	Clostridia	Ruminococcaceae	UBA1819	23.47	9.70	8.97	0.24
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_UCG-001	116.52	149.00	27.09	0.25
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Merdibacter	11.55	7.83	2.77	0.25
Bacteroidetes	Bacteroidia	Prevotellaceae	Prevotella_7	88.13	43.88	26.66	0.25
Proteobacteria	Deltaproteobacteria	Desulfovibrionaceae	NA	5.57	4.36	1.09	0.26
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-010	84.22	71.79	10.01	0.26
Firmicutes	Clostridia	Ruminococcaceae	Fournierella	6.28	4.60	1.16	0.27
Firmicutes	Clostridia	Family_XIII	Mogibacterium	1.57	0.60	0.60	0.27
Firmicutes	Clostridia	Lachnospiraceae	Hungatella	4.93	2.33	1.83	0.27
Firmicutes	Clostridia	Ruminococcaceae	Subdoligranulum	3311.80	2935.40	466.37	0.32
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Holdemanella	265.34	296.06	50.79	0.32
Bacteroidetes	Bacteroidia	Prevotellaceae	Paraprevotella	30.78	29.03	5.20	0.34
Proteobacteria	Gammaproteobacteria	Enterobacteriaceae	Klebsiella	22.57	76.22	38.88	0.34
Firmicutes	Clostridia	Ruminococcaceae	Ruminiclostridium_6	235.78	183.68	48.31	0.35
Firmicutes	Negativicutes	Acidaminococcaceae	Acidaminococcus	20.93	11.89	6.68	0.35
Firmicutes	Clostridia	NA	NA	1.23	0.97	0.24	0.35

Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_ND3007_group	377.15	409.98	36.50	0.35
Bacteroidetes	Bacteroidia	Marinifilaceae	Odoribacter	47.55	53.98	6.33	0.36
Actinobacteria	Actinobacteria	Bifidobacteriaceae	Bifidobacterium	942.23	1163.59	178.29	0.37
Firmicutes	Clostridia	Ruminococcaceae	Fecalibacterium	5154.16	4869.92	399.52	0.37
Firmicutes	Bacilli	Streptococcaceae	Lactococcus	11.00	15.63	4.44	0.38
Firmicutes	Clostridia	Lachnospiraceae	Coprococcus_2	689.90	804.51	140.26	0.38
Actinobacteria	Coriobacteriia	Eggerthellaceae	Enterorhabdus	66.77	58.18	10.73	0.41
Firmicutes	Clostridia	Lachnospiraceae	GCA-900066575	17.58	15.46	2.08	0.44
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-002	1131.35	1052.08	146.65	0.44
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Erysipelotrichaceae_UCG-003	226.99	192.24	41.24	0.44
Firmicutes	Clostridia	Peptostreptococcaceae	Terrisporobacter	62.71	81.48	21.69	0.45
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_NK4A136_group	457.00	383.24	68.29	0.45
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-014	841.07	754.52	108.58	0.47
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_AC2044_group	10.98	18.65	7.50	0.48
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Turicibacter	91.35	111.28	23.94	0.48
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-011	1.14	1.56	0.42	0.48
Firmicutes	Negativicutes	Acidaminococcaceae	Phascolarctobacterium	181.57	198.77	41.31	0.50
Firmicutes	Bacilli	Carnobacteriaceae	Granulicatella	0.83	0.60	0.25	0.50
Firmicutes	Clostridia	Ruminococcaceae	Flavonifractor	12.46	11.17	1.75	0.51
Firmicutes	NA	NA	NA	10.54	9.57	2.29	0.51
Actinobacteria	Coriobacteriia	Eggerthellaceae	Gordonibacter	1.35	1.70	0.37	0.52
Firmicutes	Clostridia	Ruminococcaceae	Caproiciproducens	7.87	6.98	1.59	0.53
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcaceae_UCG-004	50.34	44.88	7.47	0.54
Firmicutes	Clostridia	Ruminococcaceae	Phocea	0.47	0.68	0.25	0.55
Firmicutes	Clostridia	Ruminococcaceae	Anaerotruncus	6.00	5.36	2.19	0.59
Bacteroidetes	Bacteroidia	Barnesiellaceae	Barnesiella	145.83	132.43	25.70	0.62

Firmicutes	Clostridia	Lachnospiraceae	NA	1847.16	1918.00	114.99	0.62
Firmicutes	Clostridia	Ruminococcaceae	GCA-900066225	5.69	4.94	1.27	0.63
Firmicutes	Clostridia	Christensenellaceae	Christensenellaceae_R-7_group	1502.70	1417.41	160.78	0.63
Firmicutes	Clostridia	Ruminococcaceae	Intestinimonas	76.14	71.03	10.33	0.63
Firmicutes	Clostridia	Lachnospiraceae	Eisenbergiella	2.93	2.23	1.06	0.63
Firmicutes	Clostridia	Lachnospiraceae	Tyzzerella_3	22.09	27.75	11.21	0.64
Actinobacteria	Coriobacteriia	Atopobiaceae	Olsenella	12.79	13.86	3.33	0.65
Firmicutes	Clostridia	Ruminococcaceae	Ruminiclostridium_9	104.62	109.01	11.21	0.65
Firmicutes	Clostridia	Christensenellaceae	NA	214.41	243.77	60.02	0.65
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Catenibacterium	284.89	243.09	70.12	0.66
Firmicutes	Clostridia	Lachnospiraceae	Anaerostipes	507.04	553.95	84.98	0.66
Firmicutes	Clostridia	Ruminococcaceae	Oscillibacter	60.39	53.86	11.86	0.68
Firmicutes	Clostridia	Lachnospiraceae	Sellimonas	3.94	4.37	0.77	0.68
Actinobacteria	Actinobacteria	Actinomycetaceae	Actinomyces	20.75	19.50	3.32	0.70
Firmicutes	Clostridia	Ruminococcaceae	Ruminococcus_1	456.75	501.79	83.25	0.71
Firmicutes	Clostridia	Ruminococcaceae	Ruminiclostridium	1.36	1.54	0.37	0.73
Firmicutes	Negativicutes	Veillonellaceae	Veillonella	93.28	106.86	33.72	0.73
Firmicutes	Clostridia	Lachnospiraceae	Blautia	2789.05	2726.91	167.00	0.74
Bacteroidetes	Bacteroidia	Barnesiellaceae	Coprobacter	4.93	5.36	1.77	0.75
Proteobacteria	Gammaproteobacteria	Burkholderiaceae	Oxalobacter	4.41	4.02	1.04	0.75
Actinobacteria	Coriobacteriia	Coriobacteriaceae	Collinsella	722.44	688.30	80.96	0.76
Firmicutes	Clostridia	Ruminococcaceae	Pseudoflavonifractor	2.55	2.34	0.66	0.76
Firmicutes	Clostridia	Lachnospiraceae	Lachnoclostridium	263.34	252.68	40.26	0.79
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Coprobacillus	3.91	5.07	3.25	0.80
Firmicutes	Clostridia	Ruminococcaceae	CAG-352	242.31	290.23	155.19	0.81
Firmicutes	Clostridia	Lachnospiraceae	Agathobacter	2661.19	2575.52	373.58	0.81
Firmicutes	Clostridia	Lachnospiraceae	Dorea	510.65	518.70	35.98	0.85

Lentisphaerae	Lentisphaeria	Victivallaceae	Victivallis	4.60	4.46	2.12	0.86
Proteobacteria	Alphaproteobacteria	NA	NA	45.86	48.97	20.09	0.89
Firmicutes	Bacilli	Streptococcaceae	Streptococcus	450.58	469.33	124.06	0.92
Actinobacteria	Coriobacteriia	Eggerthellaceae	Slackia	20.54	20.13	3.02	0.92
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Holdemania	3.49	3.40	0.83	0.93
Firmicutes	Clostridia	Lachnospiraceae	Lachnospiraceae_UCG-004	79.11	80.21	10.32	0.94
Firmicutes	Clostridia	NA	NA	307.27	303.76	104.14	0.95
Firmicutes	Clostridia	Ruminococcaceae	Papillibacter	1.95	1.91	0.53	0.95
Firmicutes	Clostridia	NA	NA	57.60	56.64	28.21	0.97
Firmicutes	Clostridia	Peptostreptococcaceae	NA	1.84	1.87	0.57	0.97
Lentisphaerae	Lentisphaeria	vadinBE97	NA	1.76	1.75	0.79	0.99
Bacteroidetes	Bacteroidia	Bacteroidaceae	Bacteroides	3890.86	3885.54	358.32	0.99
Firmicutes	Erysipelotrichia	Erysipelotrichaceae	Erysipelatoclostridium	7.32	7.34	1.99	0.99

*The least square mean and standard error of genera abundance was obtained by mixed modelling (n=20 subjects). The effects of diet were evaluated using a generalized linear mixed model that included a fixed effect of diet, sequence of allocation, and their interaction. Bold letters denote bacterial genera that significantly differed between meat and vegetarian diets.

Genera selected using multilevel random forest modelling as optimal for discriminating vegetarian diet from meat diet.

Table S9. Fecal levels of short chain fatty acids and branched chain fatty acids relative to dietary intervention.

	Post-MD*	Post-VD*	SEM	Percent difference
Acetate	90.3	94.0	8.3	4.1
Butyrate	34.0	35.7	4.9	5
Propionate	29.1	32	3.6	9.9
Lactate	0.64	0.3	0.3	-53.1
Succinate	0.1	0.1	0.03	12
Isobutyrate	3.23	3.3	0.2	2.2
Isovalerate	2.7	2.8	0.2	5.6
Total BCFAs	5.9	6.2	0.4	5.8
Total SCFAs	154.0	162.0	15.0	5.2

*The least square mean and standard error of fecal fatty acid level was obtained from mixed model (n=20 subjects). The effects of diet were evaluated using a generalized linear mixed model that included a fixed effect of diet, sequence of allocation, and their interaction. Percent difference indicates the median difference in concentration in vegetarian vs. meat diet. Total branched chain fatty acids (BCFA) = the sum of isobutyrate and isovalerate. Total short chain fatty acids (SCFA) = the sum of acetate, butyrate, and propionate.

Table S10. Plasma levels of selected metabolites with respect to dietary intervention.

Metabolite	Ionization	m/z	Retention time	Post MD*	Post VD	SEM	*P Value*
Unknown 180.8988	**RP-**	**182.8988**	**11.38**	**16843.29**	**14557.47**	**633.66**	**0.002**
Cysteinyl-Cysteine	RP-	260.9793	0.70	6631.55	7853.38	492.19	0.066
Lignoceric acid	**RP-**	**367.3586**	**9.02**	**36810.40**	**43195.67**	**1933.87**	**0.025**
dihydroxy-stearic acid	**RP-**	**375.2750**	**7.00**	**196729.93**	**169679.79**	**10085.60**	**0.018**
Unknown 481.2818	**RP-**	**481.2818**	**6.24**	**16467.75**	**26236.58**	**5620.74**	**0.023**
PC (14:0/O-1:0)	**RP-**	**526.3512**	**7.12**	**15228.39**	**11015.75**	**906.87**	**0.004**
lysoPC (16:1)	**RP-**	**552.3308**	**6.82**	**13045.53**	**10808.43**	**680.58**	**0.009**
Unknown 570.8316	RP-	570.8316	0.63	3844.64	4421.80	299.94	0.106
lysoPE (22:0)	**RP-**	**592.3600**	**7.05**	**12193.78**	**8386.79**	**947.67**	**0.011**
DG (16:0/20:3)	**RP-**	**653.4922**	**9.86**	**4283.02**	**5275.64**	**334.29**	**0.027**
PE (18:1/20:4)	**RP-**	**748.5318**	**8.85**	**18748.37**	**12565.47**	**1133.24**	**0.000**
2-Hydroxylauroylcarnitine	**RP-**	**777.5494**	**8.46**	**15513.48**	**13221.52**	**961.62**	**0.035**
PE (18:1/18:1)	**RP-**	**786.5671**	**8.89**	**11655.84**	**8956.61**	**733.66**	**0.004**
PE (20:3/18:1)	**RP-**	**810.5666**	**8.80**	**23648.56**	**17826.32**	**1149.66**	**<0.001**
PE (20:2/18:1)	**RP-**	**812.5822**	**8.96**	**30155.11**	**22896.73**	**1162.19**	**<0.001**
PC (20:2/16:0)	RP-	820.5644	9.23	51624.88	44215.94	2679.98	0.066
PE (18:0/22:5)	**RP-**	**822.5641**	**9.22**	**21394.62**	**16708.67**	**1493.55**	**0.040**
PC (18:1/22:4)	**RP-**	**836.5812**	**8.88**	**13050.88**	**10243.25**	**640.24**	**0.004**
3-[3,5-dihydroxy-4-(sulfo-oxy)phenyl]-2-oxopropanoic acid	**RP+**	**168.9820**	**11.48**	**155146.44**	**182929.37**	**6860.20**	**0.010**
3-Methylhistidine	**RP+**	**170.0908**	**0.63**	**1943.89**	**865.23**	**355.01**	**0.025**
Hippurate	RP+	180.0651	2.90	515914.00	450011.66	58837.15	0.349
3-Indolepropionic acid	RP-	190.0867	4.39	98007.09	122411.46	17291.84	0.259
2-Methylbutyroylcarnitine	RP+	246.1697	2.52	38209.45	32777.99	3639.34	0.181
Subaphylline	**RP+**	**247.1446**	**2.44**	**52076.92**	**118952.27**	**14585.80**	**0.002**
Acoric acid	**RP+**	**286.2014**	**3.91**	**147642.67**	**215322.85**	**17346.72**	**0.002**
4-hydroxy nonenal mercapturic acid	**RP+**	**287.1510**	**5.80**	**84412.33**	**40256.93**	**11244.85**	**0.012**
N-Acetylanonaine	**RP+**	**308.1297**	**5.80**	**27288.67**	**9587.51**	**3534.59**	**0.001**
Fatty acid 346.1231	**RP+**	**346.1231**	**4.55**	**80258.08**	**218453.19**	**39899.08**	**0.024**
Tetracosanedione	**RP+**	**366.3749**	**7.90**	**84840.86**	**45100.68**	**9876.02**	**0.008**
Uknown 464.193	**RP+**	**464.1931**	**4.60**	**19418.79**	**9724.71**	**2506.99**	**0.011**
lysoPC (16:0)	**RP+**	**482.3620**	**7.12**	**95512.54**	**66500.01**	**6965.84**	**0.004**

PC (16:0/18:1)	**RP+**	**742.5793**	**8.87**	**39397.84**	**27681.81**	**2943.77**	**0.004**
PC (18:1/18:1)	**RP+**	**768.5931**	**8.92**	**126228.97**	**82032.18**	**9985.77**	**<0.001**

*The least square mean and standard error of metabolite level was obtained via mixed modelling (n=21 subjects). The effects of diet were evaluated using a generalized linear mixed model that included a fixed effect of diet, sequence of allocation, and their interaction. Bold letters denote the bacterial genera that significantly differed between meat and vegetarian diets.

DG, diacylglycerol, PE, phosphatidylethanolamine; PC, phosphatidylcholine. RP+: reverse phase chromatography positive ionization mode; RP-: reverse phase chromatography negative ionization mode.

Table S11. Spearman correlation of bacterial genera and plasma metabolites with cardiometabolic risk factors, vegetarian diet.

Variables		Oxidized LDL		TC		LDL		BMI		Weight	
		r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
Genus	Zotu1114_GCA.900066755	-0.36	0.02	-0.30	0.05	-0.38	0.01	-0.20	0.21	-0.13	0.42
Genus	Zotu74_Ruminococcaceae_NK4A214_group	-0.51	0.00	-0.30	0.06	-0.37	0.02	-0.19	0.22	-0.25	0.11
Genus	Zotu822_Ruminococcaceae_UCG.007	0.24	0.13	0.26	0.10	0.36	0.02	-0.03	0.83	0.00	1.00
Genus	Zotu647_Eggerthella	0.31	0.04	0.38	0.01	0.35	0.02	0.09	0.58	0.17	0.28
Genus	Zotu62_Coprococcus_1	-0.37	0.02	-0.29	0.06	-0.33	0.03	-0.06	0.69	-0.12	0.46
Genus	Zotu87_Roseburia	0.20	0.21	0.45	0.00	0.32	0.04	-0.12	0.44	-0.06	0.72
Genus	Zotu412_Butyricimonas	0.05	0.76	0.28	0.07	0.31	0.04	0.00	0.99	0.02	0.90
Genus	Zotu10_Ruminococcus_2	-0.34	0.03	-0.23	0.14	-0.31	0.05	-0.14	0.39	-0.12	0.43
Genus	Zotu25_Escherichia.Shigella	0.29	0.06	0.38	0.01	0.31	0.05	-0.21	0.19	-0.16	0.31
Genus	Zotu152_Marvinbryantia	-0.29	0.06	-0.40	0.01	-0.28	0.07	-0.35	0.03	-0.27	0.08
Genus	Zotu397_Oscillospira	-0.11	0.49	-0.11	0.49	-0.28	0.07	0.00	1.00	-0.02	0.89
Genus	Zotu728_Shuttleworthia	-0.43	0.00	-0.32	0.04	-0.27	0.08	-0.05	0.76	-0.10	0.53
Genus	Zotu832_Anaerofilum	0.27	0.09	0.27	0.08	0.27	0.08	-0.09	0.56	0.02	0.90
Genus	Zotu57_Parabacteroides	0.19	0.24	0.35	0.02	0.27	0.09	0.09	0.58	0.09	0.59
Genus	Zotu576_Angelakisella	0.08	0.61	0.28	0.07	0.26	0.10	0.18	0.27	0.23	0.15
Genus	Zotu239_NA	-0.21	0.18	-0.28	0.08	-0.24	0.13	-0.05	0.75	0.01	0.97
Genus	Zotu398_DTU089	0.17	0.30	0.28	0.07	0.22	0.15	0.08	0.63	0.11	0.49
Genus	Zotu788_NA	-0.42	0.01	-0.11	0.48	-0.20	0.20	-0.07	0.66	-0.07	0.66
Genus	Zotu63_Clostridium_sensu_stricto_1	0.02	0.89	0.11	0.50	0.20	0.21	0.28	0.07	0.30	0.05
Genus	Zotu191_Senegalimassilia	0.15	0.36	0.03	0.86	0.19	0.22	0.50	0.00	0.42	0.01
Genus	Zotu676_Hydrogenoanaerobacterium	-0.32	0.04	-0.23	0.14	-0.16	0.32	0.04	0.80	-0.08	0.62
Genus	Zotu58_Butyrivibrio	0.02	0.92	-0.09	0.56	-0.15	0.34	0.31	0.05	0.30	0.06
Genus	Zotu13_Fusicatenibacter	-0.17	0.29	-0.14	0.36	-0.15	0.34	-0.20	0.21	-0.14	0.36
Genus	Zotu50_Intestinibacter	0.12	0.45	0.11	0.48	0.14	0.37	0.05	0.74	0.17	0.29
Genus	Zotu307_NA	0.04	0.81	-0.21	0.18	-0.13	0.42	0.08	0.62	0.01	0.96
Genus	Zotu262_Lachnospiraceae_UCG.010	0.29	0.06	-0.11	0.49	0.13	0.42	-0.03	0.85	0.02	0.90
Genus	Zotu60_Ruminiclostridium_5	0.04	0.81	0.14	0.38	0.12	0.45	0.25	0.11	0.27	0.09

Genus	Zotu145_Butyricicoccus	-0.11	0.50	-0.09	0.59	-0.12	0.46	-0.04	0.82	-0.13	0.40
Genus	Zotu34_Ruminococcaceae_UCG.005	-0.29	0.07	-0.23	0.13	-0.11	0.47	0.01	0.93	-0.10	0.55
Genus	Zotu38_Alistipes	-0.08	0.61	0.17	0.28	0.11	0.49	0.01	0.95	0.00	0.98
Genus	Zotu334_NA	-0.21	0.18	-0.16	0.31	-0.11	0.49	0.23	0.14	0.19	0.24
Genus	Zotu481_UC5.1.2E3	0.36	0.02	0.15	0.33	0.10	0.52	-0.23	0.14	-0.20	0.21
Genus	Zotu512_NA	-0.05	0.73	0.07	0.65	0.10	0.53	0.07	0.67	0.07	0.66
Genus	Zotu169_Lachnospiraceae_FCS020_group	0.25	0.11	0.07	0.66	0.10	0.53	-0.03	0.83	0.02	0.90
Genus	Zotu357_Family_XIII_UCG.001	0.35	0.02	0.12	0.46	0.10	0.53	0.03	0.84	-0.05	0.75
Genus	Zotu629_DNF00809	-0.05	0.76	-0.20	0.21	-0.09	0.56	0.16	0.31	0.09	0.57
Genus	Zotu180_Lactobacillus	0.04	0.81	0.21	0.18	0.09	0.56	0.19	0.22	0.11	0.51
Genus	Zotu36_NA	-0.39	0.01	-0.17	0.27	-0.07	0.65	0.15	0.33	0.12	0.47
Genus	Zotu35_Dialister	-0.15	0.34	-0.18	0.24	-0.07	0.66	0.13	0.41	-0.01	0.95
Genus	Zotu364_Negativibacillus	0.05	0.74	0.08	0.63	0.07	0.66	0.04	0.82	0.14	0.39
Genus	Zotu114_Methanobrevibacter	-0.16	0.32	-0.25	0.11	-0.07	0.66	0.05	0.77	-0.03	0.83
Genus	Zotu279_Adlercreutzia	0.02	0.88	0.13	0.40	0.07	0.66	0.20	0.20	0.18	0.24
Genus	Zotu2541_NA	0.12	0.44	0.17	0.28	0.04	0.78	-0.03	0.84	-0.02	0.88
Genus	Zotu399_NA	-0.29	0.06	0.05	0.75	-0.04	0.79	-0.07	0.67	-0.12	0.45
Genus	Zotu12_Akkermansia	-0.14	0.37	-0.09	0.57	-0.03	0.85	0.13	0.42	0.05	0.76
Genus	Zotu215_Parasutterella	-0.15	0.35	0.12	0.46	-0.03	0.86	-0.10	0.53	-0.23	0.14
Metabolite	PC (18:1/18:1)	0.55	0.00	0.21	0.19	0.33	0.04	-0.14	0.38	-0.17	0.29
Metabolite	lysoPC (16:0)	0.39	0.01	0.39	0.01	0.29	0.07	-0.01	0.95	0.01	0.97
Metabolite	DG (16:0/20:3)	-0.35	0.03	-0.47	0.00	-0.44	0.01	-0.31	0.05	-0.33	0.04
Metabolite	lysoPC (16:1)	0.35	0.03	0.38	0.01	0.25	0.12	0.19	0.23	0.14	0.40
Metabolite	PE (18:0/22:5)	0.34	0.03	0.28	0.08	0.37	0.02	-0.06	0.69	-0.17	0.29
Metabolite	PC (14:0/O-1:0)	0.25	0.12	0.27	0.09	0.23	0.15	-0.03	0.87	-0.13	0.43
Metabolite	Subaphylline	-0.25	0.13	0.01	0.94	-0.08	0.61	-0.06	0.71	-0.08	0.60
Metabolite	PC (20:2/16:0)	0.23	0.15	0.28	0.08	0.28	0.08	0.04	0.80	0.00	0.99
Metabolite	PC (16:0/18:1)	0.23	0.16	0.19	0.25	0.12	0.47	-0.30	0.06	-0.26	0.11
Metabolite	lysoPE (22:0)	0.21	0.18	0.20	0.22	0.21	0.18	-0.08	0.62	-0.09	0.59
Metabolite	Lignoceric acid	-0.20	0.21	-0.37	0.02	-0.31	0.05	-0.04	0.79	-0.07	0.69

Metabolite	Acoric acid	-0.19	0.23	-0.30	0.06	-0.27	0.09	-0.08	0.64	-0.07	0.66
Metabolite	Tetracosanedione	0.18	0.26	0.09	0.60	0.19	0.23	-0.01	0.97	0.00	0.99
Metabolite	PE (20:2/18:1)	0.16	0.32	-0.16	0.34	-0.07	0.65	-0.21	0.19	-0.31	0.05
Metabolite	2-Hydroxylauroylcarnitine	0.15	0.35	0.39	0.01	0.25	0.12	0.26	0.11	0.14	0.39
Metabolite	Hippurate	0.15	0.36	0.28	0.09	0.13	0.42	0.33	0.04	0.24	0.14
Metabolite	3-Indolepropionic acid	0.14	0.38	0.15	0.34	0.25	0.12	0.24	0.14	0.15	0.34
Metabolite	Unknown 464.193	-0.11	0.50	0.13	0.43	0.17	0.28	0.06	0.71	0.02	0.88
Metabolite	Unknown 481.2818	-0.10	0.55	-0.08	0.61	-0.22	0.17	0.31	0.05	0.27	0.09
Metabolite	3-[3.5-dihydroxy-4-(sulfoxy)phenyl]-2-oxopropanoic acid	0.10	0.55	0.15	0.34	0.02	0.89	0.15	0.34	0.21	0.19
Metabolite	N-Acetylanonaine	0.10	0.56	0.35	0.03	0.22	0.17	0.16	0.32	0.18	0.27
Metabolite	Unknown180.8988	0.09	0.57	0.02	0.91	-0.08	0.61	0.36	0.02	0.24	0.14
Metabolite	3-Methylhistidine	-0.09	0.58	-0.10	0.55	-0.16	0.34	-0.13	0.43	-0.20	0.22
Metabolite	PE (18:1/18:1)	-0.09	0.59	-0.10	0.56	-0.11	0.49	-0.20	0.22	-0.27	0.09
Metabolite	2-Methylbutyroylcarnitine	0.08	0.63	0.04	0.81	-0.05	0.78	-0.24	0.14	-0.30	0.06
Metabolite	Cysteinyl-Cysteine	-0.07	0.65	-0.09	0.58	-0.13	0.42	0.36	0.02	0.20	0.21
Metabolite	Unknown570.8316	-0.07	0.67	0.05	0.74	-0.12	0.47	0.06	0.70	0.09	0.57
Metabolite	PE (18:1/20:4)	-0.04	0.81	0.13	0.43	0.07	0.66	0.07	0.65	0.01	0.94
Metabolite	4-hydroxy nonenal mercapturic acid	0.03	0.84	0.22	0.17	0.17	0.29	0.21	0.19	0.17	0.30
Metabolite	PC (18:1/22:4)	0.03	0.87	0.06	0.72	0.06	0.71	-0.12	0.46	-0.26	0.11
Metabolite	dihydroxy-stearic acid	0.02	0.91	0.20	0.22	0.12	0.44	0.14	0.38	0.20	0.23
Metabolite	PE (20:3/18:1)	0.01	0.94	-0.12	0.48	-0.08	0.60	-0.22	0.17	-0.28	0.08
Metabolite	Fatty acid 346.1231	0.00	1.00	0.07	0.67	0.16	0.32	0.16	0.32	0.19	0.23

DG, diglycerides, PE, phatidylethanolamine; PC, phosphatidylcholines.

Figure S1. Descriptive analysis of abundance (A) and prevalence (B) of gut microbiota across samples.

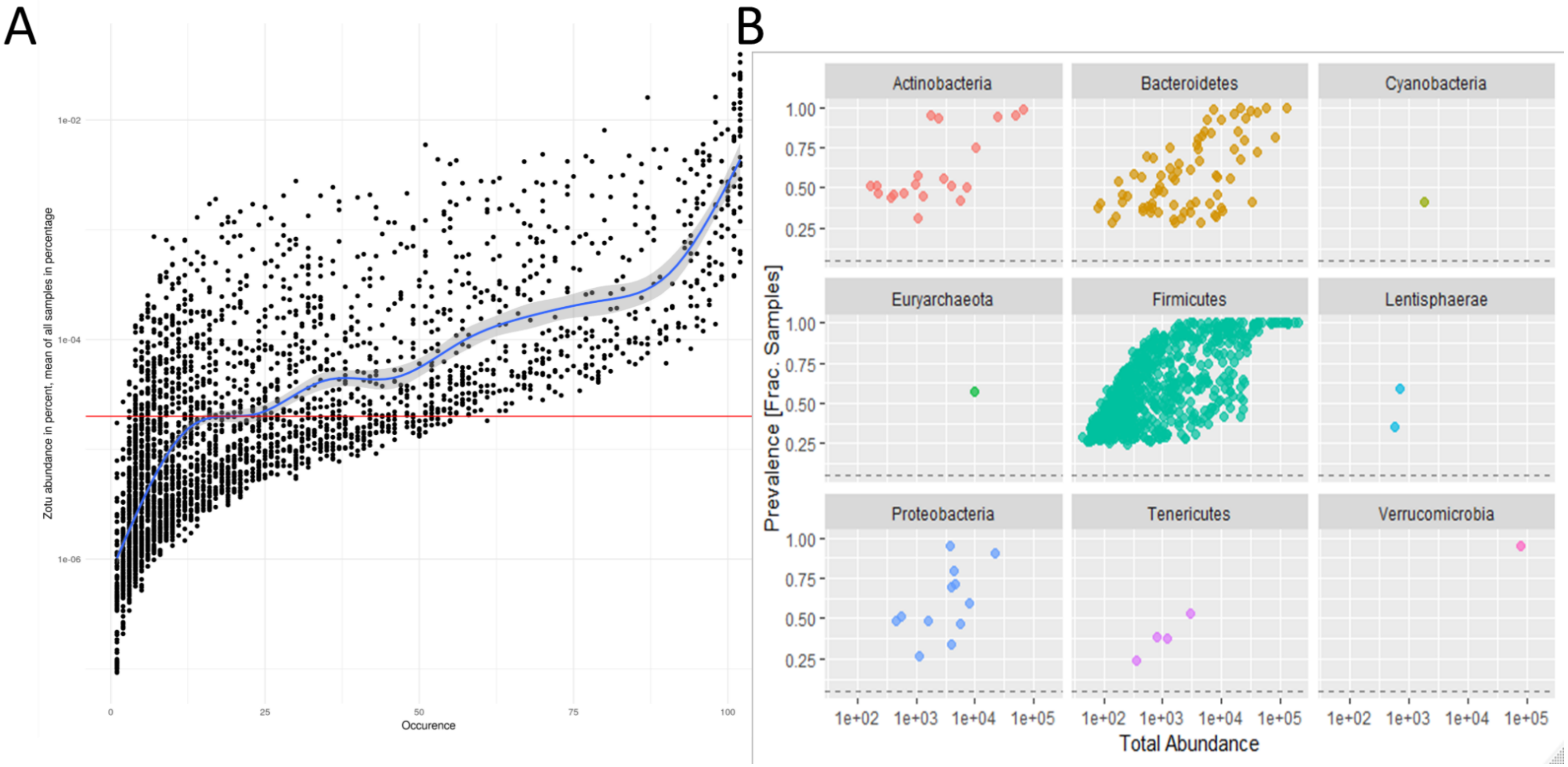


Figure S2. Structure of the effective dataset representing the within-individual variations between treatments. The effective dataset was subjected to multilevel random forest modelling.

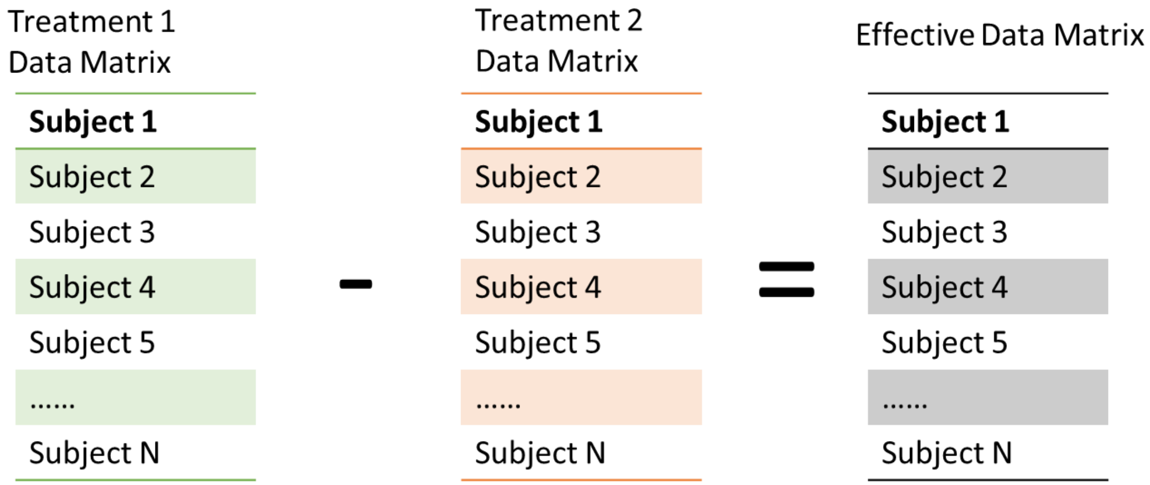
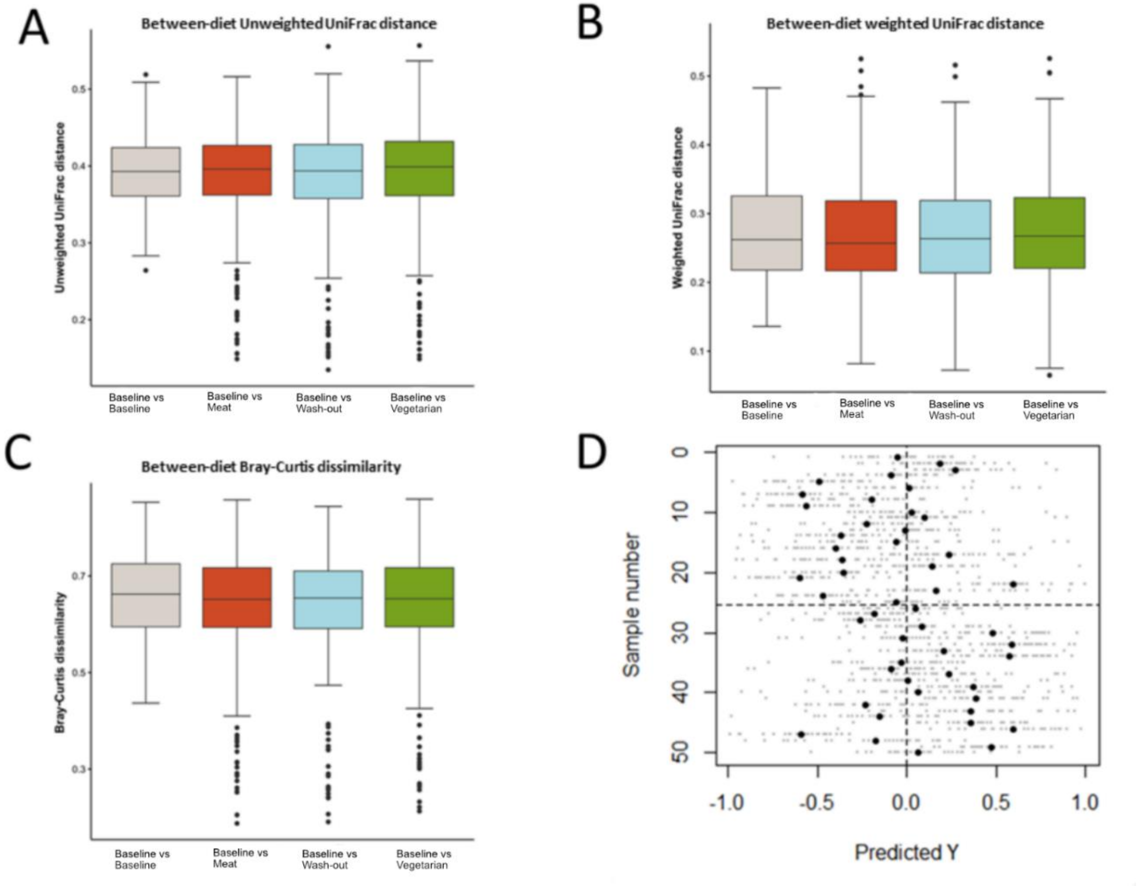
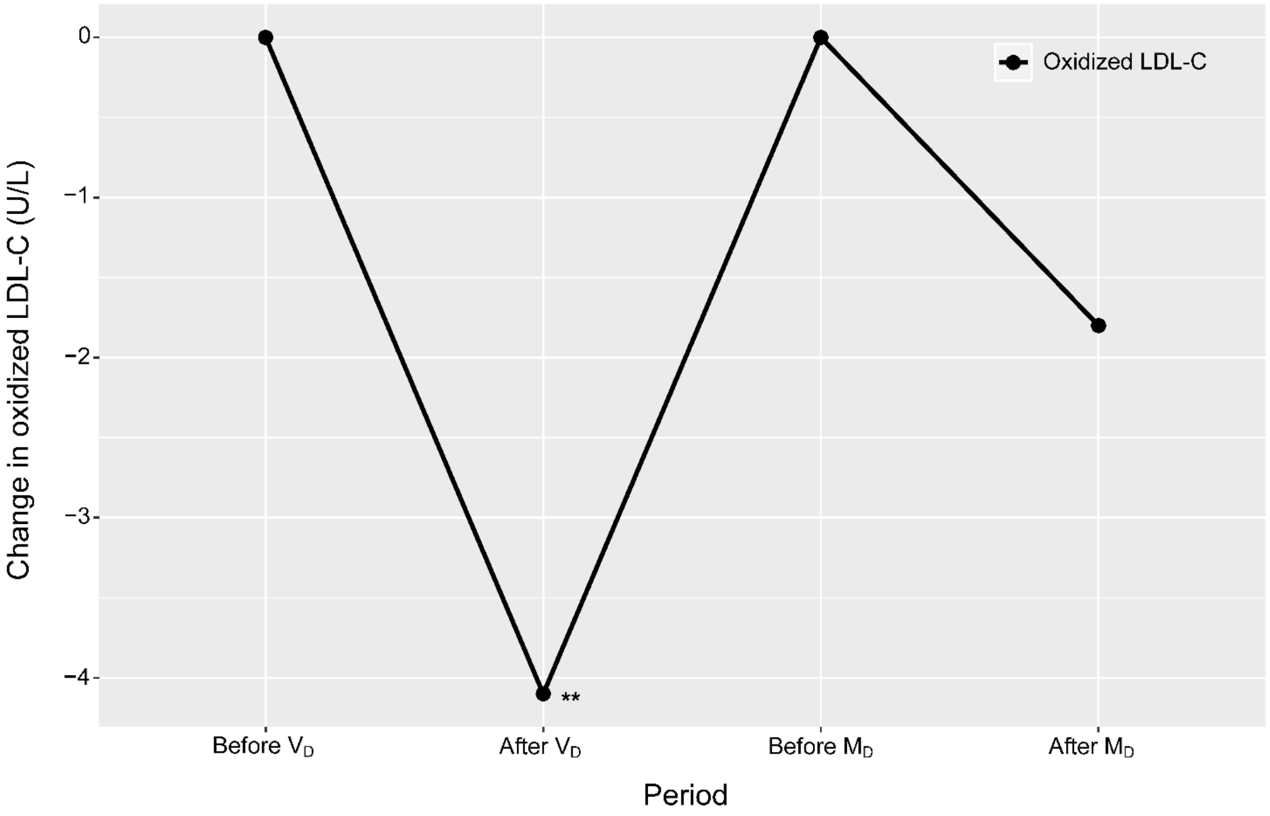


Figure S3. Difference in microbiota diversity and plasma metabolome of baseline and wash-out period.



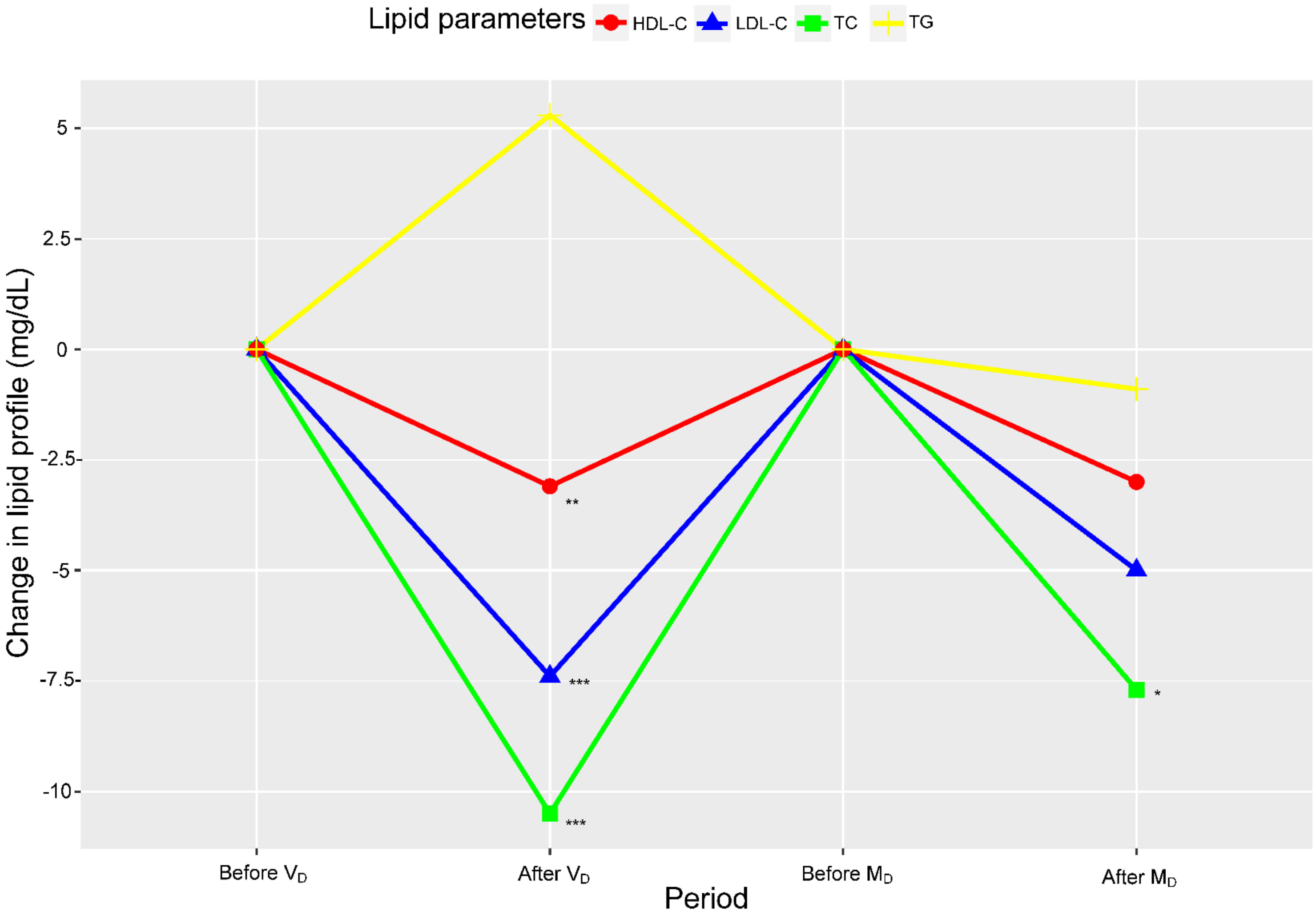
The between-diet distance in gut microbiota for all samples was assessed using (A) unweighted UniFrac, (B) weighted UniFrac and (C) Bray-Curtis. Random forest modeling of plasma metabolome between baseline and wash-out was conducted; model performance is shown in D. No significant difference in metabolome between sampling times was observed.

Figure S4. Time series analysis and mean changes in oxidized LDL according to dietary intervention.



Within-group change P-value was calculated with paired t-test. **P<0.01. LDL-C, low-density lipoprotein cholesterol; MD, meat diet; VD, vegetarian diet.

Figure S5. Time series analysis and mean changes in lipid profile according to dietary intervention.



Within-group change P-value was calculated with paired t-test. *P<0.05; **P<0.01; ***P<0.001. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MD, meat diet; TC, total cholesterol; TG, triglycerides; VD, vegetarian diet.

Figure S6. Relative abundance of gut microbiota at phylum (A) and genus level (B) representing the microbiome pattern across individuals with respect to diet period.

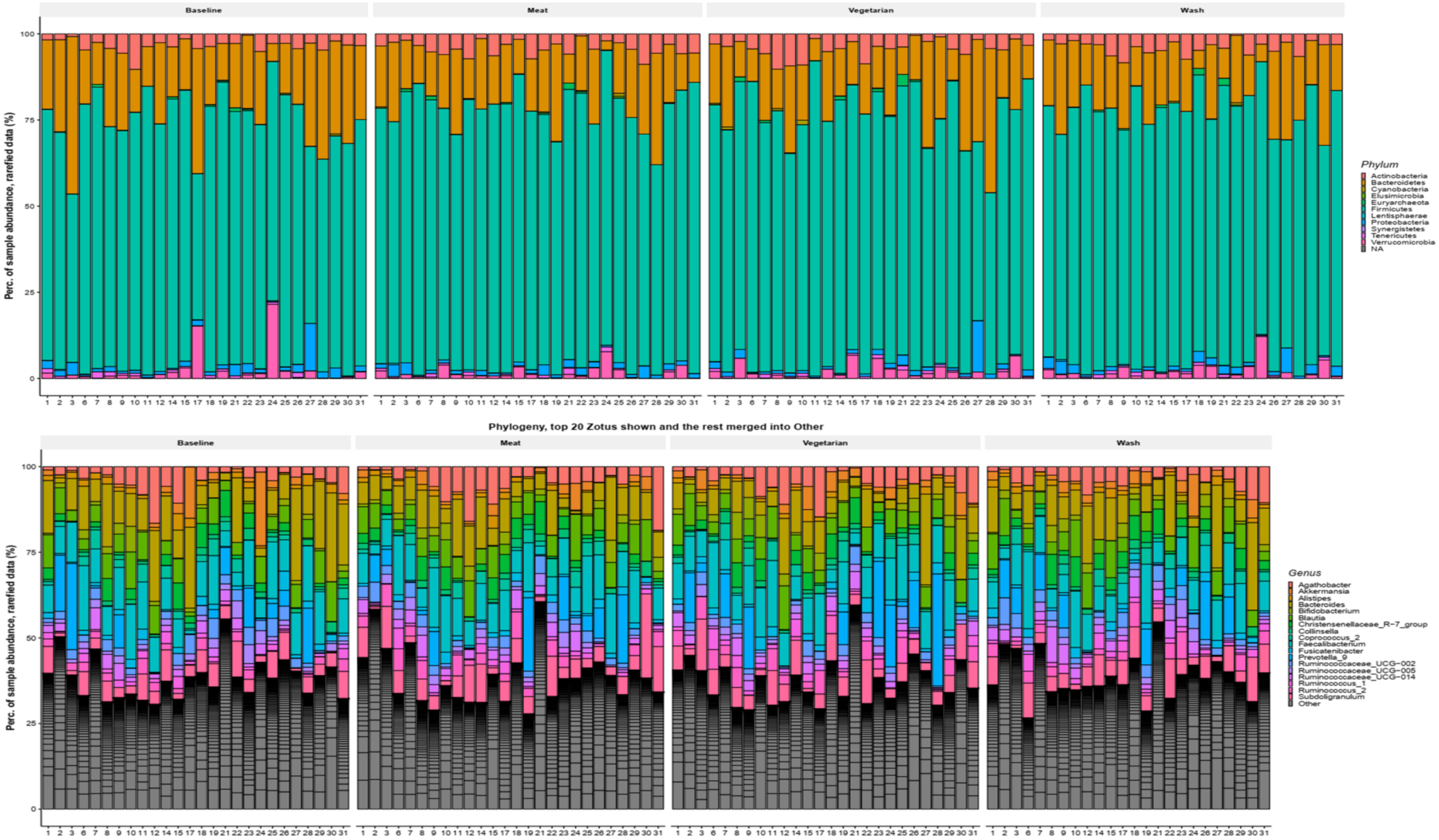
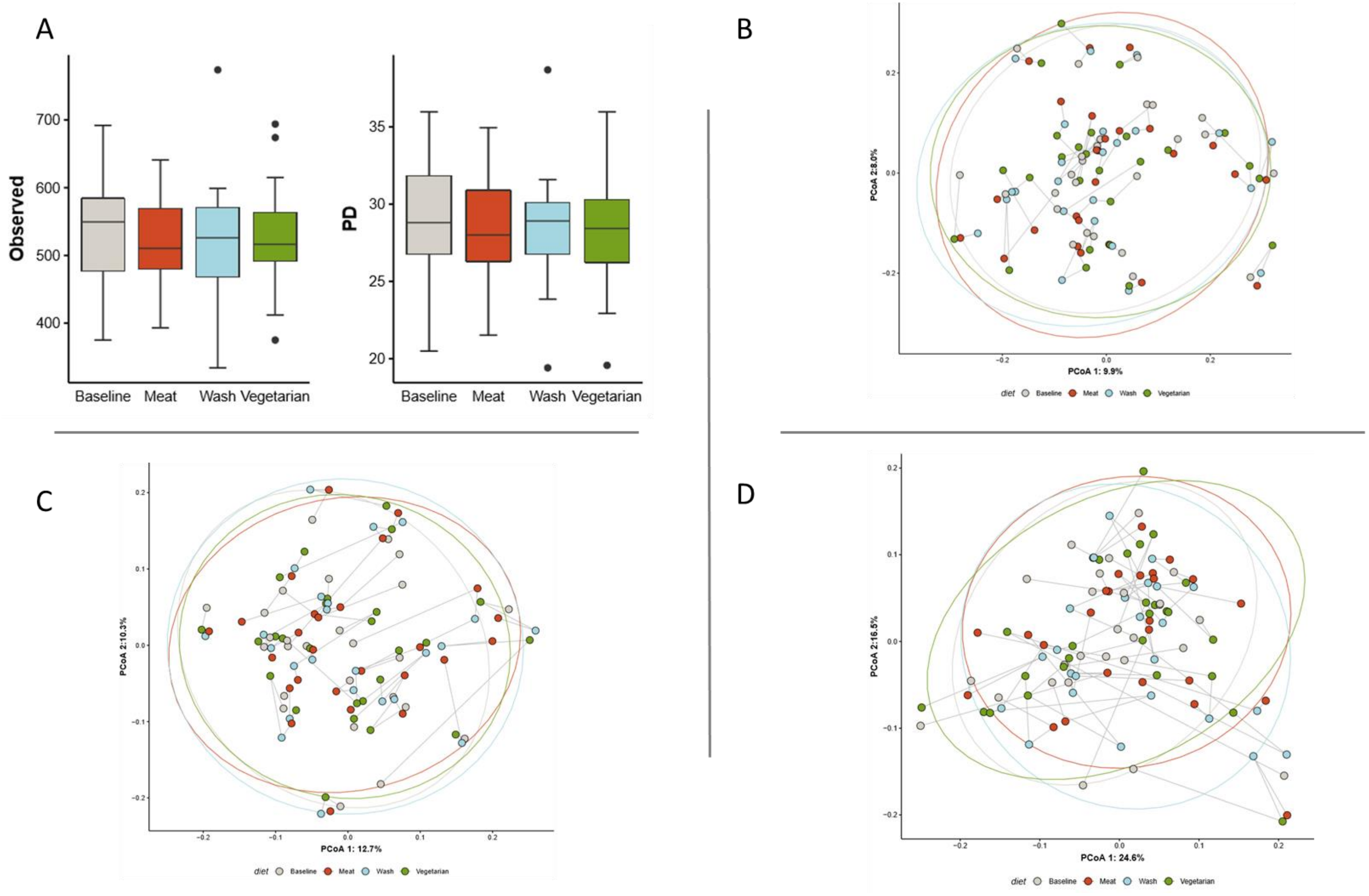
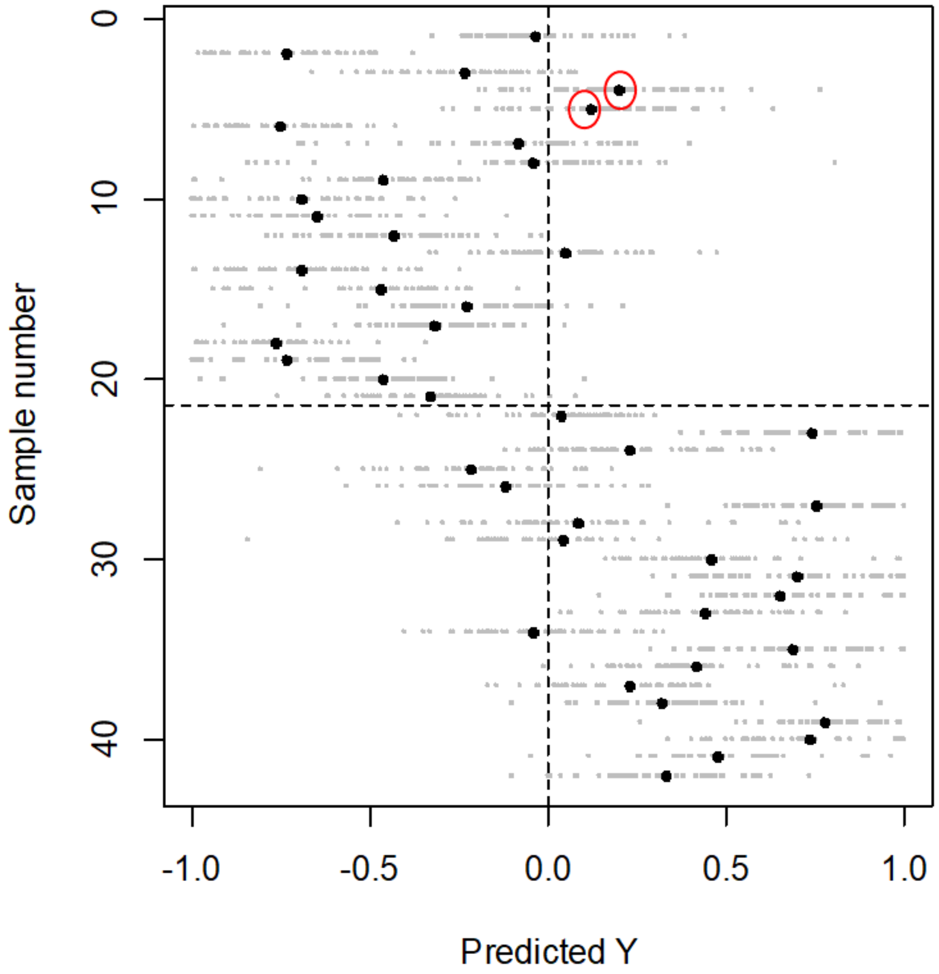


Figure S7. Gut microbiome diversity at four sampling times.



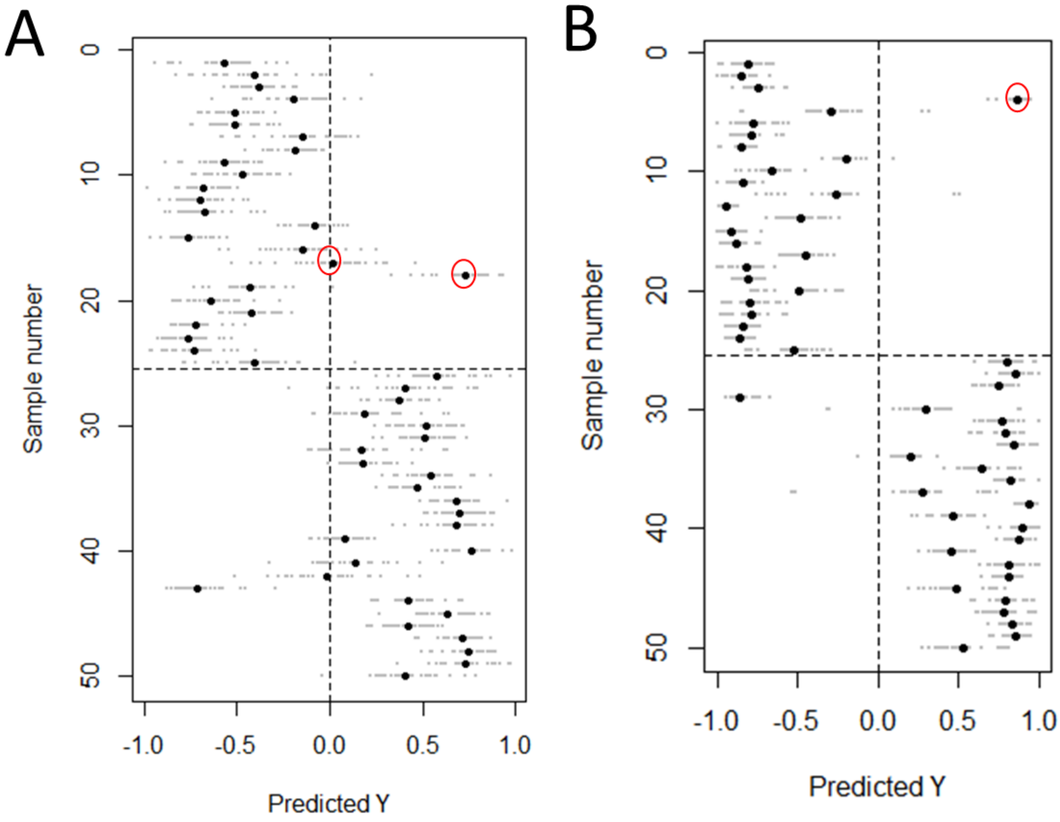
Observed species and Faith's Phylogentic Diversity (A), PCoA plots for Bray-Curtis dissimilarity (B), Unweighted UniFrac (C), and weighted UniFrac (D). Grey lines in panels B, C, and D link samples obtained from an individual at different sampling times.

Figure S8. Prediction of optimal selected bacteria genera using the random forest modeling based multilevel data analysis.



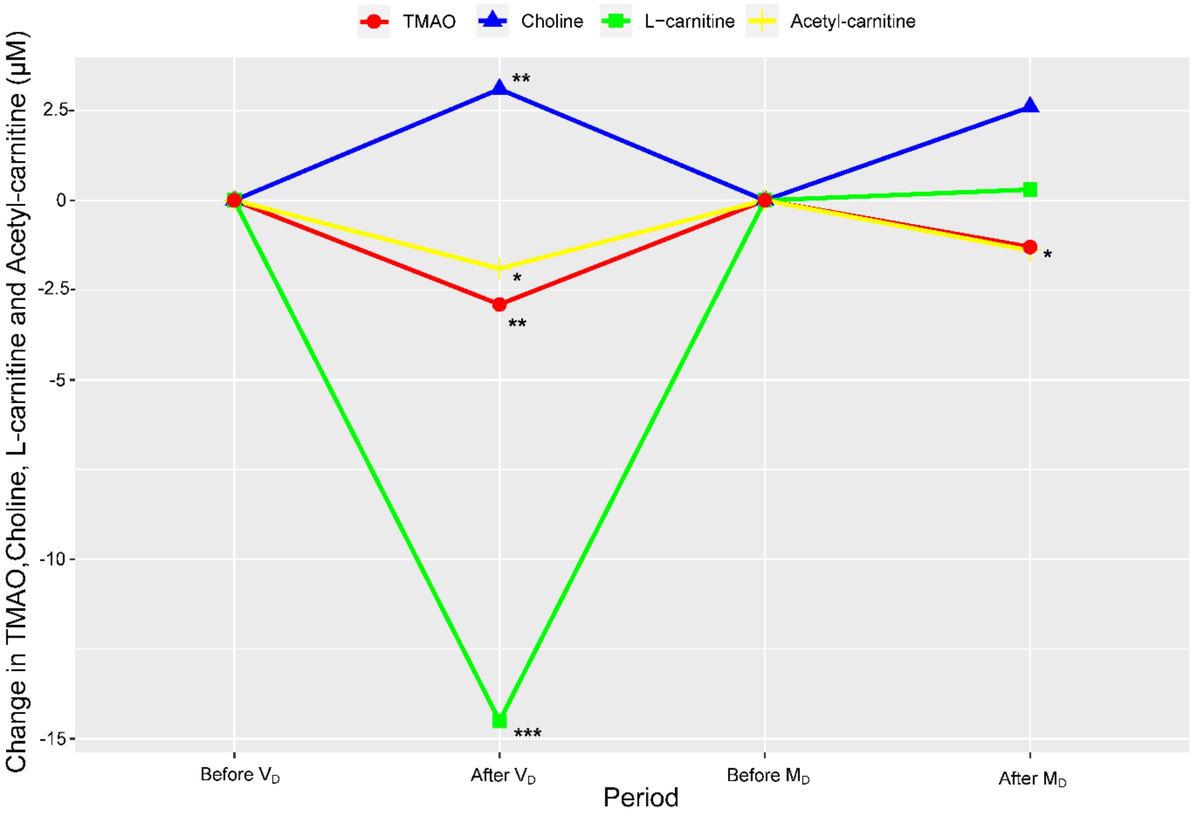
Samples are matched row-wise between upper and lower half for the treatment-effect matrix. Prediction estimates are shown in grey for each repetition of repeat double cross-validation and in black for the prediction estimates averaged over all repetitions. Misclassified samples are circled. The models showed high accuracy in discriminating the vegetarian diet from the meat diet.

Figure S9. Prediction of optimally selected metabolites using the random forest modeling based multilevel data analysis of plasma metabolome by ESI+ (A) and ESI- (B).



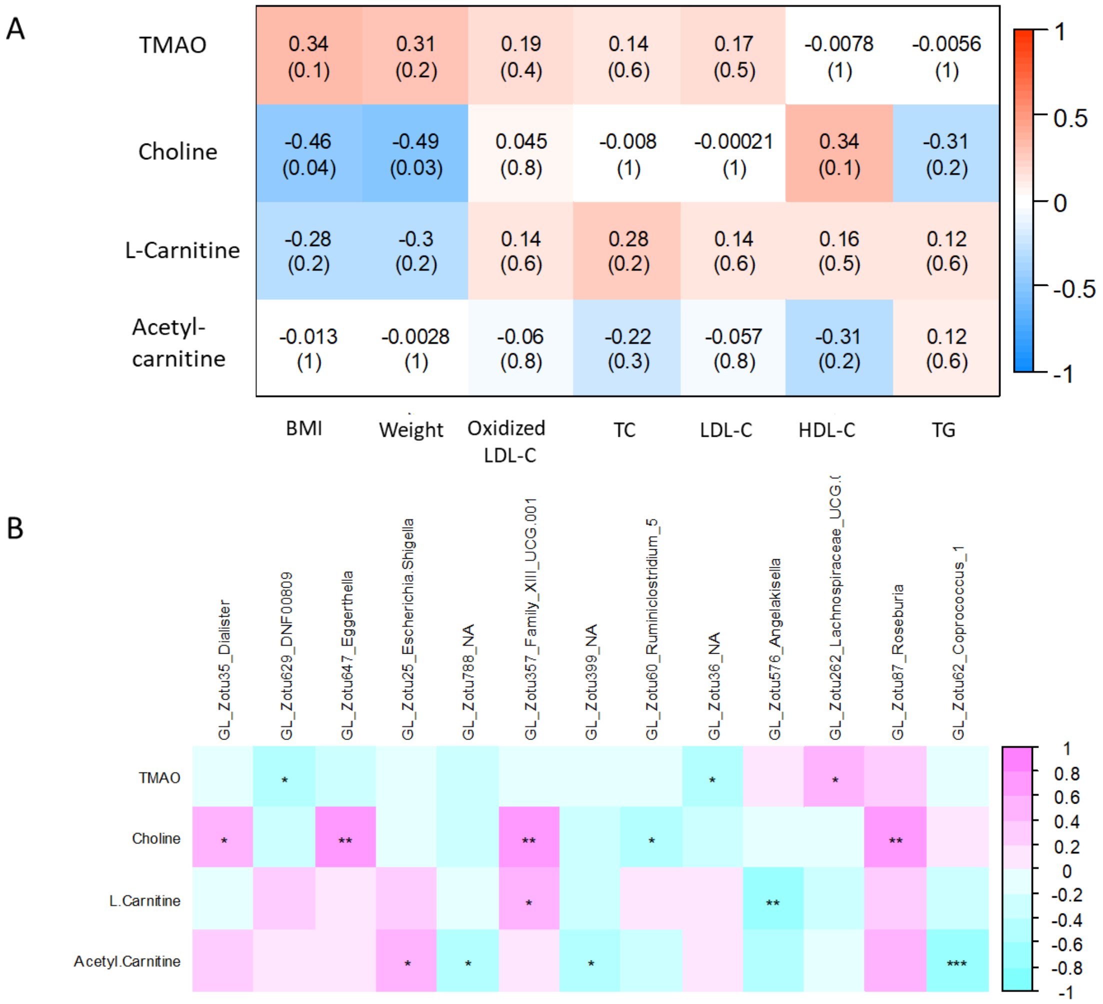
Samples are matched row-wise between upper and lower half for the treatment effect matrix. Prediction estimates are shown in grey for each repetition of repeat double cross-validation and in black for the estimates averaged over all repetitions. Misclassified samples are circled. The models showed high accuracy in discriminating the vegetarian diet from the meat diet.

Figure S10. Time series analysis and mean changes in TMAO, Choline, L-carnitine and Acetyl-carnitine according to dietary intervention.



Within-group change P-value was calculated with paired t-test. *P<0.05; **P<0.01; ***P<0.001. μM, micromolar concentration. MD, meat diet; TMAO, trimethylamine N-oxide; VD, vegetarian diet.

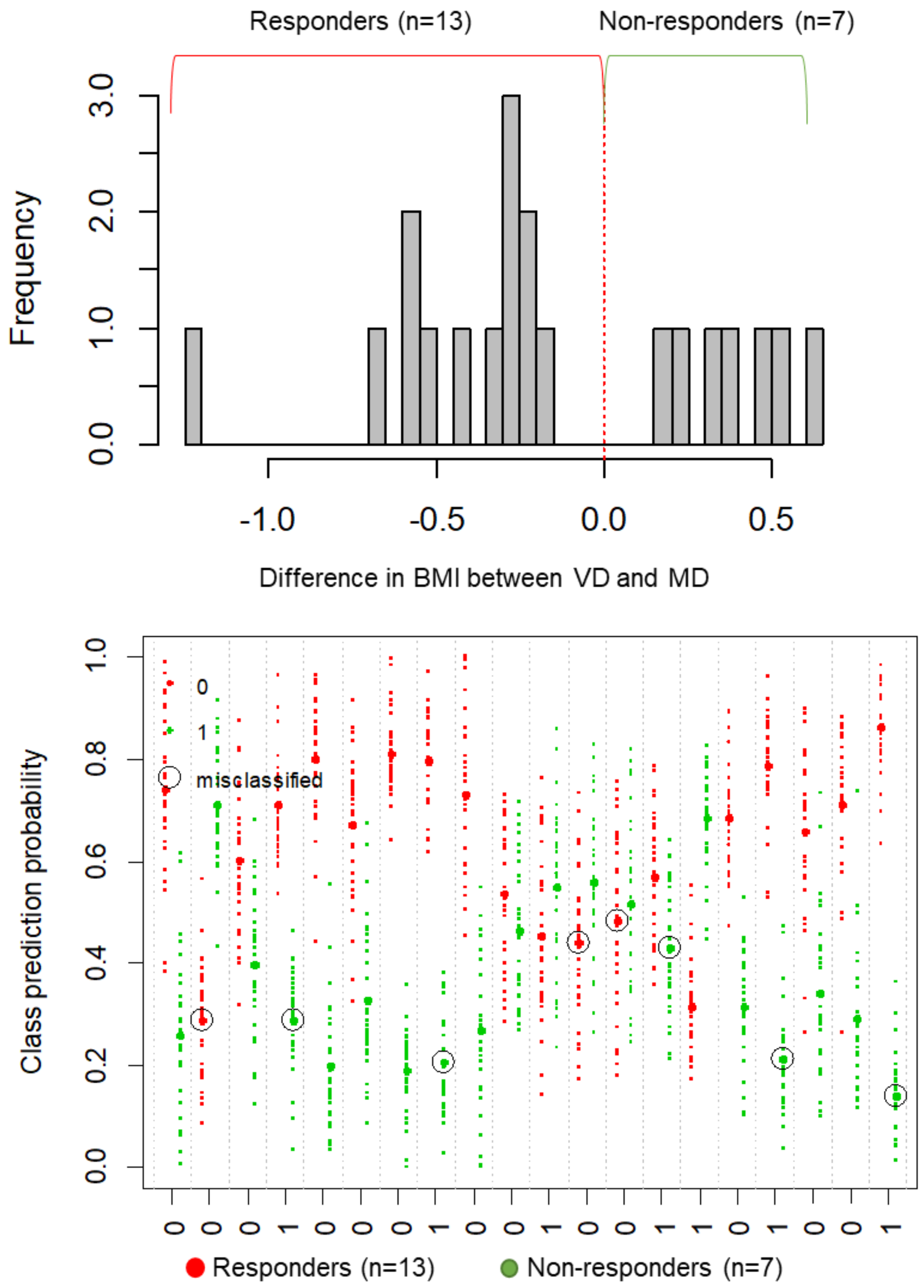
Figure S11. Correlations between plasma concentrations of trimethylamine N-oxide (TMAO), choline, L-carnitine and acetyl-carnitine and cardiometabolic risk factors (A) or the microbial genera (B) that were optimally selected to distinguish the vegetarian diet and the isocaloric meat diet using multilevel random forest algorithm.



Only microbial genera that were significantly correlated with at least one of plasma metabolites are present (B).

*P<0.05; **P<0.01; ***P<0.001. None of the correlations remained significant after false-discovery-rate correction for multiple testing.

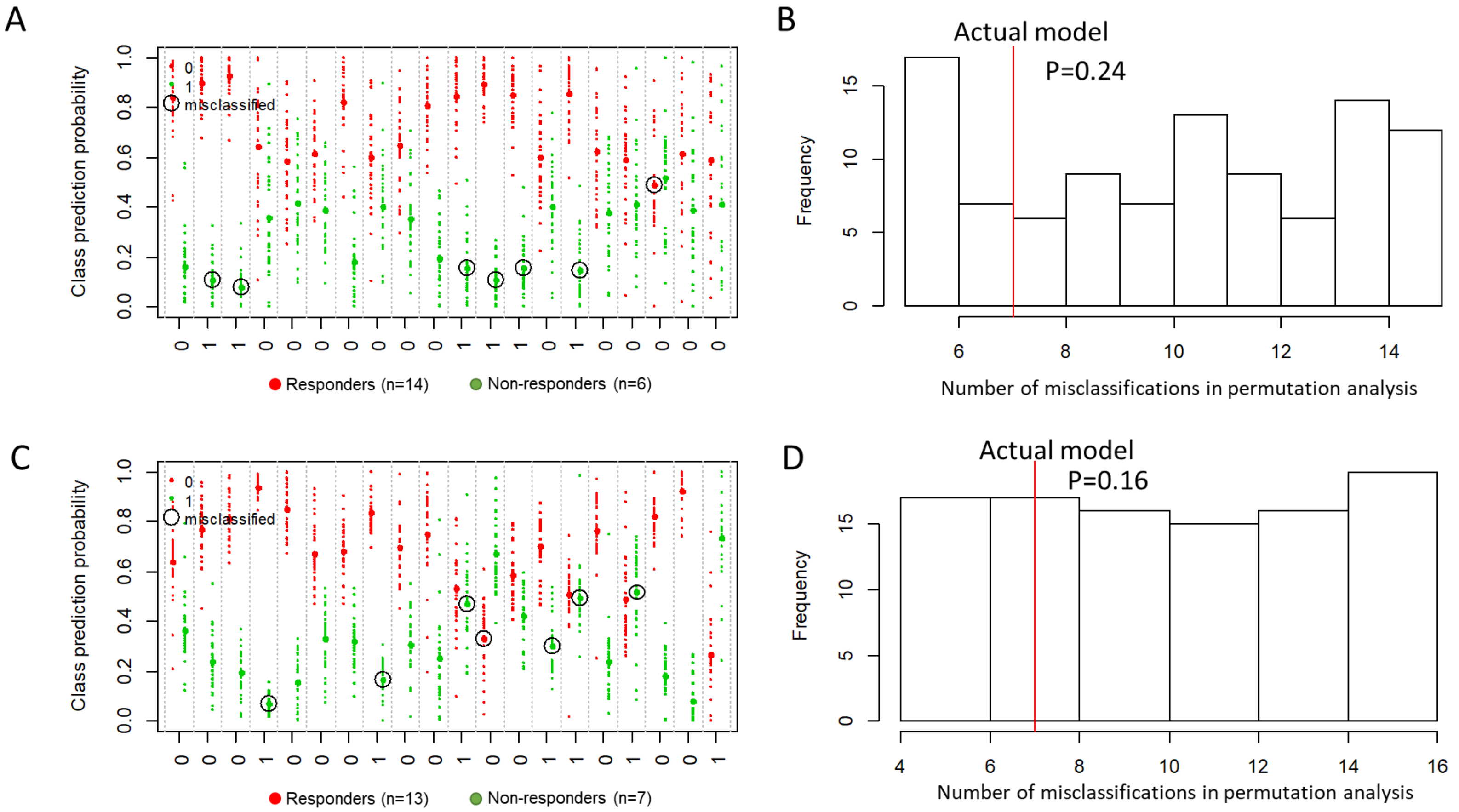
Figure S12. Baseline gut microbiota associated with response to diet with respect to BMI.



Subjects with lower BMI post-VD compared with post-MD were defined as responders.

Patients who had higher BMI after VD than MD were categorized as non-responders.

Figure S13. Baseline plasma metabolome showed no association with diet-related change in oxidized LDL-C (A and B) or BMI (C and D).



Accuracy of baseline plasma metabolome in discriminating responders from non-responders using random forest algorithm (A and C) and results from permutation analysis (B and D) is presented.