Effects of Fish Oil Intervention on Type 2 Diabetes Early Risk Novel Biomarkers in Healthy Middle-Aged and Elderly Adults: a Double-Blind Randomized Controlled Trial

Zhaoyang Nian[a], Yuting Lin[a], Wei Tang[a], Chunxia Quan[a], Jing Wen[a], Xinqian Jin[a], Zheqing Zhang[a], Limei Mao[a*]

Table S1. Baseline characteristics of subjects (PP Set).

		Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
Age (years)		61.00 (56.00,66.00)	60.00 (57.00,67.00)	59.00 (54.00,65.75)	61.00 (56.00,67.00)	0.540
Gender [n(%)]	**Male**	10 (21.28)	15 (29.41)	13 (25.0)	19 (37.25)	0.326
	Female	37 (78.72)	36 (70.59)	39 (75.0)	32 (62.75)	
Physical activities [n(%)]	**Every day**	29 (61.70)	29 (56.86)	23 (44.23)	24 (47.06)	0.151
	≥ 1 time per week	11 (23.40)	15 (29.41)	13 (25.00)	17 (33.33)	
	< 1 time per week	2 (4.26)	1 (1.96)	4 (7.70)	0 (0.00)	
	Never	5 (10.64)	6 (11.76)	12 (23.08)	10 (19.60)	
Height (cm)		158.14 ± 6.59	157.31 ± 7.95	156.66 ± 7.50	160.00 ± 6.80	0.109
Weight (kg)		55.50 (52.50,60.00)	56.20 (48.40,63.00)	55.00 (50.28,64.60)	60.20 (54.00,66.60)	0.207
BMI (kg/m²)		22.86 (20.79,24.77)	22.53 (20.67,24.76)	22.29 (20.74,24.47)	23.23 (21.66,25.56)	0.709
Waist measurement (cm)		80.00 (76.00,84.00)	81.20 (75.00,87.50)	81.00 (75.00,87.88)	85.00 (80.00,91.00)	0.057
Hip measurement (cm)		94.53 ± 5.20	93.58 ± 7.70	95.24 ± 7.18	96.32 ± 7.18	0.237
WHR		0.86 (0.81,0.90)	0.85 (0.82,0.92)	0.86 (0.80,0.91)	0.87 (0.83,0.92)	0.142

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
SBP (mmHg)	128.00 (120.00,135.00)	126.00 (111.00,139.00)	120.00 (109.25,135.75)	124.00 (118.00,132.00)	0.539
DBP (mmHg)	76.00 (71.00,84.00)	78.00 (70.00,84.00)	77.50 (69.25,85.00)	75.00 (70.00,80.00)	0.853

Data are presented as means ± SD or median and quartiles. Baseline comparisons between groups were performed using ANOVA, Kruskal-Wallis H rank sum tests, or chi-square tests. BMI: body mass index; WHR: waist-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure. BMI = weight (kg) / [height (m) * height (m)]. WHR = waist circumference(cm) / hip circumference(cm).

Table S2. Daily intake of dietary energy and nutrients during the intervention (PP Set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
Energy (kcal)	1437.28 ± 277.23	1499.99 ± 396.23	1497.10 ± 330.61	1559.41 ± 363.13	0.386
Protein (g)	60.76(54.01,68.54)	60.89(48.98,85.28)	67.11(57.94,82.68)	65.88(56.39,87.11)	0.182
Total Fat (g)	40.04(34.35,55.58)	46.72(34.73,58.60)	45.10(32.77,59.96)	45.99(31.78,61.50)	0.437
Carbohydrates (g)	204.92(175.47,230.18)	217.36(168.54,252.31)	197.61(170.07,245.96)	217.13(180.92,251.39)	0.766
Triglycerides (mg)	284.73 ± 138.81	292.78 ± 160.03	299.44±148.22	296.36 ± 136.07	0.964
Total fatty acid (g)	19.18(11.88,27.57)	19.00(12.49,27.82)	18.57(14.83,26.71)	18.02(11.68,27.30)	0.666
SFA (g)	6.51(3.07,8.04)	5.33(3.65,8.27)	6.05(4.15,7.91)	4.99(3.43,8.41)	0.868
MUFA (g)	7.61(4.22,12.81)	8.01(5.06,10.45)	8.34(6.39,11.46)	7.46(4.67,12.44)	0.725
PUFA (g)	4.66(2.79,5.95)	4.89(3.49,7.57)	4.68(3.32,6.87)	5.43(3.03,7.70)	0.609
EPA (g)	0.03(0.01,0.07)	0.05(0.00,0.14)	0.02(0.01,0.13)	0.04(0.01,0.08)	0.890
DHA (g)	0.04(0.01,0.09)	0.06(0.01,0.18)	0.04(0.01,0.13)	0.06(0.02,0.11)	0.527
Calcium (mg)	394.67(311.15,554.46)	511.21(352.42,747.23)	411.54(357.88,539.14)	462.32(349.69,634.53)	0.107
Iron (mg)	12.99(10.57,15.52)	14.53(11.71,18.19)	13.85(11.50,16.65)	15.28(10.86,19.55)	0.210
Zinc (mg)	8.14(7.62,9.28)	8.49(7.21,10.74)	8.53(7.46,9.83)	8.36(6.80,10.76)	0.747
Vitamin A (μgRAE)	558.63(351.60,916.66)	561.20(407.55,701.13)	572.69(402.85,970.08)	548.77(309.87,963.62)	0.898
Vitamin C (mg)	112.32(82.15,139.20)	105.77(83.73,149.60)	104.39(79.73,151.07)	121.95(91.75,141.33)	0.735
Vitamin E (mg)	10.36(7.55,13.30)	11.54(7.88,16.40)	10.63(8.95,15.36)	12.14(8.64,16.29)	0.333

Data are presented as means ± SD or median and quartiles. Dietary intake between groups were performed using ANOVA or Kruskal-Wallis H rank sum tests. SFA: saturated fatty acid;

MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid.

Table S3. Primary outcomes at the baseline and week 12 (PP Set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	P_{ANOVA}	P_{time}	P_{group}	$P_{interaction}$
FBG (mmol/L)						< 0.001	0.586	0.016
Baseline	4.96 ± 1.26	5.00 ± 0.96	4.87 ± 0.85	5.17 ± 0.95	0.509			
Week 12	4.71 ± 1.05	4.46 ± 0.83$^{\#\#}$	4.37 ± 0.58$^{\#\#}$	4.30 ± 0.48$^{\#\#}$	0.054			
Change	-0.26 ± 0.95	-0.53 ± 0.99	-0.49 ± 0.93	-0.87 ± 0.89**	0.016			
FINS (μIU/mL)								
Baseline	14.71 ± 5.75	11.68 ± 5.91	12.74 ± 7.78	13.95 ± 6.15	0.157	0.003	0.014	0.140
Week 12	14.07 ± 6.68	11.51 ± 5.49*	9.69 ± 4.26$^{**,\#}$	10.71 ± 5.58$^{**,\#\#}$	0.005			
Change	-0.64 ± 7.73	-0.17 ± 7.45	-3.05 ± 7.54	-3.24 ± 8.07	0.140			
HOMA-IR								
Baseline	3.14 ± 1.33	2.51 ± 1.47	2.67 ± 1.64	3.21 ± 1.54	0.103	< 0.001	0.011	0.021
Week 12	2.99 ± 1.55	2.35 ± 1.27*	1.90 ± 0.87$^{**,\#\#,\wedge\wedge}$	2.01 ± 1.14$^{**,\#\#,\wedge\wedge}$	< 0.001			
Change	-0.15 ± 1.75	-0.16 ± 1.80	-0.77 ± 1.58	-1.20 ± 1.95*	0.021			

Data are presented as means ± SD. Change = week 12 - baseline. HOMA-IR = FINS * FBG / 22.5. # $P < 0.05$ versus baseline. ## $P < 0.01$ versus baseline. * $P < 0.05$ versus control. ** $P < 0.01$ versus control. ^ $P < 0.05$ versus control in time × group ANOVA post hoc test. ^^ $P < 0.01$ versus control in time × group ANOVA post hoc test.

Table S4. Analysis of covariance for primary outcomes[§] (PP set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
FBG Change (mmol/L)					
Model 1[Φ]	-0.28 ± 0.10[a]	-0.53 ± 0.10[b]	-0.58 ± 0.09[b]	-0.76 ± 0.10[b]	0.007
Model 2[φ]	-0.30 ± 0.10[a]	-0.54 ± 0.10[a]	-0.58 ± 0.10[b]	-0.73 ± 0.10[b]	0.023
FINS Change (μIU/mL)					
Model 1[Φ]	0.62 ± 0.90[a]	-1.47 ± 0.83[b]	-3.46 ± 0.83[b]	-2.63 ± 0.81[b]	0.007
Model 2[φ]	0.53 ± 0.92[a]	-1.40 ± 0.84[a]	-3.65 ± 0.86[b]	-2.44 ± 0.82[b]	0.012
HOMA-IR Change					
Model 1[Φ]	0.07 ± 0.21[a]	-0.49 ± 0.20[b]	-0.96 ± 0.19[b]	-0.92 ± 0.18[b]	< 0.001
Model 2[φ]	0.03 ± 0.21[a]	-0.48 ± 0.20[b]	-0.98 ± 0.20[b]	-0.88 ± 0.18[b]	0.002

Data are presented as means ± SD. Change = week 12 - baseline. § Corrected model: corrected means ± SD. Same letter means no statistical difference between groups.

Φ: Adjusted baseline primary outcomes.

φ: Adjusted baseline primary outcomes, gender, age, BMI, physical activity, dietary energy, protein, carbohydrates, and total fat.

Table S5. Secondary outcomes at the baseline and week 12 (PP Set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	P_{ANOVA}	P_{time}	P_{group}	$P_{interaction}$
Lg(MASP1) (ng/mL)						0.006	0.226	0.764
Baseline	1.96 ± 0.85	2.34 ± 0.98	2.02 ± 1.07	2.21 ± 1.03	0.331			
Week 12	1.76 ± 0.68	2.03 ± 0.75	1.87 ± 0.93	1.80 ± 0.81$^{\#}$	0.496			
Change	-0.20 ± 1.09	-0.30 ± 1.13	-0.15 ± 1.29	-0.40 ± 1.15	0.764			
Lg(UA) (μmol/L)						0.159	0.019	0.903
Baseline	5.45 ± 0.42	5.56 ± 0.40	5.45 ± 0.52	5.68 ± 0.39	0.065			
Week 12	5.38 ± 0.47	5.47 ± 0.43	5.44 ± 0.47	5.57 ± 0.40	0.330			
Change	-0.06 ± 0.62	-0.10 ± 0.67	-0.02 ± 0.63	-0.11 ± 0.59	0.903			
Lg(UHR)						< 0.001	0.046	0.487
Baseline	5.16 ± 0.58	5.43 ± 0.64	5.15 ± 0.67	5.48 ± 0.68*	0.040			
Week 12	4.97 ± 0.63	5.15 ± 0.52$^{\#}$	5.09 ± 0.57	5.19 ± 0.59$^{\#}$	0.392			
Change	-0.19 ± 0.75	-0.28 ± 0.78	-0.06 ± 0.75	-0.28 ± 0.71	0.487			
Lg(ApoC-III) (mg/L)						0.126	0.846	0.527
Baseline	4.08 ± 0.27	3.99 ± 0.36	3.95 ± 0.41	3.98 ± 0.40	0.517			
Week 12	3.95 ± 0.34	3.93 ± 0.31	3.96 ± 0.36	3.95 ± 0.35	0.987			
Change	-0.12 ± 0.40	-0.05 ± 0.35	0.01 ± 0.44	0.03 ± 0.45	0.527			

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	P_{ANOVA}	P_{time}	P_{group}	$P_{interaction}$
Lg(LAP)						< 0.001	0.352	0.049
Baseline	3.17 ± 0.59	3.18 ± 0.67	3.22 ± 0.76	3.43 ± 0.84	0.247			
Week 12	3.17 ± 0.52	3.01 ± 0.62##	3.05 ± 0.64#	3.20 ± 0.75##	0.377			
Change	0.00 ± 0.35	-0.17 ± 0.38	-0.17 ± 0.46*	-0.23 ± 0.43**	0.049			
Lg(VAI)						< 0.001	0.927	0.020
Baseline	0.47 ± 0.68	0.54 ± 0.61	0.51 ± 0.68	0.70 ± 0.78	0.378			
Week 12	0.34 ± 0.60	0.27 ± 0.53##	0.29 ± 0.55##	0.24 ± 0.77##	0.873			
Change	-0.12 ± 0.49	-0.27 ± 0.53	-0.22 ± 0.48	-0.45 ± 0.60**	0.020			

Data are presented as means ± SD. Change = week 12 - baseline. UHR = UA / HDL-C; LAP (male) = (WC - 65) * TG; LAP (female) = (WC - 58) * TG; VAI (male) = WC / (39.68 + 1.88 *BMI) * TG / 1.03 * 1.31 / HDL-C; VAI (female) = WC / (36.58 + 1.89 * BMI) * TG / 0.81 * 1.52 / HDL-C. # $P < 0.05$ versus baseline. ## $P < 0.01$ versus baseline. * $P < 0.05$ versus control. ** $P < 0.01$ versus control. ^ $P < 0.05$ versus control in time × group ANOVA post hoc test. ^^ $P < 0.01$ versus control in time × group ANOVA post hoc test.

Table S6. Analysis of covariance for secondary outcomes[§] (PP set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
Lg(MASP1) Change (ng/mL)					
Model 1[Φ]	-0.34 ± 0.13	-0.12 ± 0.14	-0.24 ± 0.12	-0.33 ± 0.13	0.610
Model 2[φ]	-0.34 ± 0.13	-0.07 ± 0.14	-0.30 ± 0.12	-0.31 ± 0.13	0.491
Lg(UA) Change (μmol/L)					
Model 1[Φ]	-0.15 ± 0.07	-0.07 ± 0.08	-0.10 ± 0.07	0.03 ± 0.07	0.343
Model 2[φ]	-0.12 ± 0.07	-0.05 ± 0.08	-0.10 ± 0.07	0.00 ± 0.07	0.675
Lg(UHR) Change					
Model 1[Φ]	-0.28 ± 0.09	-0.17 ± 0.10	-0.16 ± 0.08	-0.14 ± 0.09	0.736
Model 2[φ]	-0.26 ± 0.09	-0.17 ± 0.10	-0.15 ± 0.09	-0.17 ± 0.10	0.836
Lg(ApoC-III) Change (mg/L)					
Model 1[Φ]	-0.07 ± 0.05	-0.06 ± 0.05	-0.02 ± 0.05	-0.04 ± 0.05	0.902
Model 2[φ]	-0.07 ± 0.05	-0.05 ± 0.05	-0.02 ± 0.05	-0.04 ± 0.05	0.904
Lg(LAP) Change					
Model 1[Φ]	-0.02 ± 0.05	-0.19 ± 0.05	-0.18 ± 0.05	-0.18 ± 0.05	0.082
Model 2[φ]	-0.01 ± 0.05	-0.19 ± 0.05	-0.19 ± 0.05	-0.17 ± 0.05	0.057
Lg(VAI) Change					
Model 1[Φ]	-0.16 ± 0.07	-0.28 ± 0.07	-0.24 ± 0.06	-0.40 ± 0.07	0.077

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
Model 2φ	-0.17 ± 0.07	-0.27 ± 0.07	-0.25 ± 0.06	-0.38 ± 0.07	0.183

Data are presented as means ± SD. Change = week 12 - baseline. § Corrected model: corrected means ± SD. Same letter means no statistical difference between groups.

Φ: Adjusted baseline secondary outcomes.

φ: Adjusted baseline secondary outcomes, gender, age, BMI, physical activity, dietary energy, protein, carbohydrates, and total fat.

Table S7. Compliance evaluation (PP Set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	P_{ANOVA}	P_{time}	P_{group}	$P_{interaction}$
EPA (%)						< 0.001	< 0.001	< 0.001
Baseline	0.90 ± 0.55	0.77 ± 0.48	0.91 ± 0.61	0.86 ± 0.58	0.581			
Week 12	0.78 ± 0.55	1.04 ± 0.63$^{\#\#}$	1.33 ± 0.77$^{**,\#\#,\wedge\wedge}$	1.60 ± 0.96$^{**,\#\#,\wedge\wedge}$	< 0.001			
Change	−0.11 ± 0.78	0.27 ± 0.70*	0.43 ± 0.90**	0.74 ± 0.97**	< 0.001			
DHA (%)						< 0.001	0.044	< 0.001
Baseline	3.89 ± 1.00	3.73 ± 1.02	4.07 ± 1.02	3.78 ± 0.97	0.317			
Week 12	3.88 ± 1.07	4.28 ± 1.17$^{\#\#}$	4.46 ± 1.35$^{*,\#,\wedge}$	4.88 ± 1.05$^{**,\#\#,\wedge}$	< 0.001			
Change	−0.01 ± 1.18	0.55 ± 1.23*	0.39 ± 1.30	1.11 ± 1.22**	< 0.001			

Data are presented as means ± SD. Change = week 12 - baseline. # $P < 0.05$ versus baseline. ## $P < 0.01$ versus baseline. * $P < 0.05$ versus control. ** $P < 0.01$ versus control. ^ $P < 0.05$ versus control in time × group ANOVA post hoc test. ^^ $P < 0.01$ versus control in time × group ANOVA post hoc test.

Table S8. Analysis of covariance for compliance evaluation[§] (PP set).

	Control (n=47)	FO1 (n=51)	FO2 (n=52)	FO3 (n=51)	*P*
EPA (%) Change					
Model 1[Φ]	-0.08 ± 0.11[a]	0.20 ± 0.10[b]	0.46 ± 0.10[b]	0.74 ± 0.10[c]	< 0.001
Model 2[φ]	-0.09 ± 0.11[a]	0.21 ± 0.10[b]	0.47 ± 0.10[b]	0.74 ± 0.10[c]	< 0.001
DHA (%) Change					
Model 1[Φ]	0.00 ± 0.16[a]	0.47 ± 0.16[b]	0.51 ± 0.15[b]	1.05 ± 0.16[c]	< 0.001
Model 2[φ]	-0.05 ± 0.16[a]	0.46 ± 0.16[b]	0.55 ± 0.15[b]	1.07 ± 0.16[c]	< 0.001

Data are presented as means ± SD. Change = week 12 - baseline. § Corrected model: corrected means ± SD. Same letter means no statistical difference between groups.

Φ: Adjusted baseline EPA or DHA.

φ: Adjusted baseline EPA or DHA, gender, age, BMI, physical activity, dietary energy, protein, carbohydrates, and total fat.

Table S9. Primary outcomes at the baseline and week 12 (Sensitivity analysis).

		Control (n=60)	FO1 (n=60)	FO2 (n=60)	FO3 (n=60)	P_{ANOVA}
FBG (mmol/L)						
Baseline	Linear Regression	5.13 ± 1.31	4.88 ± 1.05	4.91 ± 0.99	5.02 ± 0.99	0.573
	PMM	4.93 ± 1.14	4.97 ± 0.93	4.92 ± 0.85	5.10 ± 0.94	0.732
	MCMC	4.83 ± 1.35	5.12 ± 1.04	4.86 ± 0.91	5.26 ± 1.19	0.112
	P_M					0.926
Week 12	Linear Regression	4.63 ± 1.02$^{\#\#}$	4.42 ± 0.84$^{\#\#}$	4.37 ± 0.71$^{\#\#}$	4.31 ± 0.55$^{\#\#}$	0.131
	PMM	4.62 ± 0.95$^{\#\#}$	4.49 ± 0.78$^{\#\#}$	4.36 ± 0.57$^{\#\#}$	4.26 ± 0.49$^{**,\#\#}$	0.041
	MCMC	4.71 ± 1.07	4.51 ± 0.84$^{\#\#}$	4.32 ± 0.80$^{*,\#\#}$	4.32 ± 0.72$^{*,\#\#}$	0.039
	P_M					0.264
FINS (μIU/mL)						
Baseline	Linear Regression	13.86 ± 6.45	12.62 ± 6.47	13.07 ± 8.48	15.38 ± 9.00	0.219
	PMM	14.35 ± 5.53	11.64 ± 5.54	12.93 ± 7.22	13.36 ± 6.05	0.112
	MCMC	14.56 ± 7.34	12.88 ± 8.41	13.02 ± 8.79	13.91 ± 6.75	0.610
	P_M					0.611
Week 12	Linear Regression	13.97 ± 6.47	11.47 ± 5.52*	9.06 ± 5.60$^{**,\#\#}$	11.87 ± 6.54$^{\#}$	< 0.001
	PMM	13.21 ± 6.41	11.67 ± 5.61	9.29 ± 5.06$^{**,\#\#}$	10.80 ± 5.48$^{*,\#}$	0.002
	MCMC	14.93 ± 7.23	11.89 ± 5.56**	10.31 ± 6.07$^{**,\#}$	10.30 ± 5.99$^{**,\#\#}$	< 0.001
	P_M					0.180
HOMA-IR						
Baseline	Linear Regression	3.15 ± 1.66	2.69 ± 1.40	2.88 ± 2.04	3.35 ± 1.88	0.174

		Control (n=60)	FO1 (n=60)	FO2 (n=60)	FO3 (n=60)	P_{ANOVA}
Week 12	PMM	3.07 ± 1.21	2.59 ± 1.33	2.84 ± 1.66	3.00 ± 1.48	0.251
	MCMC	3.16 ± 1.96	3.00 ± 2.09	2.85 ± 2.18	3.23 ± 1.74	0.736
	P_M					0.453
	Linear Regression	2.95 ± 1.75	2.26 ± 1.14**	1.76 ± 1.13$^{**,\#\#}$	2.30 ± 1.42$^{*,\#\#}$	< 0.001
	PMM	2.76 ± 1.53	2.32 ± 1.15*	1.80 ± 1.01$^{**,\#\#}$	2.04 ± 1.11$^{**,\#\#}$	< 0.001
	MCMC	3.19 ± 1.88	2.38 ± 1.19$^{**,\#}$	2.00 ± 1.36$^{**,\#\#}$	1.99 ± 1.27$^{**,\#\#}$	< 0.001
	P_M					0.220

Data are presented as means ± SD. HOMA-IR = FINS * FBG / 22.5. # $P <$ 0.05 versus baseline. ## $P <$ 0.01 versus baseline. * $P <$ 0.05 versus control. ** $P <$ 0.01 versus control.

Table S10. Secondary outcomes at the baseline and week 12 (Sensitivity analysis).

		Control (n=60)	FO1 (n=60)	FO2 (n=60)	FO3 (n=60)	P_{ANOVA}
Lg(MASP1) (ng/mL)						
Baseline	Linear Regression	2.02 ± 0.81	2.33 ± 1.02	2.07 ± 1.00	2.13 ± 1.05	0.323
	PMM	2.20 ± 1.01	2.55 ± 1.06	2.21 ± 1.13	2.12 ± 1.07	0.194
	MCMC	2.12 ± 0.93	2.47 ± 1.00	2.06 ± 1.07	2.35 ± 1.15	0.163
	P_M					0.368
Week 12	Linear Regression	1.87 ± 0.72	1.94 ± 0.76$^{\#}$	1.97 ± 0.92	1.83 ± 0.85	0.771
	PMM	1.86 ± 0.83$^{\#}$	2.09 ± 0.84$^{\#}$	1.90 ± 0.97	1.84 ± 0.84	0.480
	MCMC	1.84 ± 0.68	2.20 ± 0.81	1.94 ± 0.94	2.00 ± 0.87$^{\#}$	0.185
	P_M					0.172
Lg(UA) (μmol/L)						
Baseline	Linear Regression	5.52 ± 0.41	5.58 ± 0.39	5.50 ± 0.51	5.66 ± 0.42	0.176
	PMM	5.47 ± 0.49	5.51 ± 0.43	5.42 ± 0.70	5.73 ± 0.42**	0.009
	MCMC	5.45 ± 0.56	5.33 ± 0.88	5.42 ± 0.76	5.51 ± 0.70	0.674
	P_M					0.071

		Control (n=60)	FO1 (n=60)	FO2 (n=60)	FO3 (n=60)	P_{ANOVA}
	Linear Regression	5.41 ± 0.47	5.50 ± 0.40	5.41 ± 0.49	5.52 ± 0.46	0.412
Week 12	PMM	5.29 ± 0.58	5.45 ± 0.58	5.48 ± 0.48	5.54 ± 0.44$^{\#}$	0.073
	MCMC	5.31 ± 0.65	5.29 ± 0.80	5.31 ± 0.81	5.50 ± 0.47	0.392
	P_M					0.144
Lg(UHR)						
	Linear Regression	5.23 ± 0.60	5.35 ± 0.60	5.21 ± 0.67	5.51 ± 0.69*	0.045
Baseline	PMM	5.26 ± 0.75	5.34 ± 0.70	5.11 ± 0.91	5.56 ± 0.74*	0.024
	MCMC	5.23 ± 0.83	5.19 ± 1.23	5.07 ± 0.87	5.32 ± 0.89	0.621
	P_M					0.192
	Linear Regression	5.06 ± 0.69	5.19 ± 0.57	5.07 ± 0.59	5.14 ± 0.70$^{\#\#}$	0.661
Week 12	PMM	4.96 ± 0.76$^{\#}$	5.14 ± 0.58	5.14 ± 0.59	5.15 ± 0.65$^{\#\#}$	0.335
	MCMC	4.90 ± 0.75$^{\#\#}$	4.96 ± 0.86	4.96 ± 0.85	5.15 ± 0.62	0.405
	P_M					0.352
Lg(ApoC-III) (mg/L)						
	Linear Regression	4.05 ± 0.30	3.98 ± 0.34	3.94 ± 0.38	3.98 ± 0.39	0.450
Baseline	PMM	4.02 ± 0.58	3.97 ± 0.40	3.95 ± 0.43	3.90 ± 0.49	0.630

		Control (n=60)	FO1 (n=60)	FO2 (n=60)	FO3 (n=60)	P_{ANOVA}
	MCMC	4.03 ± 0.33	4.04 ± 0.38	3.93 ± 0.59	3.92 ± 0.50	0.318
	P_M					0.949
	Linear Regression	4.00 ± 0.33	3.96 ± 0.32	3.97± 0.35	3.98 ± 0.35	0.950
Week 12	PMM	3.83 ± 0.43#	3.87 ± 0.47	3.95 ± 0.40	3.93 ± 0.43	0.421
	MCMC	3.87 ± 0.55#	3.95 ± 0.38	3.96 ± 0.44	3.94 ± 0.41	0.695
	P_M					0.092
Lg(LAP)						
	Linear Regression	3.19 ± 0.69	3.25 ± 0.65	3.23 ± 0.73	3.43 ± 0.80	0.273
Baseline	PMM	3.22 ± 0.65	3.25 ± 0.72	3.28 ± 0.75	3.48 ± 0.79	0.186
	MCMC	3.16 ± 0.82	3.16 ± 0.84	3.22 ± 0.78	3.44 ± 0.82	0.181
	P_M					0.122
	Linear Regression	3.11 ± 0.59	3.06 ± 0.61##	3.07 ± 0.63#	3.17 ± 0.71##	0.793
Week 12	PMM	3.25 ± 0.54	3.09 ± 0.65##	3.09 ± 0.67##	3.15 ± 0.81##	0.551
	MCMC	3.11 ± 0.57	3.03 ± 0.62	3.04 ± 0.67#	3.19 ± 0.76##	0.510
	P_M					0.549
Lg(VAI)						
Baseline	Linear Regression	0.47 ± 0.65	0.55 ± 0.61	0.53 ± 0.68	0.71 ± 0.75	0.251

		Control (n=60)	FO1 (n=60)	FO2 (n=60)	FO3 (n=60)	P_{ANOVA}
	PMM	0.55 ± 0.73	0.64 ± 0.78	0.58 ± 0.74	0.75 ± 0.83	0.524
	MCMC	0.51 ± 0.90	0.44 ± 0.72	0.49 ± 0.77	0.67 ± 0.78	0.447
	P_M					0.112
	Linear Regression	0.32 ± 0.58#	0.30 ± 0.58##	0.30 ± 0.61##	0.22 ± 0.72##	0.837
Week 12	PMM	0.44 ± 0.61	0.36 ± 0.58##	0.30 ± 0.55##	0.21 ± 0.83##	0.275
	MCMC	0.28 ± 0.63#	0.23 ± 0.60#	0.25 ± 0.67##	0.27 ± 0.77##	0.983
	P_M					0.779

Data are presented as means ± SD. UHR = UA / HDL-C ; LAP (male) = (WC - 65) * TG; LAP (female) = (WC - 58) * TG; VAI (male) = WC / (39.68 + 1.88 * BMI) * TG / 1.03 * 1.31 / HDL-C; VAI (female) = WC / (36.58 + 1.89 * BMI) * TG / 0.81 * 1.52 / HDL-C. # $P <$ 0.05 versus baseline. ## $P <$ 0.01 versus baseline. * $P <$ 0.05 versus control. ** $P <$ 0.01 versus control.

Table S11. Compliance evaluation(Sensitivity analysis).

		Control(n=60)	FO1(n=60)	FO2(n=60)	FO3(n=60)	P_{ANOVA}
EPA (%)						
Baseline	Linear Regression	0.83 ± 0.60	0.81 ± 0.56	0.88 ± 0.67	0.90 ± 0.60	0.867
	PMM	0.89 ± 0.55	0.75 ± 0.46	0.93 ± 0.60	0.89 ± 0.58	0.280
	MCMC	0.89 ± 0.65	0.81 ± 0.50	0.87 ± 0.63	0.89 ± 0.62	0.881
	P_M					0.926
Week 12	Linear Regression	0.72 ± 0.69	1.02 ± 0.64$^{*,\#}$	1.40 ± 0.89$^{**,\#\#}$	1.65 ± 1.01$^{**,\#\#}$	< 0.001
	PMM	0.79 ± 0.59	1.01 ± 0.62$^{\#\#}$	1.36 ± 0.78$^{**,\#\#}$	1.63 ± 0.96$^{**,\#\#}$	< 0.001
	MCMC	0.77 ± 0.70	0.89 ± 0.84	1.38 ± 0.77$^{**,\#\#}$	1.62 ± 1.00$^{**,\#\#}$	< 0.001
	P_M					0.836
DHA (%)						
Baseline	Linear Regression	3.87 ± 1.13	3.81 ± 1.15	3.97 ± 1.20	3.90 ± 1.14	0.887
	PMM	3.83 ± 0.91	3.70 ± 0.99	4.09 ± 1.03	3.88 ± 0.99	0.194
	MCMC	3.88 ± 1.14	3.81 ± 1.07	3.98 ± 1.08	3.75 ± 0.96	0.690
	P_M					0.264
Week 12	Linear Regression	3.67 ± 1.41	4.24 ± 1.22$^{*,\#}$	4.45 ± 1.48$^{**,\#}$	5.00 ± 1.16$^{**,\#\#}$	< 0.001
	PMM	3.82 ± 1.13	4.31 ± 1.14$^{*,\#\#}$	4.44 ± 1.29$^{**,\#}$	4.91 ± 1.03$^{**,\#\#}$	< 0.001

	Control(n=60)	FO1(n=60)	FO2(n=60)	FO3(n=60)	P_{ANOVA}
MCMC	3.83 ± 1.16	4.17 ± 1.31	4.46 ± 1.30**,##	4.87 ± 1.09**,##	< 0.001
P_M					0.584

Data are presented as means ± SD. # $P < 0.05$ versus baseline. ## $P < 0.01$ versus baseline.

* $P < 0.05$ versus control. ** $P < 0.01$ versus control.