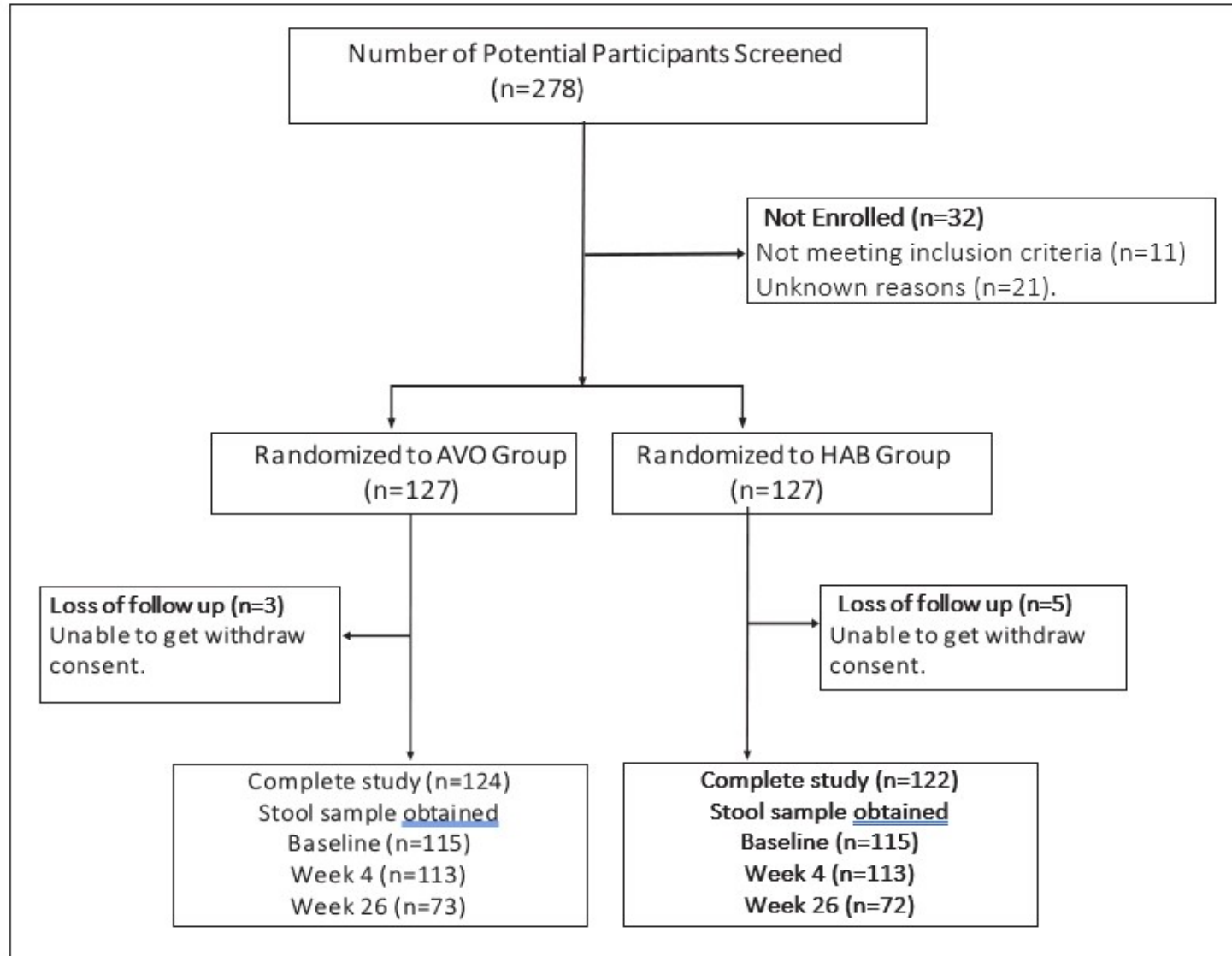


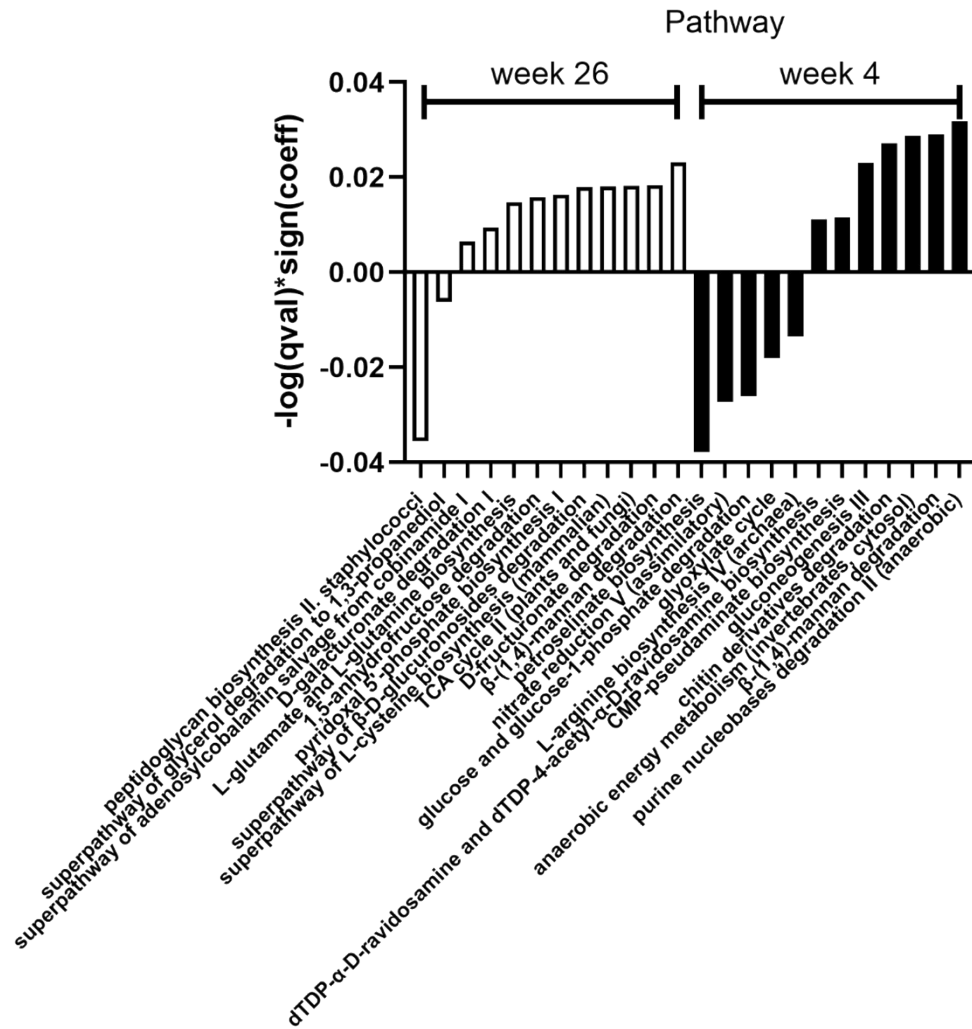
Supplementary materials

1) Sleep quality and physical activities.

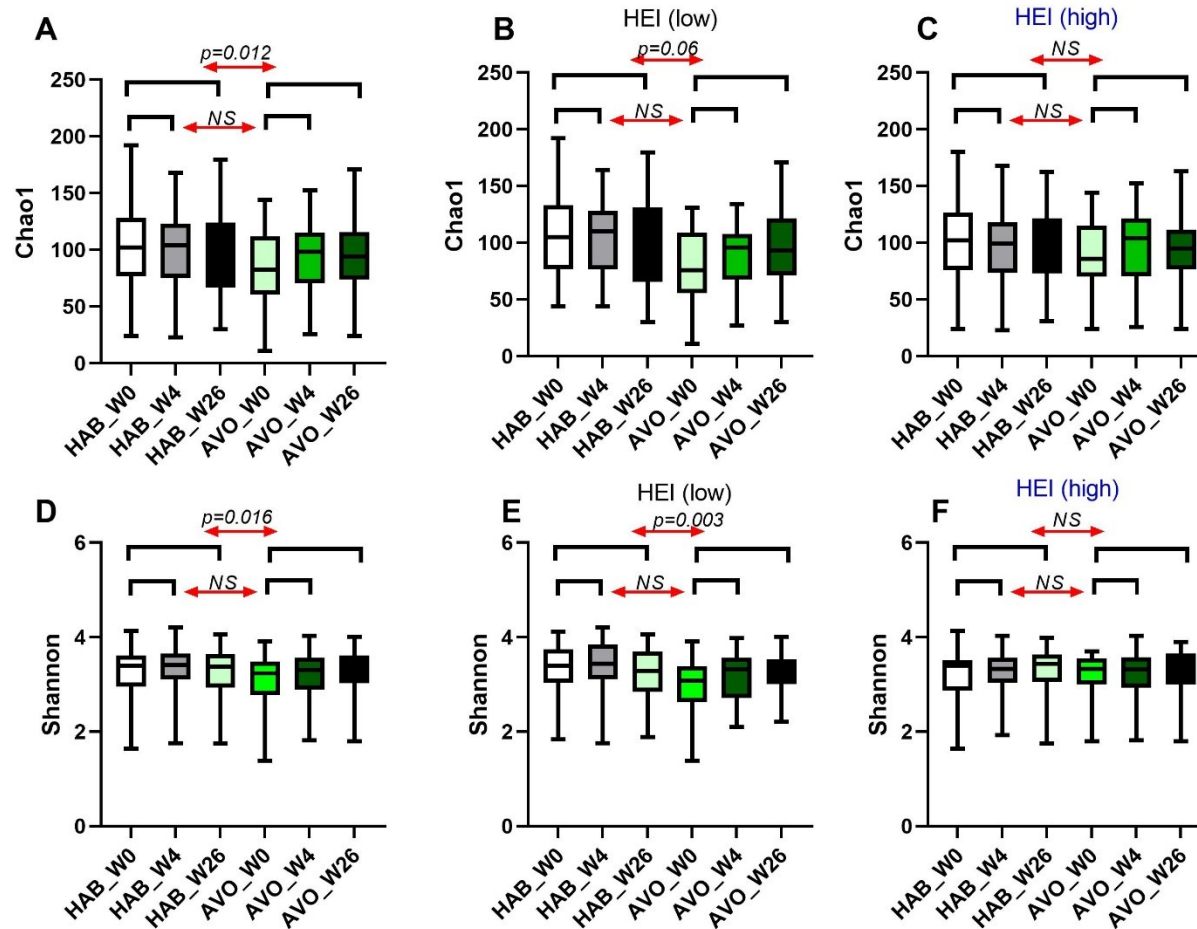
This ancillary study included data collected at baseline and 26 weeks. An in-house health and demographics questionnaire was used to qualitatively measure physical activity (binary response: Yes/No). Sleep health was evaluated using the Pittsburgh Sleep Quality Index (PSQI).¹⁶ A logistic regression test was used to evaluate whether changes in physical activity were associated with avocado intake. Out of 230 participants, 67.5% in the HAB group and 66% in the AVO group reported engaging in regular physical activity at week 0, while 63.2% in the HAB group and 61.3% in the AVO group reported engaging in regular physical activity at week 26. We did not detect significant changes in physical activity associated with avocado intake. Sleep quality index was analyzed using mixed linear model. At week 0, participants in the HAB group had a PSQI score of 1.06 (SD = 0.82), while those in the AVO group had scores of 1.07 (SD = 0.93). At week 26, the PSQI scores were 1.11 (SD = 0.89) for the HAB group and 1.03 (SD = 0.81) for the AVO group. We did not detect significant changes in sleep quality with avocado intake.



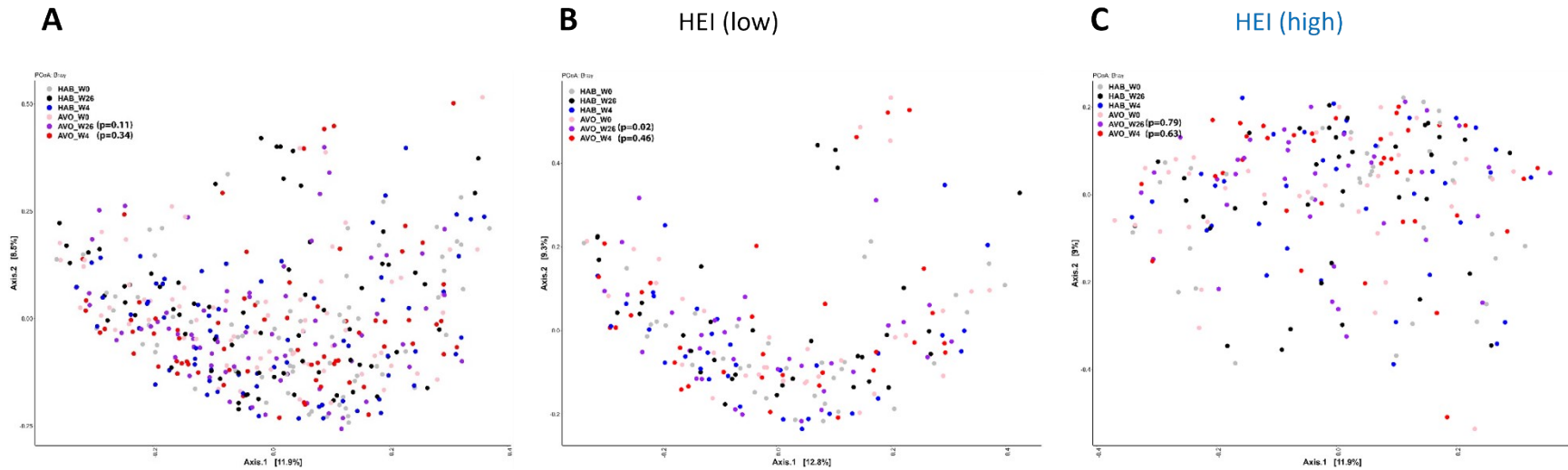
Supplementary Figure 1



Supplementary Figure 2: MaAsLin2 analysis showing the association of metabolic pathways with avocado intake at week 4 and 26 in all participants with $P < 0.05$.



Supplementary Figure 4: A linear mixed effects model showed significant increases in alpha diversity indices Chao 1 and Shannon for (A, D) participants who completed baseline, week 4 and week 26 tool sample collections (AVO: $n=70$; HAB: $n=71$). Significant differences were also noted for (B, E) participants with low HEI (AVO: $n=32$; HAB: $n=33$) and (E, F) high HEI (AVO: $n=37$; HAB: $n=37$) in the AVO group after 26 weeks of intervention compared to the HAB group ($p<0.05$). P-values atop each figure indicate significant changes from baseline at week 4 or 26 between AVO and HAB groups.



Supplementary Figure 5: PCoA plot based on Bray-Curtis dissimilarity, with each point corresponding to a sample and colored-coded for the different group. Analysis was performed in (A) all participants who completed 26 week's intervention (B) Participants with (B) low HEI scores or high HEI scores who completed 26 week's intervention. PERMANOVA showed that the separation of bacterial communities in between baseline and week 26 was significant between AVO and HAB groups in HEI low participants ($p=0.015$, Repeated measures PERMANOVA).

Supplementary table 1: Anthropometric and biochemical measures of HEI_high participants over time.

	AVO			HAB			P wk4	P wk26
	Baseline	Week 4	Week 26	Baseline	Week 4	Week 26		
N	63	63	37	56	56	37		
BMI (kg/m ²)	32.93(5.81)	—	33.96(6.13)	32.27(5.59)	—	32.57(5.03)		NS
HEI-2015	64.96(8.9)	—	65.99(10.31)	67.25(11.01)	—	63.88(15.09)		NS
VAT (L)	2.9(1.23)	—	3.02(1.29)	2.79(1.27)	—	2.85(1.23)		NS
HFF (%)	0.1(0.12)	—	0.08(0.09)	0.1(0.11)	—	0.09(0.12)		NS
DBP (mmHg)	77(12)	75(9)	76(7)	78(11)	77(8)	77(7)	NS	NS
SBP (mmHg)	121(19)	120(16)	121(11)	122(16)	120(13)	124(18)	NS	NS
Pulse	68.67(8.93)	74.1(9.52)	69.78(8.48)	68.8(9.89)	74.07(10.01)	69.86(10.21)	NS	NS
Insulin (μ U/mL)	16.9(17.4)	—	14.39(8.72)	14.68(9.56)	—	16.15(11.59)		NS
hsCRP (mg/L)	6.36(8.85)	—	7.48(8.24)	5.24(5.61)	—	6.06(6.23)		NS
Glucose (mg/dL)	98.57(32.64)	—	101.89(21.72)	95.91(16.51)	—	105.24(26.24)		NS
TC (mg/dL)	172(35)	—	176(31)	191(44)	—	198(44)		NS
Trig (mg/dL)	126(101)	—	119(87)	121(57)	—	121(58)		NS
HDL-C (mg/dL)	53(12)	—	54(10)	58(13)	—	55(12)		NS
VLDL-C (mg/dL)	25(20)	—	24(17)	24(11)	—	24(12)		NS
LDL-C (mg/dL)	95(31)	—	100(29)	109(35)	—	118(37)		NS

Values are presented as mean (SD); P \geq 0.05, no significance (NS).

Supplementary table 2: Significant interactions ($q < 0.25$) between time and intervention at the species level at both week 4 and week 26 in HEI_low participants

feature	metadata	coef	stderr	pval	qval
Bacterium_AF16_15	Time_W24_Avo	1.66	0.35	0.00	0.01
Clostridium_leptum	Time_W24_Avo	1.16	0.32	0.00	0.10
Roseburia_hominis	Time_W24_Avo	0.61	0.17	0.00	0.10
GGB3653_SGB4964	Time_W24_Avo	1.34	0.38	0.00	0.10
Faecalibacterium_SGB15346	Time_W24_Avo	1.22	0.35	0.00	0.10
Roseburia_inulinivorans	Time_W24_Avo	0.59	0.17	0.00	0.10
Faecalibacterium_prausnitzii	Time_W24_Avo	0.50	0.15	0.00	0.10
Roseburia_intestinalis	Time_W24_Avo	1.14	0.34	0.00	0.10
Blautia_faecis	Time_W24_Avo	0.81	0.25	0.00	0.13
Neglectibacter_timonensis	Time_W24_Avo	0.47	0.15	0.00	0.18
Collinsella_SGB14861	Time_W24_Avo	0.36	0.12	0.00	0.18
Alistipes_finegoldii	Time_W24_Avo	0.40	0.13	0.00	0.19
GGB45432_SGB63101	Time_W24_Avo	0.65	0.22	0.00	0.19
Bacteroides_ovatus	Time_W24_Avo	0.83	0.28	0.00	0.19
GGB9522_SGB14921	Time_W24_Avo	0.46	0.15	0.00	0.19
GGB51441_SGB71759	Time_W24_Avo	0.47	0.16	0.00	0.19
Lachnospiraceae_bacterium	Time_W24_Avo	1.03	0.36	0.00	0.20
Dorea_formicigenerans	Time_W24_Avo	0.82	0.28	0.00	0.20
GGB9758_SGB15368	Time_W24_Avo	0.81	0.28	0.00	0.21
Coprococcus_eutactus	Time_W24_Avo	1.09	0.39	0.01	0.21
GGB9501_SGB14898	Time_W24_Avo	-0.69	0.24	0.01	0.21
GGB9186_SGB14125	Time_W24_Avo	0.77	0.28	0.01	0.22
GGB9765_SGB15382	Time_W24_Avo	0.70	0.25	0.01	0.22
GGB3588_SGB4808	Time_W24_Avo	-0.45	0.16	0.01	0.22
Collinsella_intestinalis	Time_W24_Avo	0.26	0.10	0.01	0.22
GGB53985_SGB6367	Time_W24_Avo	0.20	0.07	0.01	0.22
GGB9787_SGB15410	Time_W24_Avo	0.65	0.24	0.01	0.23
GGB35068_SGB47850	Time_W24_Avo	-0.67	0.25	0.01	0.23
GGB9813_SGB15447	Time_W24_Avo	0.72	0.27	0.01	0.23
Streptococcus_australis	Time_W24_Avo	0.83	0.32	0.01	0.23
GGB3602_SGB4574	Time_W24_Avo	0.27	0.10	0.01	0.23
Amedibacillus_dolichus	Time_W24_Avo	0.27	0.10	0.01	0.23
Anaeromassilibacillus_sp_An250	Time_W4_Avo	1.03	0.30	0.00	0.10
Bacteroides_caccae	Time_W4_Avo	-0.50	0.17	0.00	0.19
GGB3653_SGB4964	Time_W4_Avo	0.59	0.21	0.01	0.21
Bacteroides_ovatus	Time_W4_Avo	0.39	0.14	0.01	0.21
Eisenbergiella_tayi	Time_W4_Avo	0.83	0.30	0.01	0.22
Hungatella_hathewayi	Time_W4_Avo	0.85	0.32	0.01	0.23
Alistipes_communis	Time_W4_Avo	0.85	0.32	0.01	0.23
Holdemanella_biformis	Time_W4_Avo	0.61	0.23	0.01	0.23
Streptococcus_australis	Time_W4_Avo	0.60	0.23	0.01	0.23

Supplementary table 3: Causal mediation analysis

Tests	Total effect	Mediation proportion
Mediator: Energy intake Outcome: <i>AF16_15</i>	5.08 (0.002)	0.02 (0.478)
Mediator: Energy intake Outcome: <i>Faecalibacterium prausnitzii</i>	2.34 (0.006)	0.03 (0.48)
Mediator: Energy intake Outcome: <i>Chao1</i>	12.51(0.036)	-0.02 (0.576)
Mediator: Energy intake Outcome: <i>Shannon</i>	0.18 (0.028)	-0.02 (0.704)
Mediator: Total fruits Outcome: <i>AF16_15</i>	5.11 (0.000)	0.02 (0.784)
Mediator: Total fruits Outcome: <i>Faecalibacterium prausnitzii</i>	2.38 (0.01)	0.01 (0.908)
Mediator: Total fruits Outcome: <i>Chao1</i>	12.79 (0.026)	0.14 (0.210)
Mediator: Total fruits Outcome: <i>Shannon</i>	0.18 (0.02)	0.07 (0.582)
Mediator: Whole fruits Outcome: <i>AF16_15</i>	5.07 (0.000)	0.07 (0.338)
Mediator: Whole fruits Outcome: <i>Faecalibacterium prausnitzii</i>	2.38 (0.012)	0.02 (0.814)
Mediator: Whole fruits Outcome: <i>Chao1</i>	12.77 (0.014)	0.17 (0.168)

Mediator: Whole fruits Outcome: <i>Shannon</i>	0.18 (0.038)	0.06 (0.632)
Mediator: Fatty acids Outcome: <i>AF16_15</i>	5.09 (0.000)	0.05(0.258)
Mediator: Fatty acids Outcome: <i>Faecalibacterium prausnitzii</i>	2.35 (0.006)	-0.01 (0.848)
Mediator: Fatty acids Outcome: <i>Chao1</i>	12.54 (0.030)	-0.001 (0.986)
Mediator: Fatty acids Outcome: <i>Shannon</i>	0.18 (0.036)	-0.05 (0.462)
Mediator: HEI2015 total score Outcome: <i>AF16_15</i>	5.07 (0.000)	0.02 (0.464)
Mediator: Fatty HEI2015 total score Outcome: <i>Faecalibacterium prausnitzii</i>	2.31 (0.008)	0.07 (0.132)
Mediator: HEI2015 total score Outcome: <i>Chao1</i>	12.95 (0.020)	0.11 (0.068)
Mediator: HEI2015 total score Outcome: <i>Shannon</i>	0.18 (0.042)	0.08 (0.156)

Total effect (estimate (p value)) and mediation proportion (MP) (estimate (p value)) are presented.

Supplementary table 4: Interactions ($p < 0.05$) between time and intervention at the species level in participants who completed 26 weeks' intervention.

feature	metadata	coef	stderr	pval	qval
Firmicutes_bacterium_AF16_15	Time_W26_Avo	1.09	0.30	0.00	0.17
Faecalibacterium_prausnitzii	Time_W26_Avo	0.66	0.20	0.00	0.44
Clostridium_leptum	Time_W26_Avo	0.90	0.29	0.00	0.62
Roseburia_intestinalis	Time_W26_Avo	0.91	0.33	0.01	0.89
GGB9765_SGB15382	Time_W26_Avo	0.35	0.13	0.01	0.89
Anaeromassilibacillus_sp_An250	Time_W26_Avo	0.68	0.25	0.01	0.93
Sanguibacter_SGB15121	Time_W26_Avo	0.38	0.15	0.01	0.97
Eubacterium_SGB6276	Time_W26_Avo	0.63	0.24	0.01	0.97
GGB9186_SGB14125	Time_W26_Avo	0.28	0.11	0.01	0.97
GGB9522_SGB14921	Time_W26_Avo	0.37	0.16	0.02	0.97
Neglectibacter_timonensis	Time_W26_Avo	0.42	0.18	0.02	0.97
Roseburia_inulinivorans	Time_W26_Avo	0.86	0.37	0.02	0.97
Hungatella_hathewayi	Time_W26_Avo	0.43	0.19	0.02	0.97
Parasutterella_SGB9260	Time_W26_Avo	-0.30	0.13	0.02	0.97
Amedibacillus_dolichus	Time_W26_Avo	-0.48	0.21	0.02	0.99
Clostridiales_bacterium_NSJ_40	Time_W26_Avo	-0.22	0.10	0.03	0.99
GGB3491_SGB4665	Time_W26_Avo	0.15	0.07	0.03	0.99
Erysipelotrichaceae_bacterium_3_1_53	Time_W26_Avo	0.25	0.11	0.03	0.99
GGB9760_SGB15373	Time_W26_Avo	0.56	0.26	0.03	0.99
Anaerostipes_hadrus	Time_W26_Avo	0.29	0.14	0.03	0.99
GGB3175_SGB4191	Time_W26_Avo	0.32	0.15	0.03	0.99
Bacteroides_ovatus	Time_W26_Avo	0.68	0.32	0.03	0.99
GGB3653_SGB4964	Time_W26_Avo	0.73	0.35	0.03	0.99
Eubacterium_siraeum	Time_W26_Avo	0.46	0.22	0.03	0.99
Clostridiaceae_bacterium_AF18_31LB	Time_W26_Avo	0.43	0.20	0.04	0.99
GGB9559_SGB14969	Time_W26_Avo	0.35	0.17	0.04	0.99
Alistipes_putredinis	Time_W26_Avo	0.61	0.29	0.04	0.99
GGB9719_SGB15273	Time_W26_Avo	0.43	0.21	0.04	0.99
Bacteroides_caccae	Time_W26_Avo	0.62	0.31	0.05	0.99
GGB9758_SGB15368	Time_W26_Avo	0.49	0.25	0.05	0.99
GGB9302_SGB14263	Time_W26_Avo	-0.24	0.12	0.05	0.99
GGB51441_SGB71759	Time_W26_Avo	0.38	0.19	0.05	0.99
Mediterraneibacter_SGB48424	Time_W26_Avo	0.22	0.11	0.05	0.99
Clostridiaceae_bacterium_Marseille_Q4145	Time_W4_Avo	0.19	0.07	0.01	0.97
Eisenbergiella_tayi	Time_W4_Avo	0.54	0.22	0.01	0.97
Anaerostipes_caccae	Time_W4_Avo	0.45	0.18	0.01	0.97
Bacteroides_ovatus	Time_W4_Avo	0.78	0.32	0.02	0.97
Anaeromassilibacillus_sp_An250	Time_W4_Avo	0.62	0.25	0.02	0.97
Eggerthella_lenta	Time_W4_Avo	0.69	0.30	0.02	0.97
Acidaminococcus_intestini	Time_W4_Avo	-0.35	0.16	0.02	0.99
GGB4596_SGB6358	Time_W4_Avo	-0.21	0.10	0.03	0.99
Catenibacterium_SGB4425	Time_W4_Avo	0.38	0.18	0.04	0.99

Ruthenibacterium_lactatiformans	Time_W4_Avo	0.55	0.27	0.04	0.99
GGB33928_SGB15225	Time_W4_Avo	0.23	0.11	0.04	0.99
Roseburia_faecis	Time_W4_Avo	0.59	0.29	0.04	0.99
Negativibacillus_massiliensis	Time_W4_Avo	0.22	0.11	0.04	0.99
Mediterraneibacter_SGB48424	Time_W4_Avo	0.23	0.11	0.04	0.99
GGB9719_SGB15273	Time_W4_Avo	0.42	0.21	0.05	0.99
Clostridium_leptum	Time_W4_Avo	0.58	0.29	0.05	0.99
Oscillospiraceae_bacterium_Marseille_Q3528	Time_W4_Avo	0.51	0.26	0.05	0.99
Lachnospiraceae_bacterium_NSJ_29	Time_W4_Avo	0.54	0.27	0.05	0.99

Supplementary table 5: Interactions ($p < 0.05$) between time and intervention at the species level in HEI_low participants who completed 26 weeks' intervention

feature	metadata	coef	stderr	pval	qval
Firmicutes_bacterium_AF16_15	Time_W26_Avo	2.10	0.47	0.00	0.02
Clostridium_leptum	Time_W26_Avo	1.53	0.45	0.00	0.34
GGB9522_SGB14921	Time_W26_Avo	0.53	0.16	0.00	0.34
Blautia_faecis	Time_W26_Avo	0.66	0.21	0.00	0.34
GGB3653_SGB4964	Time_W26_Avo	1.19	0.37	0.00	0.34
GGB9813_SGB15447	Time_W26_Avo	0.23	0.07	0.00	0.34
GGB53985_SGB6367	Time_W26_Avo	0.36	0.12	0.00	0.34
Neglectibacter_timonensis	Time_W26_Avo	0.68	0.22	0.00	0.34
Collinsella_SGB14861	Time_W26_Avo	1.13	0.37	0.00	0.34
Faecalibacterium_SGB15346	Time_W26_Avo	0.99	0.34	0.00	0.40
GGB4578_SGB6328	Time_W26_Avo	0.41	0.14	0.00	0.40
GGB33469_SGB15236	Time_W26_Avo	0.57	0.20	0.01	0.40
Lachnospiraceae_bacterium	Time_W26_Avo	0.75	0.26	0.01	0.40
GGB3588_SGB4808	Time_W26_Avo	0.47	0.17	0.01	0.41
Collinsella_intestinalis	Time_W26_Avo	0.39	0.14	0.01	0.41
Bacteroides_ovatus	Time_W26_Avo	1.15	0.43	0.01	0.44
Streptococcus_australis	Time_W26_Avo	-0.45	0.17	0.01	0.44
Faecalibacterium_prausnitzii	Time_W26_Avo	0.89	0.33	0.01	0.44
Roseburia_intestinalis	Time_W26_Avo	1.25	0.48	0.01	0.47
GGB9501_SGB14898	Time_W26_Avo	0.44	0.17	0.01	0.49
GGB9707_SGB15229	Time_W26_Avo	0.57	0.22	0.01	0.49
Alistipes_finegoldii	Time_W26_Avo	0.89	0.35	0.01	0.49
Dorea_formicigenerans	Time_W26_Avo	0.67	0.26	0.01	0.49
Roseburia_hominis	Time_W26_Avo	0.90	0.36	0.01	0.49
GGB9765_SGB15382	Time_W26_Avo	0.52	0.21	0.01	0.49
GGB9787_SGB15410	Time_W26_Avo	0.33	0.13	0.01	0.50
GGB45432_SGB63101	Time_W26_Avo	0.68	0.28	0.02	0.50
Parabacteroides_merdae	Time_W26_Avo	0.81	0.33	0.02	0.50
Bacteroides_intestinalis	Time_W26_Avo	0.60	0.25	0.02	0.59
GGB51441_SGB71759	Time_W26_Avo	0.70	0.30	0.02	0.60
GGB9559_SGB14969	Time_W26_Avo	0.54	0.23	0.02	0.60
Coprococcus_eutactus	Time_W26_Avo	0.55	0.24	0.02	0.60
Solibaculum_mannosilyticum	Time_W26_Avo	0.43	0.19	0.02	0.62
Anaeromassilibacillus_sp_An250	Time_W26_Avo	0.85	0.37	0.03	0.64
Alistipes_putredinis	Time_W26_Avo	1.01	0.45	0.03	0.64
Amedibacillus_dolichus	Time_W26_Avo	-0.74	0.33	0.03	0.66
Blautia_sp_MSK_20_85	Time_W26_Avo	0.81	0.37	0.03	0.66
GGB9758_SGB15368	Time_W26_Avo	0.81	0.37	0.03	0.66
GGB9186_SGB14125	Time_W26_Avo	0.23	0.11	0.03	0.66
GGB3277_SGB4327	Time_W26_Avo	0.85	0.39	0.03	0.66
Roseburia_inulinivorans	Time_W26_Avo	1.04	0.48	0.03	0.66
Ruminococcus_gnavus	Time_W26_Avo	-0.95	0.45	0.04	0.66

Lachnospiraceae_bacterium_AM48_27BH	Time_W26_Avo	0.15	0.07	0.04	0.66
Blautia_producta	Time_W26_Avo	-0.71	0.33	0.04	0.66
Eubacterium_siraeum	Time_W26_Avo	0.60	0.28	0.04	0.66
GGB80140_SGB15224	Time_W26_Avo	0.31	0.14	0.04	0.66
Oscillospiraceae_bacterium_Marseille_Q3528	Time_W26_Avo	0.56	0.27	0.04	0.66
Coprococcus_SGB4669	Time_W26_Avo	0.41	0.20	0.04	0.70
GGB4684_SGB6478	Time_W26_Avo	0.29	0.14	0.04	0.70
Clostridium_butyricum	Time_W26_Avo	-0.73	0.36	0.05	0.70
Oscillibacter_sp_ER4	Time_W26_Avo	0.80	0.40	0.05	0.70
GGB9641_SGB15117	Time_W26_Avo	0.41	0.21	0.05	0.70
Erysipelotrichaceae_bacterium_3_1_53	Time_W26_Avo	0.35	0.17	0.05	0.70
Lawsonibacter_asaccharolyticus	Time_W26_Avo	0.61	0.31	0.05	0.70
GGB51647_SGB4348	Time_W26_Avo	-0.26	0.13	0.05	0.70
Gemella_sanguinis	Time_W26_Avo	-0.18	0.09	0.05	0.70
Bacteroides_fragilis	Time_W26_Avo	0.56	0.28	0.05	0.70
Roseburia_sp_BX1005	Time_W26_Avo	0.39	0.19	0.05	0.70
Streptococcus_australis	Time_W4_Avo	-0.46	0.17	0.01	0.41
Anaeromassilibacillus_sp_An250	Time_W4_Avo	1.02	0.37	0.01	0.41
Bacteroides_ovatus	Time_W4_Avo	1.04	0.43	0.02	0.50
GGB2998_SGB3988	Time_W4_Avo	0.30	0.13	0.02	0.58
GGB9635_SGB15106	Time_W4_Avo	0.48	0.21	0.02	0.63
GGB9512_SGB14909	Time_W4_Avo	0.53	0.24	0.03	0.64
Bacteroides_caccae	Time_W4_Avo	0.84	0.39	0.03	0.66
Cuneatibacter_caecimuris	Time_W4_Avo	0.24	0.11	0.03	0.66
Holdemanella_biformis	Time_W4_Avo	0.34	0.16	0.04	0.66
Lactonifactor_sp_BIOML_A6	Time_W4_Avo	0.45	0.22	0.05	0.70
Oscillospiraceae_bacterium_Marseille_Q3528	Time_W4_Avo	0.53	0.27	0.05	0.70
Coprobacillus_cateniformis	Time_W4_Avo	0.34	0.17	0.05	0.70