

Table S1: Reported symptoms and inventory of collected samples.

Number	Age	Reported Symptoms	Completed trial (C) / Dropout (DO)	Blood samples		Stool samples	
				V1	V7	V1	V7
CAE-001	23	Little	C	-	-	-	-
CAE-002	20	Little. Vomiting. Transient constipation	C	-	-	-	-
CAE-003	40	At first: Cramps and diarrhea. then constipation. stomach ache	C	-	-	-	-
Pla-004	39	At first: Headache. heartburn. stools more frequent and loose	C	-	-	-	-
Pla-005	19	None	C	-	-	-	-
CAE-006	27	None	C	-	-	-	-
Pla-007	34	None	C	-	-	-	-
CAE-008	31	At first: Stools more frequent. headache. heartache	C	-	-	-	-
Pla-009	23	None	DO	-	-	-	-
CAE-010	44	Burning sensation in the rectum a few days. diarrhea. nausea. stomach ache. vomiting	C	-	-	-	-
CAE-011	27	V5 and up: nausea. sweating. intestinal burning	C	-	-	-	-
Pla-012	40	At first: Sensation of acidity in the stomach 1 time	C	-	-	-	-
CAE-013	44	None	C	-	-	-	-
CAE-014	24	At first: Bowel pain. lower abmen. poor appetite	DO	-	-	-	-
Pla-015	21	None	C	-	-	-	-
Pla-016	28	None	C	-	-	-	-
Pla-017	34	V3 and V5: heartburn	C	-	-	-	-
Pla-018	40	None	DO	-	-	-	-
Pla-019	41	None	C	x	x	x	x
CAE-020	25	Intestine and stomach level bar. cramps. V3: Sweating. V5-6: Belly ache	C	x	x	-	-
Pla-022	34	At first: Stool more frequent. then constipation. nausea	C	x	x	-	-
CAE-023	26	Heat and sweats. more appetite. hot flashes. gas and bloating	C	x	x	-	-
Pla-024	25	None	DO	-	-	-	-
CAE-025	21	Burning sensation. stomach pain. vomiting in PM. previous stomach ache	C	x	x	-	-
Pla-026	50	None	C	x	x	x	x
CAE-027	47	V3: Red urine. Migraine	DO	x	-	x	-
CAE-028	28	Headache. burning and stomach pain. vomiting. pain	DO	x	-	x	-

		and burning during bowel movements					
Pla-029	21	None	C	x	x	x	x
Pla-030	25	None	C	-	-	-	-
CAE-031	35	None	C	x	x	x	x
Pla-032	29	At first: Diarrhea	DO	x	-	x	-
CAE-033	26	At first: Gastro-oesophageal reflux. flatulence. diarrhea	C	x	x	x	x
CAE-034	26	None	DO	x	-	-	-
Pla-035	26	At first: Dry mouth. flatulence and night sweats	C	x	x	x	x
Pla-036	21	V3: no symptoms but nausea if not eating within hours of taking	DO	x	-	x	-
CAE-037	47	Gurgling the first days	DO	x	-	-	-
CAE-038	22	None	C	-	-	x	-
Pla-039	26	None	C	x	x	-	-
CAE-040	30	Diarrhea and heartburn. headache. vomiting	DO	-	-	x	-
Pla-041	25	At first: Dizziness	C	x	x	x	x
Pla-042	25	V4: Bloating and stomachaches	C	x	x	x	x
CAE-043	22	Morning canceled	DO	-	-	x	-
Pla-044	23	V2: Tremors and heartaches	C	-	-	x	x
CAE-045	23	Stomach burns. spasms. reflux. bloating	DO	-	-	-	-
CAE-046	24	Heartache. vomiting. stomach cramps. loose stools	C	x	-	-	-
Pla-047	28	V3: Diarrhea and nausea	C	x	x	x	x
CAE-048	38	Constipation. blood in the stools. stinging and burning stools	C	x	x	x	x
Pla-049	25	None	C	x	x	x	x
CAE-050	22	Constipation and burning during evacuation. hard stools. diarrhea. stomachaches. headache. dizziness. intense migraine	DO	x	-	-	-
Pla-051	35	None except V6 stomach pains ++ after 6 oranges	C	x	x	x	x
Pla-052	36	None	C	-	-	x	x
CAE-053	24	Discomfort. vomiting. loose stools. cramps. abdominal pain. stinging stools. diarrhea. nausea and stomach discomfort	C	x	x	x	x
Pla-055	33	At first: Hot flashes. V6: mild heartburn	C	x	x	-	-
CAE-056	45	V4: loss of appetite. less hunger and less sugar rage	DO	x	-	-	-
Pla-057	20	At first: V2-3: Headache. 1 episode of vomiting	C	x	x	x	-

Pla-058	29	None	C	-	-	x	x
CAE-059	27	At first: Bellyache. loose stools. pressure drop	C	x	x	-	-
CAE-060	31	Vomiting. stomach pain and gas ++. heartburn. burping. bloating	C	x	x	x	x
CAE-061	20	Sudden epigastric abdominal pain 10/10. loss of consciousness. hospital transport by ambulance	DO	-	-	-	-
CAE-062	24	Bellyache. stomach. burning and swelling in the stomach. gas and burps. diarrhea	C	x	x	x	x
Pla-063	19	Gurgling	DO	-	-	-	-

Table S2: List of the lipid mediators used as deuterated internal standards for LC/MS-MS analyses

Abbreviation	Internal standards utilized
2-AG	d5-Mono-arachidonoyl-glycerol 1(3) and 2 isomers
AA	d8-Arachidonic acid
AEA	d4-Anandamide
Arachidonoyl Glycine	d8- <i>N</i> -Arachidonoyl Glycine
Arachidonoyl Serotonin	<i>N</i> -Arachidonoyl Serotonin
DHA	d5-Docosahexaenoic acid
DHEA	d4- <i>N</i> -docosahexaenoyl-ethanolamine
DPA	d5-Docosapentaenoic acid
2-DPG (n-3)	d5-Mono-docosapentaenoyl-glycerol 1(3) and 2 isomers
EPA	d5-Eicosapentaenoic acid
2-EPG	d5-Mono-eicosapentaenoyl-glycerol 1(3) and 2 isomers
EPEA	d4- <i>N</i> -eicosapentaenoyl-ethanolamine
LEA	d4- <i>N</i> -linoleoyl-ethanolamine
2-LG	d5-Mono-linoleoyl-glycerol 1(3) and 2 isomers
N-Oleyl-L-Serine	<i>N</i> -Oleyl-L-Serine
2-OG	2-oleoyl-glycerol
Oleoyl Serotonin	d17- <i>N</i> -oleoyl-serotonin
OEA	d4- <i>N</i> -oleoyl-ethanolamine
PEA	d4- <i>N</i> -palmitoyl-ethanolamine
2-PG	Mono-palmitoyl-glycerol 1(3) and 2 isomers
PGE2	d4-Prostaglandin E2
PGE2-EA	d4-Prostaglandin E2 ethanolamide (prostamide E2)
PGE2-G	d5-Prostaglandin E2 glycerol
PGF2α-EA	Prostaglandin F2 α ethanolamide (prostamide F2 α)
Stearoyl-EA	d3- <i>N</i> -stearoyl-ethanolamine

Legends to Supplementary Figures:

Figure S1: Effect of Capsimax and caloric restriction on relative abundance of fecal bacterial genera of 15 participants (9 placebo and 6 Capsimax) overweight or obese reproductive aged-women, before (Visit 1 [V1]) and after (Visit 7 [V7]) the interventions.

Figure S2: Correlation between fecal microbiota taxa at phylum (A), classed (B) and genera (C) levels and BMI, waist circumference, fat mass (FM) and fat-free mass (FFM) of 15 participants (9 placebo and 6 Capsimax) overweight or obese reproductive aged-women. The correlation analysis were performed using repeated measures correlation tests (rmcorr package). Only correlations coefficients with p-value < 0.05 are displayed.

Figure S3: Correlations between the plasma levels of eCBome mediators and BMI, waist circumference, fat mass (FM) and fat-free mass (FFM) of 15 participants (9 placebo and 6 Capsimax) overweight or obese reproductive aged-women. The correlation analysis was performed using repeated measures correlation tests (rmcorr package). Only correlations coefficients with p-value < 0.05 are displayed. OEA, *N*-oleoyl-ethanolamine; LEA, *N*-linoleoyl-ethanolamine; DPEA, *N*-docosapentaenoyl-ethanolamine; 1/2-OG, 1/2-oleoyl-glycerol; DHA, docosahexaenoic acid; DHEA, *N*-docosahexaenoyl-ethanolamine; PEA, *N*-palmitoyl-ethanolamine.

Figure S1

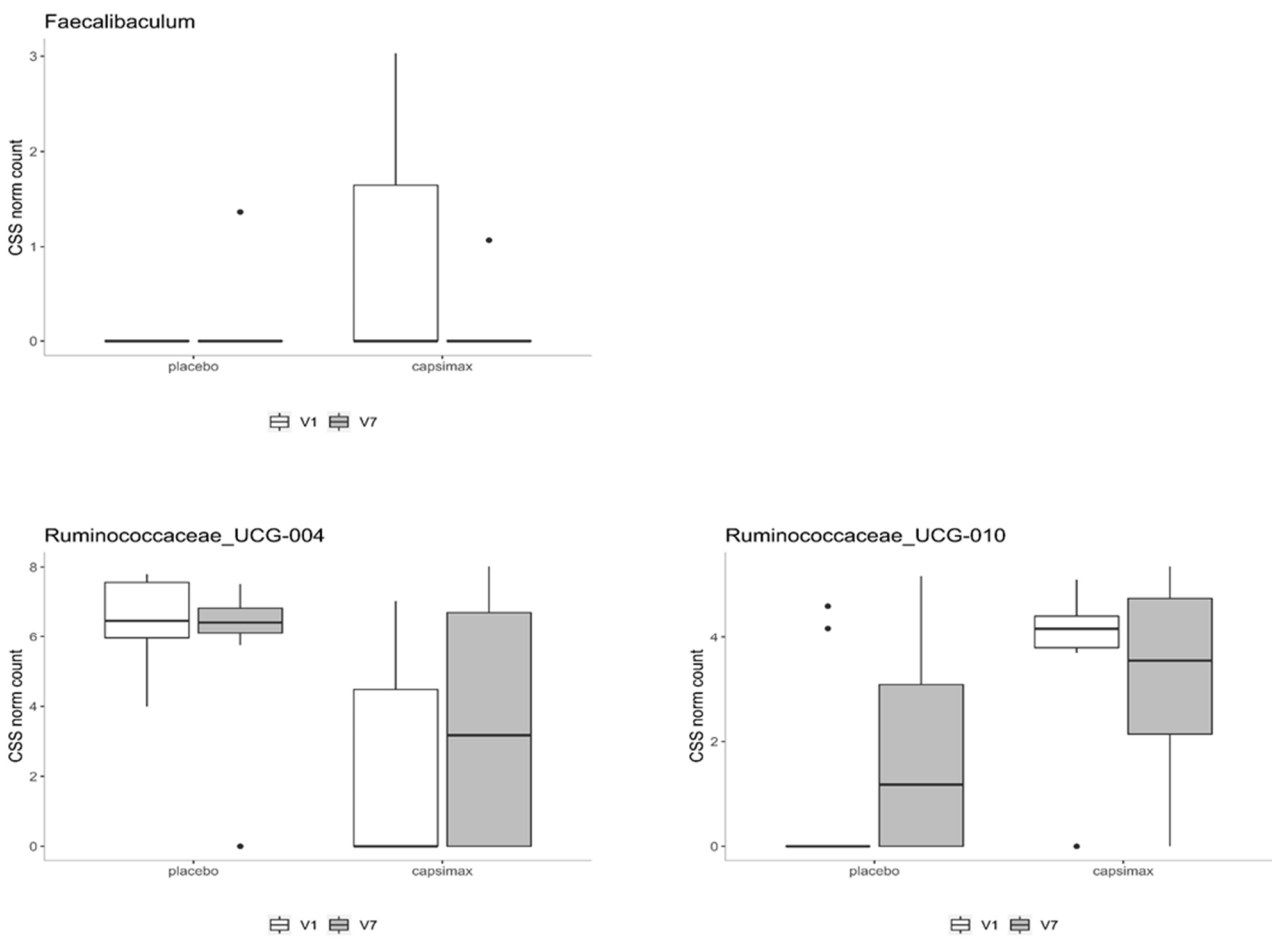
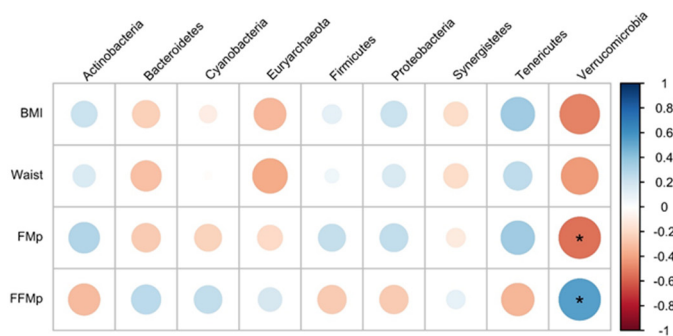
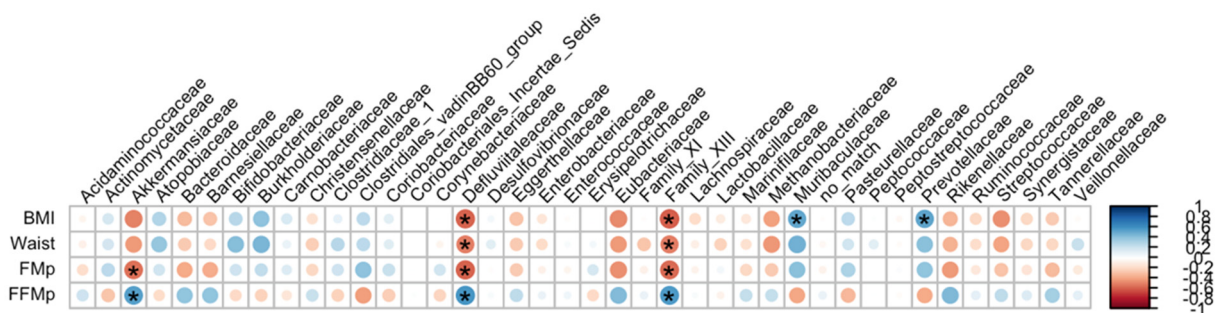


Figure S2

A)



B)



C)

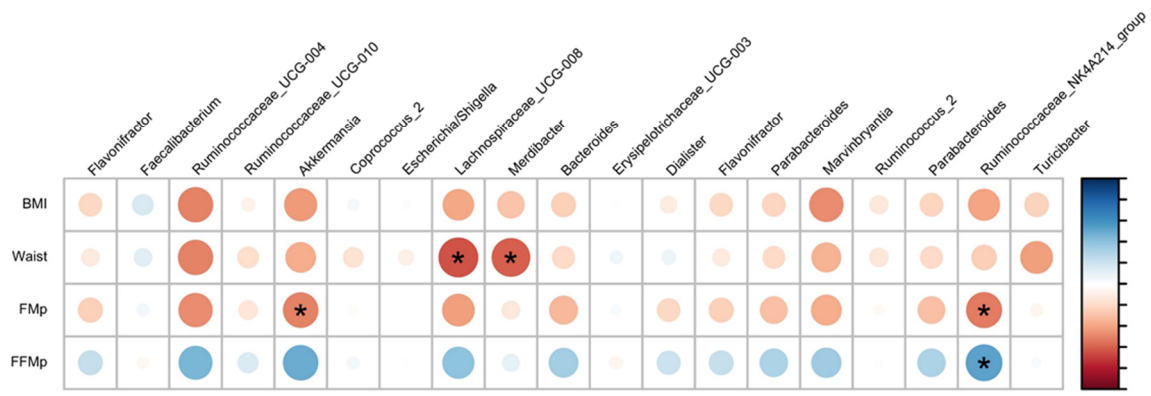


Figure S3

