

SUPPLEMENTARY MATERIAL

Table S1: Advanced lipoprotein profile characteristics at baseline by treatment allocation.

		<i>Units</i>	<i>Control group</i> <i>N=94</i>	<i>Intervention group</i> <i>N=103</i>	<i>P value</i>
Cholesterol					
	sdLDL	mmol/L	0.60 (0.53, 0.67)	0.60 (0.52, 0.68)	0.963
	sdLDL /LDL	%	16.5 (14.7,18.3)	18.3 (15.9,20.8)	0.229
	VLDL	mg/dL	31.9 (25.6, 38.2)	31.5 (25.3, 37.8)	0.932
	IDL	mg/dL	17.4 (15.1, 19.8)	15.4 (13.0, 17.8)	0.210
Triglycerides					
	VLDL	mg/dL	113 (91, 134)	112 (86, 138)	0.967
	IDL	mg/dL	16.8 (14.9, 18.8)	15.6 (13.7, 17.6)	0.380
	LDL	mg/dL	21.9 (19.4, 24.5)	20.0 (17.1, 22.9)	0.295
	HDL	mg/dL	25.9 (20.8, 31.1)	25.7 (21.9, 29.6)	0.950
Particle number					
	VLDL	nmol/L	89.4 (72.1, 106.8)	87.8 (68.3, 107.3)	0.894
	IVLDL	nmol/L	2.10 (1.75, 2.44)	2.16 (1.80, 2.52)	0.806
	mVLDL	nmolL	7.23 (5.65, 8.80)	7.64 (5.62, 9.66)	0.737
	sVLDL	nmolL	80.1 (64.2, 96.0)	78.0 (60.6, 95.3)	0.850
	IVLDL/VLDL	%	2.46 (2.28, 2.64)	2.60 (2.39, 2.80)	0.291
	mVLDL/VLDL	%	8.29 (7.28, 9.29)	8.64 (7.68, 9.60)	0.597
	sVLDL/VLDL	%	89.3 (88.3, 90.2)	88.8 (87.8, 89.7)	0.456
	LDL	nmolL	1490 (1350, 1630)	1356 (1244, 1468)	0.130
	ILDL	nmolL	178 (162, 194)	166 (149, 183)	0.303
	mLDL	nmolL	411 (348, 474)	359 (305, 412)	0.199
	sLDL	nmolL	901 (815, 987)	831 (770, 891)	0.178
	ILDL/LDL	%	12.1 (11.3, 12.9)	12.3 (11.4, 13.1)	0.763
	mLDL/LDL	%	27.2 (24.8, 29.5)	26.0 (23.7, 28.3)	0.449
	sLDL/LDL	%	60.7 (58.0, 63.5)	61.7 (58.9, 64.6)	0.588
	HDL	μmol/L	29.9 (26.9, 32.9)	29.6 (27.9, 31.2)	0.819
	IHDL	μmol/L	0.31 (0.28, 0.33)	0.28 (0.26, 0.30)	0.099
	mHDL	μmol/L	9.55 (8.63, 10.47)	8.89 (8.39, 9.40)	0.214
	sHDL	μmol/L	20.1 (17.9, 22.2)	20.4 (18.8, 21.9)	0.820
	IHDL/HDL	%	1.04 (0.97, 1.11)	0.96 (0.88, 1.05)	0.159
	mHDL/HDL	%	32.1 (30.5, 33.6)	30.4 (28.3, 32.4)	0.167
	sHDL/HDL	%	66.9 (65.3,68.5)	68.7 (66.5, 70.8)	0.162
	Non-HDL	nmolL	1550 (1411, 1688)	1414 (1300, 1527)	0.126
Particle size					
	VLDL	nm	41.8 (41.6, 41.9)	41.8 (41.7, 42.0)	0.310
	LDL	nm	20.8 (20.6, 20.9)	20.7 (20.6, 20.9)	0.747
	HDL	nm	8.25 (8.22, 8.28)	8.22 (8.18, 8.25)	0.153

Data are means (95% confidence interval). sdLDL (small dense LDL); LDL (Low Density Lipoprotein); VLDL (Very Low Density Lipoprotein); IDL (Intermediate Density Lipoprotein); HDL (High Density Lipoprotein); mVLDL (medium VLDL); sVLDL (small VLDL); ILDL (large LDL); mLDL (medium LDL); sLDL (small LDL); IHDL (large HDL); mHDL (medium HDL); sHDL (small HDL); Non-HDL (Non-HDL).

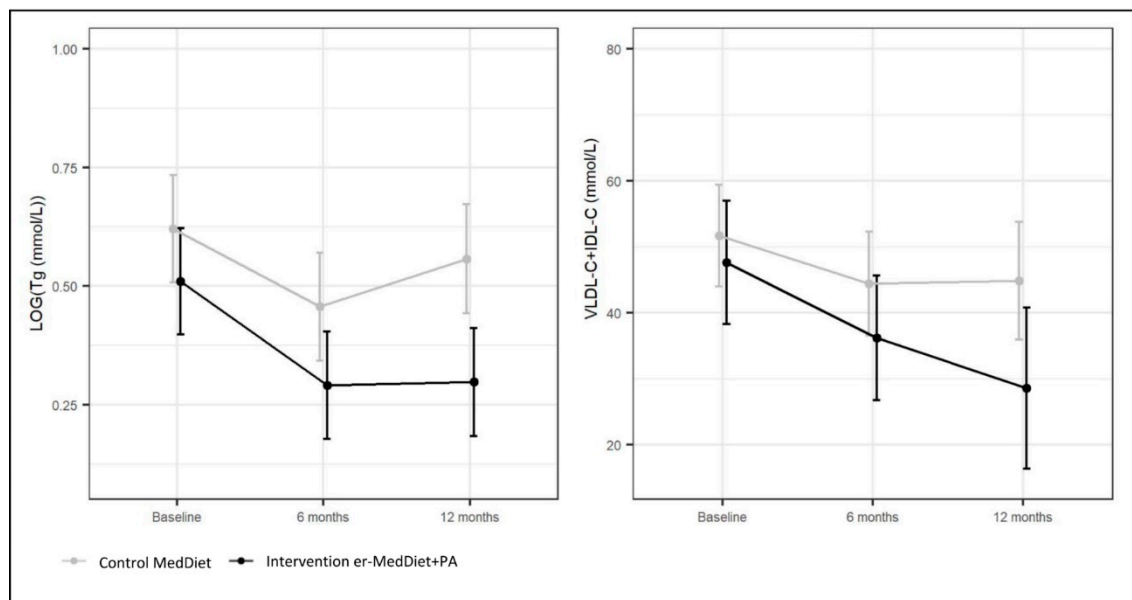


Figure S1: Effect of MetDiet and er-MetDiet+PA on Triglycerides and Remnant Lipoproteins at 6 and 12 months. LOG(Tg) (Log-transformed Triglycerides); VLDL-C (Very Low Density Lipoproteins Cholesterol); IDL-C (Intermediate Density Lipoproteins Cholesterol); MedDiet (Mediterranean Diet; er-MedDiet +PA (energy-reduced MedDiet and physical activity).

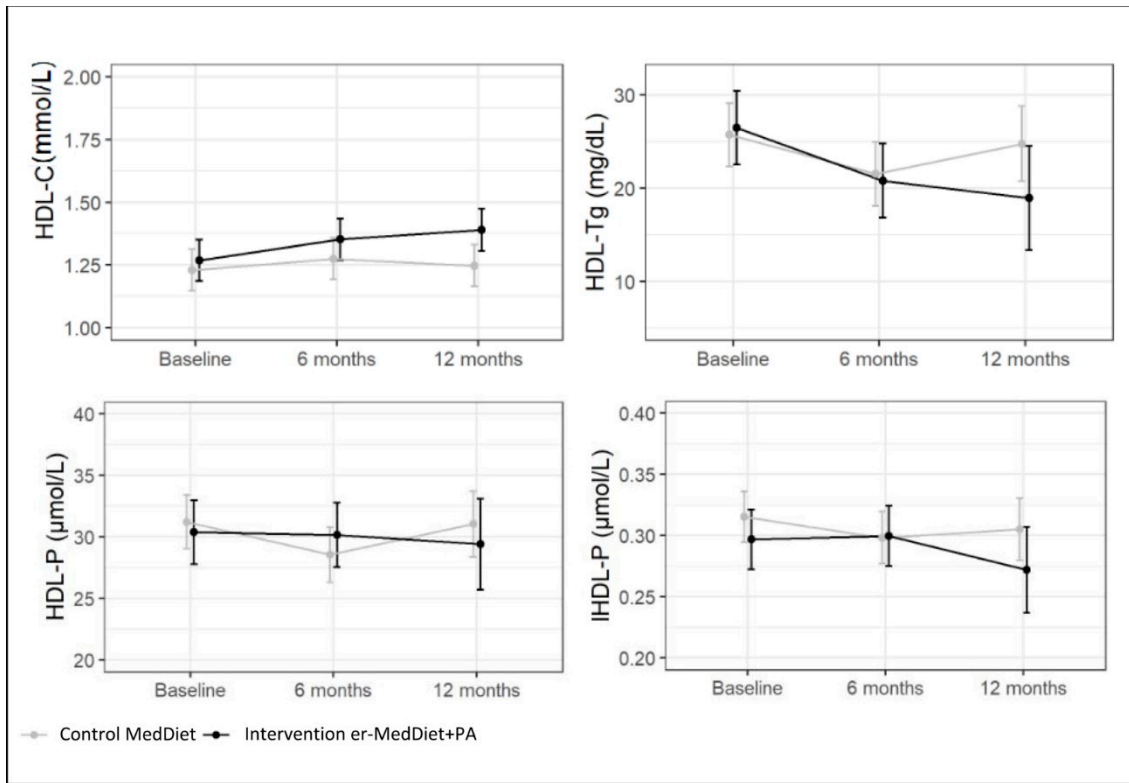


Figure S2: Effect of MetDiet and er-MetDiet+PA on HDL lipid composition and particle concentration at 6 and 12 months. HDL-C (High Density Lipoproteins Cholesterol); HDL-P (HDL Particle Number); HDL-Tg (HDL Triglycerides); IHDL-P (large HDL Particle Number); MedDiet (Mediterranean diet); er-MedDiet +PA (energy-reduced MedDiet and physical activity).

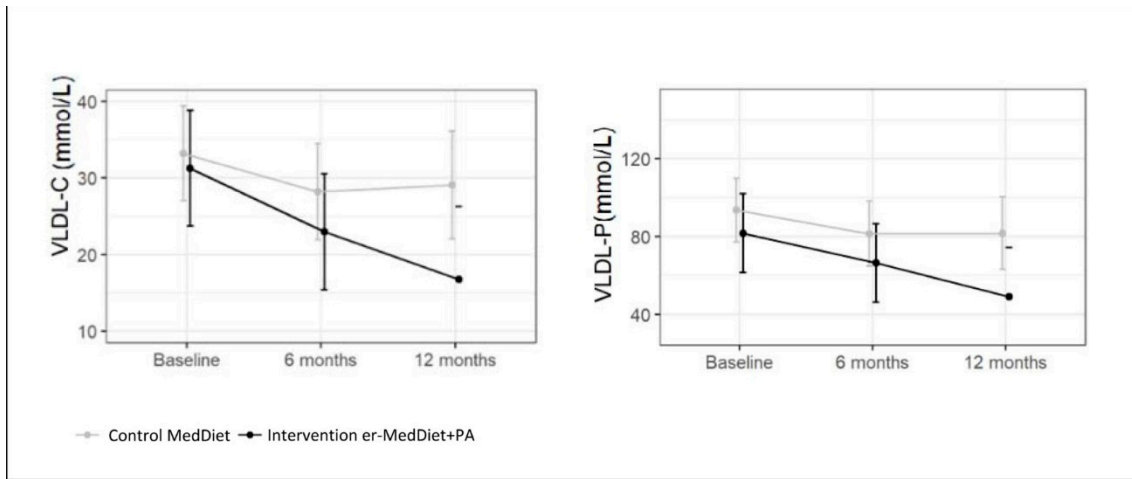


Figure S3: Effect of MetDiet and er-MetDiet+PA on VLDL advanced lipid profile results at 6 and 12 months. VLDL-C (Very Low Density Lipoproteins Cholesterol); VLDL-P (VLDL Particle Number); MedDiet (Mediterranean diet); er-MedDiet +PA (energy-reduced MedDiet and physical activity).

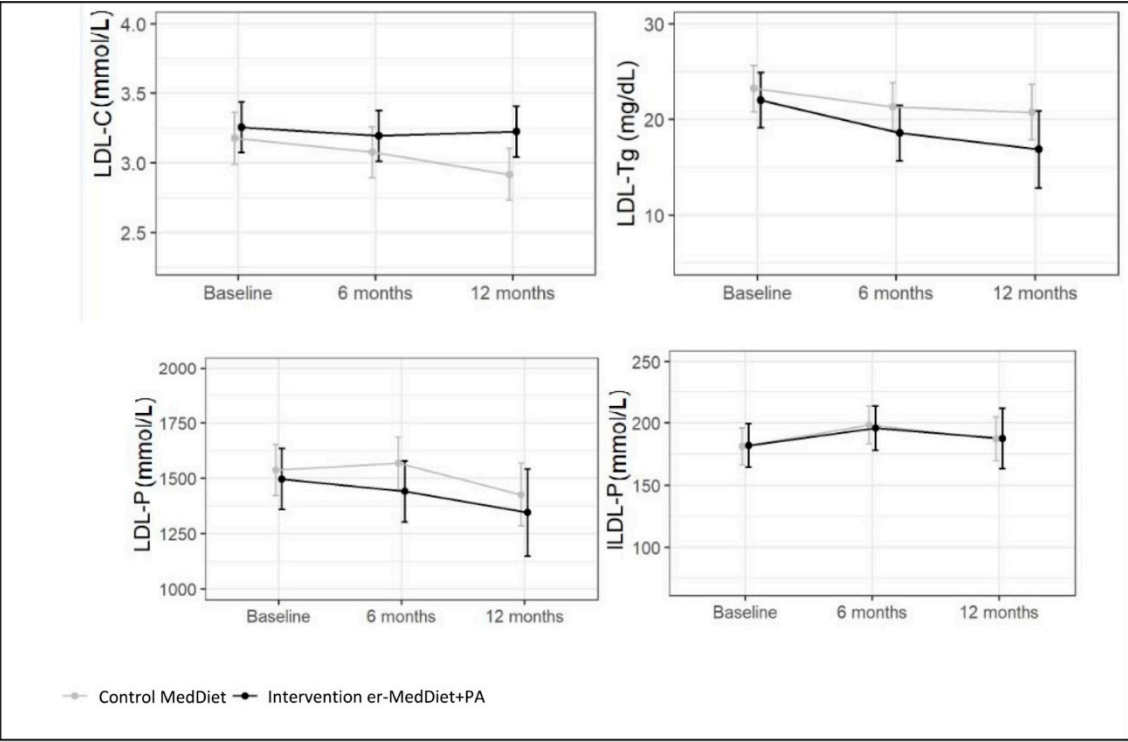


Figure S4: Effect of MetDiet and er-MetDiet+PA on LDL lipid composition and particle concentration at 6 and 12 months. LDL-C (Low Density Lipoproteins Cholesterol); LDL-P (LDL Particle Number); LDL-Tg (LDL Triglycerides); ILDL-P (large LDL Particle Number); MedDiet (Mediterranean diet); er-MetDiet +PA (energy-reduced MedDiet and physical activity).

Table S2: Effects of MedDiet and er-MedDiet+PA based intervention on lipid and anthropometric variables observed at 6 and 12 months in women.

	Time effect (Control effect*)				Interaction group and time (Intervention vs. Control effect**)			
	6 months		12 months		6 months		12 months	
	Coefficient [95%CI]	P value	Coefficient [95%CI]	P value	Coefficient [95%CI]	P value	Coefficient [95%CI]	P value
Body Mass Index (kg/m ²)	-0.53[-0.92;-0.15]	<0.01	-0.71[-1.1;-0.33]	<0.01	-1.62[-2.15;-1.08]	<0.01	-1.41[-1.95;-0.87]	<0.01
Waist circumference (cm)	-2.77[-4.42;-1.12]	<0.01	-2.01[-3.67;-0.36]	0.017	-1.81[-4.11;0.5]	0.125	-2.11[-4.43;0.21]	0.074
Cholesterol								
LDL (mmol/L)	-0.06[-0.29;0.18]	0.639	-0.28[-0.52;-0.05]	0.019	0.1[-0.22;0.43]	0.537	0.34[0.01;0.66]	0.045
sdLDL (mmol/L)	-0.11[-0.29;0.07]	0.242	-0.17[-0.36;0.03]	0.089	-0.17[-0.42;0.08]	0.192	-0.03[-0.3;0.24]	0.839
HDL (mmol/L)	0.05[-0.01;0.11]	0.078	0.01[-0.04;0.07]	0.65	-0.04[-0.12;0.04]	0.346	0.07[-0.01;0.15]	0.108
Non-HDL (mmol/L)	-0.12[-0.46;0.22]	0.494	-0.54[-0.9;-0.18]	<0.01	0.29[-0.18;0.77]	0.228	0.8[0.27;1.32]	<0.01
IDL (mg/dL)	-2.59[-7.82;2.65]	0.333	-3.74[-9.34;1.85]	0.189	0.47[-6.93;7.87]	0.901	-3.22[-11.79;5.35]	0.462
VLDL (mg/dL)	-6.86[-16.86;3.15]	0.179	-8.59[-19.27;2.08]	0.115	3.05[-11.07;17.18]	0.672	-8.86[-25.22;7.51]	0.289
VLDL+IDL (mg/dL)	-9.44[-23.16;4.28]	0.177	-12.34[-26.98;2.31]	0.099	3.52[-15.85;22.9]	0.722	-12.07[-34.52;10.37]	0.292
Triglycerides								
LOG(Tg (mmol/L))	-0.12[-0.24;0]	0.049	-0.06[-0.17;0.06]	0.357	0.01[-0.15;0.18]	0.875	-0.06[-0.22;0.11]	0.49
LDL (mg/dL)	-1.4[-7.03;4.23]	0.626	-3.25[-9.25;2.76]	0.289	-1.2[-9.15;6.74]	0.767	-4.25[-13.45;4.96]	0.366
HDL (mg/dL)	-7.36[-15.74;1.02]	0.085	-1.2[-10.17;7.76]	0.793	2.41[-9.43;14.25]	0.69	-7.27[-21.05;6.52]	0.301
IDL (mg/dL)	-2.03[-6.11;2.04]	0.329	-2.2[-6.56;2.15]	0.321	0.44[-5.32;6.19]	0.882	-4[-10.66;2.67]	0.24
VLDL (mg/dL)	-24.59[-56.15;6.96]	0.127	-27.26[-61.27;6.75]	0.116	25.38[-19.22;69.97]	0.265	-14.64[-67.44;38.16]	0.587
Particle number								
LDL (nmol/L)	-36.98[-327.12;253.16]	0.803	-247.26[-556.99;62.47]	0.118	45.04[-364.73;454.8]	0.829	37.41[-437.26;512.08]	0.877
LDL (μmol/L)	19.5[-13.81;52.8]	0.251	-5.54[-41.1;30.01]	0.76	-4.7[-51.73;42.34]	0.845	2.51[-51.98;57]	0.928
sLDL (nmol/L)	-65.28[-211.74;81.17]	0.382	-175.43[-334.41;-16.44]	0.031	74.91[-132.19;282.02]	0.478	78.19[-171.01;327.4]	0.539
HDL (μmol/L)	-5.65[-11.72;0.42]	0.068	0.02[-6.46;6.5]	0.995	4.17[-4.4;12.74]	0.34	-1.59[-11.52;8.34]	0.754
LDL (μmol/L)	-0.03[-0.08;0.02]	0.252	-0.01[-0.07;0.04]	0.616	0.02[-0.05;0.09]	0.535	-0.02[-0.1;0.06]	0.658
sHDL (μmol/L)	-3.98[-8.26;0.3]	0.068	0.25[-4.32;4.82]	0.915	2.46[-3.58;8.5]	0.425	-2.43[-9.43;4.57]	0.496
VLDL (nmol/L)	-21.53[-48.06;5]	0.112	-24.24[-52.8;4.32]	0.096	19.76[-17.73;57.25]	0.302	-13.84[-58.1;30.41]	0.54
LDL (nmol/L)	-0.31[-0.87;0.25]	0.272	-0.28[-0.88;0.32]	0.365	0.28[-0.5;1.07]	0.48	-0.49[-1.42;0.44]	0.302
sVLDL (nmol/L)	-20.74[-45.3;3.82]	0.098	-22.83[-49.31;3.65]	0.091	19.36[-15.35;54.08]	0.274	-11.89[-53;29.22]	0.571
Particle size								
VLDL (nm)	0.22[-0.06;0.5]	0.13	0.27[-0.04;0.58]	0.083	-0.18[-0.58;0.22]	0.376	0.16[-0.32;0.63]	0.518
LDL (nm)	0.18[-0.08;0.44]	0.164	0.3[0.02;0.58]	0.036	-0.11[-0.47;0.26]	0.565	-0.11[-0.55;0.32]	0.609
HDL (nm)	0.01[-0.03;0.04]	0.791	0[-0.05;0.04]	0.876	0.02[-0.03;0.08]	0.386	0.05[-0.01;0.12]	0.109

LDL (Low Density Lipoprotein); sdLDL (small dense LDL); HDL (High Density Lipoprotein); Non-HDL (Non-High-Density Lipoprotein); IDL (Intermediate Density Lipoprotein); VLDL (Very Low-Density Lipoprotein); VLDL+IDL (Remnant Lipoproteins); Tg (Triglycerides); LDL (large LDL); sLDL (small LDL); LDL (large HDL); sHDL (small HDL); VLDL (large VLDL); sVLDL (small VLDL); [IC95%] (95% confidence interval). Significant values are indicated with bold lettering. Data were analyzed by linear mixed models with intervention group, time (baseline, 6 and 12 months), interaction of group and time, and adjusted by age, the administration of lipid-lowering treatments, and smoking status. * Time effect: can be interpreted as the effect observed in the Control group. ** Interaction group and time: can be interpreted as the additional effect of the intervention group compared to the control group.

Table S3: Effects of MedDiet and er-MedDiet+PA based intervention on lipid and anthropometric variables observed at 6 and 12 months in men.

	Time effect (Control effect*)				Interaction group and time (Intervention vs. Control effect**)			
	6 months		12 months		6 months		12 months	
	Coefficient [95%CI]	P value	Coefficient [95%CI]	P value	Coefficient [95%CI]	P value	Coefficient [95%CI]	P value
Body Mass Index (kg/m ²)	-0.63[-0.98;-0.27]	<0.01	-0.52[-0.88;-0.16]	<0.01	-1.3[-1.8;-0.8]	<0.01	-1.43[-1.94;-0.92]	<0.01
Waist circumference (cm)	-1.2[-2.48;0.08]	0.067	-2.43[-3.75;-1.11]	<0.01	-4.02[-5.83;-2.21]	<0.01	-2.18[-4.02;-0.33]	0.021
Cholesterol								
LDL (mmol/L)	-0.14[-0.36;0.07]	0.186	-0.24[-0.46;-0.01]	0.037	-0.03[-0.33;0.27]	0.838	0.12[-0.18;0.42]	0.447
sdLDL (mmol/L)	-0.1[-0.26;0.06]	0.23	-0.09[-0.27;0.08]	0.305	-0.25[-0.47;-0.02]	0.03	-0.27[-0.52;-0.02]	0.031
HDL (mmol/L)	0.04[-0.03;0.1]	0.246	0.02[-0.05;0.09]	0.537	0.11[0.02;0.2]	0.019	0.14[0.04;0.23]	<0.01
Non-HDL (mmol/L)	-0.08[-0.39;0.23]	0.597	-0.21[-0.56;0.13]	0.229	-0.14[-0.58;0.3]	0.531	0.32[-0.19;0.83]	0.22
IDL (mg/dL)	-2.04[-4.27;0.2]	0.074	-1.97[-4.61;0.67]	0.145	-1.79[-5.2;1.61]	0.302	-0.85[-5.49;3.8]	0.721
VLDL (mg/dL)	-4.03[-10.65;2.6]	0.234	-1.65[-9.5;6.19]	0.679	-7.3[-17.42;2.82]	0.158	-13.18[-27.02;0.66]	0.062
VLDL+IDL (mg/dL)	-6.06[-14.47;2.34]	0.157	-3.64[-13.59;6.31]	0.474	-9.16[-22;3.67]	0.162	-14.02[-31.55;3.51]	0.117
Triglycerides								
LOG(Tg (mmol/L))	-0.21[-0.34;-0.08]	<0.01	-0.07[-0.21;0.07]	0.321	-0.12[-0.31;0.06]	0.198	-0.24[-0.43;-0.05]	0.014
LDL (mg/dL)	-1.99[-4.95;0.97]	0.187	-1.87[-5.35;1.6]	0.291	-2.18[-6.68;2.31]	0.34	-1.92[-8;4.17]	0.537
HDL (mg/dL)	-2.26[-6.57;2.04]	0.302	-0.66[-5.58;4.26]	0.792	-3.77[-10.15;2.62]	0.247	-6.02[-14.46;2.43]	0.163
IDL (mg/dL)	-1.61[-3.48;0.25]	0.09	-1.39[-3.6;0.81]	0.216	-1.55[-4.4;1.29]	0.284	-0.98[-4.87;2.9]	0.62
VLDL (mg/dL)	-9.05[-36.42;18.33]	0.517	-6.95[-39.29;25.38]	0.673	-35.85[-77.58;5.87]	0.092	-66.91[-123.79;-10.02]	0.021
Particle number								
LDL (nmol/L)	70.12[-89.84;230.08]	0.39	-39.2[-226.51;148.11]	0.682	-171.03[-413.41;71.34]	0.167	-86.08[-413.05;240.9]	0.606
lLDL (μmol/L)	17.25[-0.35;34.85]	0.055	11.03[-9.76;31.83]	0.298	-2.65[-29.48;24.18]	0.847	2.05[-34.53;38.63]	0.913
sLDL (nmol/L)	50.44[-67.52;168.4]	0.402	-24.94[-160.4;110.52]	0.718	-160.8[-337.92;16.32]	0.075	-104.49[-337.11;128.13]	0.379
HDL (μmol/L)	-1.43[-3.8;0.94]	0.236	-0.32[-3.1;2.45]	0.819	1.64[-1.95;5.23]	0.372	0.18[-4.68;5.05]	0.941
lHDL (μmol/L)	-0.01[-0.04;0.02]	0.47	-0.01[-0.05;0.03]	0.597	0.02[-0.03;0.07]	0.428	-0.02[-0.08;0.05]	0.608
sHDL (μmol/L)	-0.8[-2.98;1.38]	0.471	0.14[-2.43;2.71]	0.914	0.36[-2.96;3.68]	0.83	0.25[-4.27;4.76]	0.914
VLDL (nmol/L)	-7.28[-25.01;10.46]	0.421	-4.76[-25.77;16.25]	0.657	-17.39[-45.21;10.44]	0.221	-28.53[-67.24;10.18]	0.149
lVLDL (nmol/L)	-0.07[-0.43;0.29]	0.706	0[-0.43;0.43]	0.99	-0.57[-1.12;-0.01]	0.046	-0.97[-1.73;-0.21]	0.013
sVLDL (nmol/L)	-5.76[-25.03;13.51]	0.558	-4.1[-26.87;18.67]	0.724	-7.66[-37.03;21.71]	0.609	-7.67[-47.73;32.38]	0.707
Particle size								
VLDL (nm)	-0.04[-0.22;0.14]	0.652	-0.01[-0.22;0.2]	0.926	0.18[-0.1;0.46]	0.212	0.27[-0.09;0.63]	0.143
LDL (nm)	0.01[-0.21;0.24]	0.901	0.05[-0.21;0.31]	0.72	0.24[-0.1;0.58]	0.171	0.15[-0.3;0.6]	0.517
HDL (nm)	0[-0.04;0.03]	0.822	-0.02[-0.06;0.02]	0.37	-0.01[-0.07;0.05]	0.641	0.02[-0.06;0.1]	0.586

LDL (Low Density Lipoprotein); sdLDL (small dense LDL); HDL (High Density Lipoprotein); Non-HDL (Non-High-Density Lipoprotein); IDL (Intermediate Density Lipoprotein); VLDL (Very Low-Density Lipoprotein); VLDL+IDL (Remnant Lipoproteins); Tg (Triglycerides); lLDL (large LDL); sLDL (small LDL); lHDL (large HDL); sHDL (small HDL); lVLDL (large VLDL); sVLDL (small VLDL); [IC95%] (95% confidence interval). Significant values are indicated with bold lettering. Data were analyzed by linear mixed models with intervention group, time (baseline, 6 and 12 months), interaction of group and time, and adjusted by age, the administration of lipid-lowering treatments, and smoking status. * Time effect: can be interpreted as the effect observed in the Control group. ** Interaction group and time: can be interpreted as the additional effect of the intervention group compared to the control group.

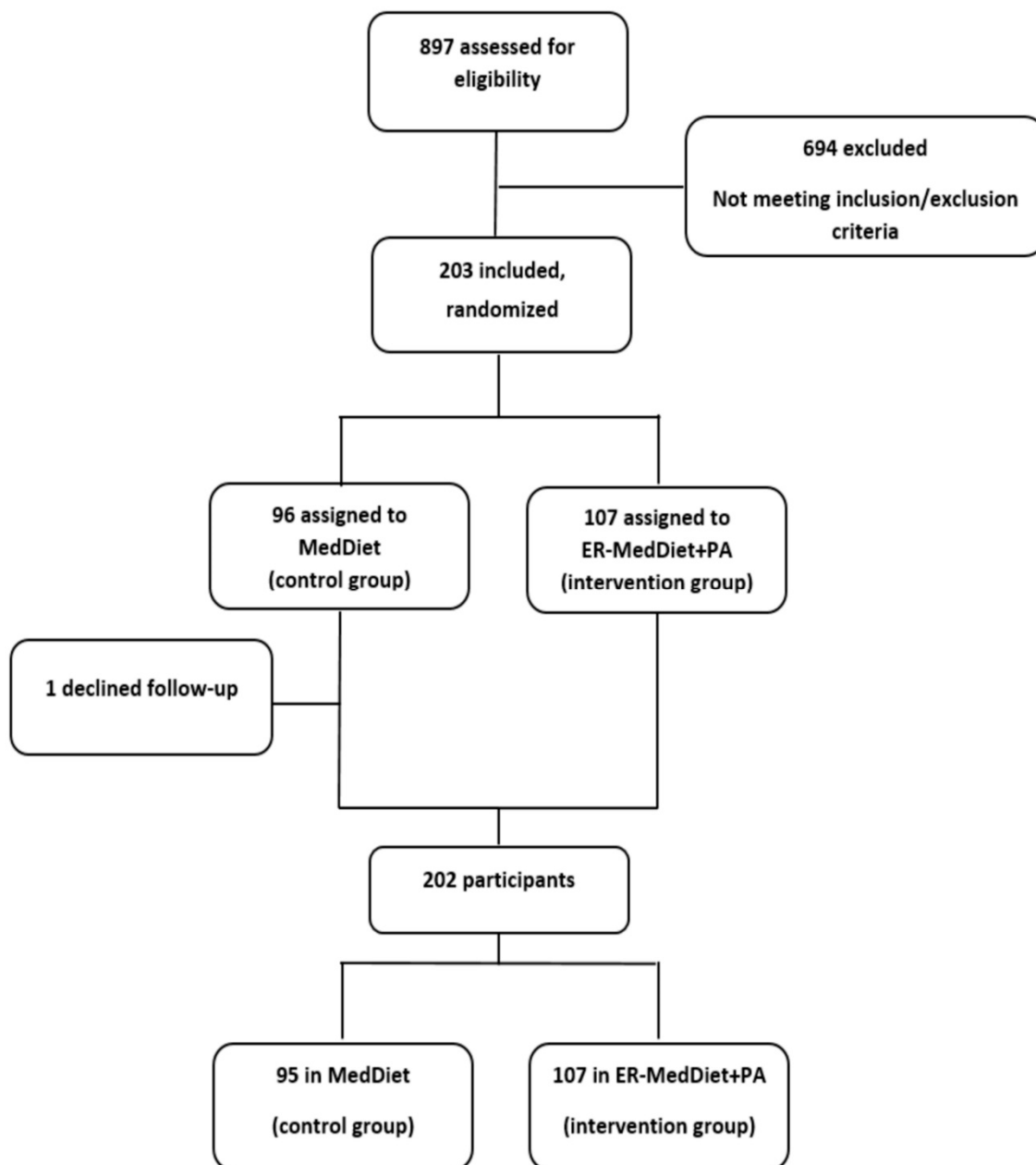


Figure S5: Trial flow chart.
MedDiet (Mediterranean diet); er-MedDiet +PA (energy-reduced MedDiet and physical activity).