

# Short-term trajectories of exercise-induced plasma lipid changes in overweight females, with a focus on HDL-cholesterol

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## Conflict of interest

None declared

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## Abstract

**Background.** Increased levels of plasma lipoproteins are among some of the modifiable risk factors for cardiovascular disease (CVD). Dietary changes and increased physical activity are the most powerful non-pharmacological interventions for achieving optimal plasma lipid levels.

**Objectives.** To investigate the effect of an intensive short-term lifestyle intervention on plasma lipid trajectories in overweight non-diabetic females.

**Materials and methods.** A total of 202 healthy overweight (body mass index (BMI) >27.5 kg/m<sup>2</sup>) females underwent an intensive short-term (ten-week) intervention (at least 4 units of one-hour exercise activity weekly at optimal energy intake) aimed at lowering body weight. Plasma lipid (total cholesterol (TC), low-density-lipoprotein cholesterol (LDL-C), high-density-lipoprotein cholesterol (HDL-C), and triglycerides (TG)) levels were examined at baseline and every 2 weeks over the course of the ten-week intervention.

**Results.** There was a significant decrease in BMI ( $\Delta$  –4.7%,  $p < 0.001$ ) and body weight ( $\Delta$  –4.9%,  $p < 0.001$ ) after the intervention. Positive changes (decreases) in TC ( $\Delta$  –8%,  $p < 0.001$ ), TG ( $\Delta$  –9%,  $p < 0.001$ ) and LDL-C ( $\Delta$  –11%,  $p < 0.001$ ) were observed immediately after 2 weeks, but levels did not decrease further thereafter. In contrast, HDL-C did not increase as expected: after 2 weeks of intervention, we observed a significant decrease of about 6% ( $p < 0.001$ ) followed by a slow return to baseline values. But even after 10 weeks of intervention, HDL-C values had not reached the values detected at baseline.

**Conclusions.** In overweight females, HDL-C decreased after short-term intensive lifestyle intervention. To confirm the protective effect of increased physical activity, plasma lipids need to be examined over a longer time period.

**Key words:** physical activity, overweight, HDL-cholesterol, short-term intervention

## Cite as

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## Background

Despite progress in diagnostics and treatment, cardiovascular diseases (CVD) are still the major cause of mortality and morbidity in developed countries.<sup>1</sup> The major CVD risk factors are age, male sex, genetic predisposition, smoking, obesity, hypertension, diabetes, and dyslipidemia.<sup>2</sup>

Plasma lipids – especially the build-up of plasma cholesterol – play an important role in atherosclerotic plaque development.<sup>3</sup> The current recommended values are <5.0 mmol/L for total cholesterol (TC), <3.0 mmol/L for low-density-lipoprotein cholesterol (LDL-C), and <1.7 mmol/L for triglycerides (TG); these values should be even lower in individuals at high risk for CVD. High-density-lipoprotein cholesterol (HDL-C) values should be >1.0 mmol/L in males and >1.2 mmol/L in females.<sup>4</sup>

Both genetic and environmental factors affect plasma lipid values.<sup>5–8</sup> Among the environmental risk factors that lead to dyslipidemia, obesity seems to be the most important. The energy imbalance resulting in increased body weight and body mass index (BMI) values is influenced not only by insufficient physical activity and excess energy intake, but also (in addition to unfavorable genetic backgrounds) by other less discussed factors, such as side effects of commonly prescribed drugs, non-exercise activity thermogenesis and air-conditioning.<sup>9,10</sup>

As one of the main factors associated with CVD, obesity correlates with plasma lipid levels. Obese individuals typically exhibit increased levels of plasma LDL-C and TG, and decreased levels of plasma HDL-C.<sup>11</sup>

Increased physical activity (any kind of exercise) is a common lifestyle intervention widely used in treating obesity. Such regimens can lead to positive changes in lipid profiles, reductions in plasma LDL-C and TG and increases in plasma HDL-C.<sup>12,13</sup> However, studies on short-term lipid trajectories during lifestyle interventions are scarce, limited by very low numbers of examined subjects (between 10 and 25) and focus almost exclusively on males.<sup>14–17</sup>

## Objectives

The aim of our study was to assess the impact of exercise on short-term trajectories (10 weeks) of plasma lipid fractions in a large sample of overweight adult females.

## Materials and methods

### Examined subjects

In total, 202 overweight (BMI at least 27.5 kg/m<sup>2</sup>) adult females within the age range of 19–71 years (with quintiles interface 34/43/50 and 58 years, respectively), recruited through an advertisement on a lifestyle website and a women's magazine, were enrolled in the study. Individuals with diabetes, endocrine/autoimmune disease or any chronic inflammatory or neoplastic disease were excluded from the study. Detailed characteristics of the subjects and a summary of the data are presented in Table 1.

Six examinations were performed: (i) before intervention (baseline); (ii) after every two-week period (4 examinations); (iii) after the 10<sup>th</sup> week of intervention.

The study protocol was approved by the ethics committees at the Institute for Clinical and Experimental Medicine (Prague, Czech Republic) and Thomayer Hospital (Prague, Czech Republic) in agreement with the Helsinki Declaration of 1975. All subjects provided voluntary informed consent to participate in the study.

### Anthropometrical parameters

Body weight was measured using an electronic weight scale (scaled to the nearest 0.1 kg). Height was measured with a stadiometer to the nearest 0.5 cm. Waist and hip circumferences were measured to an accuracy of 0.5 cm. The waist-to-hip ratio (WHR) and BMI were also calculated. To avoid potential inter-individual inaccuracies

Table 1. Characteristics of the subjects

Parameter	Time point							p-value*	p-value <sup>†</sup>
	baseline	week 2	week 4	week 6	week 8	week 10			
Age [years]	46.7 ± 11.4	n.a.	n.a.	n.a.	n.a.	n.a.	–	–	–
Body weight [kg]	89.9 ± 13.8	88.5 ± 13.6	87.5 ± 13.6	86.8 ± 13.2	86.3 ± 13.0	85.7 ± 13.0	0.0001	0.0001	0.0001
Waist [cm]	113.4 ± 11.6	111.9 ± 10.8	110.6 ± 10.6	109.6 ± 10.4	108.6 ± 9.9	107.7 ± 10.1	0.0001	0.0001	0.0001
Hip [cm]	102.4 ± 8.7	100.0 ± 10.9	98.5 ± 8.1	97.0 ± 8.4	95.9 ± 8.0	94.8 ± 10.7	0.0001	0.0001	0.0001
BMI [kg/m <sup>2</sup> ]	32.1 ± 4.4	31.6 ± 4.3	31.2 ± 4.3	31.0 ± 4.2	30.8 ± 4.1	30.6 ± 4.0	0.0001	0.0001	0.0001
TC [mmol/L]	5.3 ± 0.94	4.8 ± 0.94	4.9 ± 0.92	4.9 ± 0.91	4.9 ± 0.89	4.9 ± 0.89	0.0001	0.0001	0.0001
LDL-C [mmol/L]	3.23 ± 0.83	2.88 ± 0.84	2.94 ± 0.78	2.96 ± 0.78	2.98 ± 0.79	3.01 ± 0.80	0.0001	0.0001	0.0005
HDL-C [mmol/L]	1.46 ± 0.33	1.37 ± 0.30	1.38 ± 0.30	1.38 ± 0.30	1.40 ± 0.30	1.44 ± 0.31	0.0001	n.s.	n.s.
TG [mmol/L]	1.44 ± 0.71	1.31 ± 0.78	1.33 ± 0.67	1.27 ± 0.68	1.27 ± 0.55	1.32 ± 0.63	0.0001	0.0001	0.0001

Data are presented as mean ± standard deviation (SD); p-values denote differences between baseline and week 2 (p-value\*) and between baseline and week 10 (p-value<sup>†</sup>); n.a. – not applicable; n.s. – not significant.

in measurements, 1 trained nurse performed all of the anthropometrical examinations.

## Intervention

The program was based on supervised ten-week lifestyle modification interventions.<sup>18–20</sup> Dietary intervention involved adjusting energy intake to the age-related optimum (max. 7500 kJ/day). Three times per week, the subjects participated in a sixty-minute-long supervised training session at a fitness center. Participants were advised to carry out 2 additional sessions per week (jogging, brisk walking or cycling), with at least 1 self-reported session performed per subject. All activities included aerobic exercise.

Participants were examined every 2 weeks. Subjects completed a one-day dietary report before each examination to assess compliance with the recommended dietary changes. Dietary recommendations were optimized after each control visit.

## Lipid parameters

Blood samples were collected after twelve-hour overnight fasting at the beginning, and after every 2 weeks, of intervention. The final samples were taken after 10 weeks of intervention. Serum from blood was obtained through separation by centrifugation at 3500 rpm (10 min) and stored at  $-80^{\circ}\text{C}$ . In all cases, aliquots of samples were analyzed on the same day as the entire experiment was completed. Concentrations of plasma TG and TC and LDL-C were analyzed using Roche Diagnostics kits (Basel, Switzerland; Ref. No. for kits: TG – 11730711, TC – 11491458, LDL-C – 27714423). The HDL-C level was determined after separation of apolipoprotein B-containing particles using a phosphotungstate-based method. The Hitachi 920 autoanalyzer (Hitachi, Tokyo, Japan) was used for all measurements. The laboratory was under the External Quality Assurance program of the Centers for Disease Prevention and Control (CDC; Atlanta, USA).

## Statistical analysis

Multivariate analysis of variance (MANOVA) was used for statistical analysis. Parameter changes were adjusted for age, smoking and BMI (for plasma lipids only) at baseline. The TG values were logarithmically transformed before analysis. Results are presented as a percentage decrease, with values given as mean  $\pm$  standard deviation (SD). A  $p$ -value  $< 0.05$  was considered significant.

## Results

The characteristics of the individuals in the study examined before and after each intervention period are summarized in Table 1. The mean BMI at baseline was

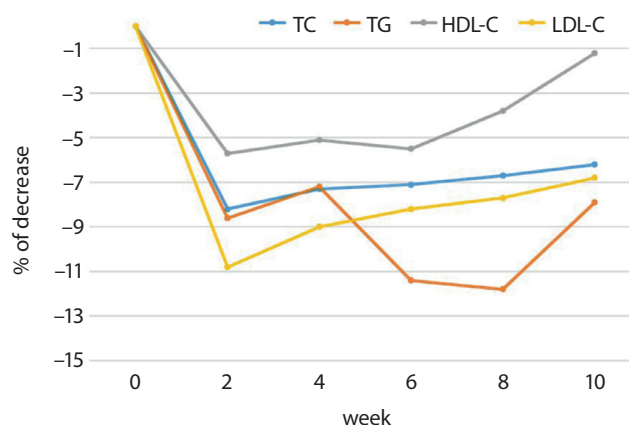


Fig. 1. Overview of short-term trajectories of plasma lipids over the ten-week intervention period

$32.3 \pm 4.3 \text{ kg/m}^2$  with a minimum of  $27.7 \text{ kg/m}^2$  and a maximum of  $50.6 \text{ kg/m}^2$ . Of the total participants, 30% were overweight while 43% had grade I obesity, 20% grade II obesity, and 7% grade III obesity.

As expected, there were significant continuous decreases in body weight ( $p < 0.0001$ ), BMI ( $p < 0.0001$ ) and waist ( $p < 0.0001$ ) and hip ( $p < 0.0001$ ) measurements after intervention (Table 1). Individual anthropometrical changes differed widely between baseline and final examinations. For example, the smallest decrease in body weight was only 0.2 kg ( $-0.3\%$ ), while the largest achieved was 15.0 kg ( $-11.3\%$ ). For mean values, all anthropometrical parameters examined revealed continuous decreases across all 5 measurements (Fig. 1).

Positive changes in anthropometrical parameters were accompanied by immediate and significant changes across all lipid parameters examined.

In the cases of both TC ( $p < 0.0001$ ) and LDL-C ( $p < 0.0001$ ), we observed a steep reduction in values (of about 8% for TC and as much as 11% for LDL-C) as early as after the first two-week intervention period (Table 1, Fig. 1). Values were relatively stable across the following measurements, with no further significant decreases observed. In fact, we observed a slight trend for a return to baseline values.

In the case of TG values, we observed a quick and highly significant ( $p < 0.0001$ ) decrease in plasma values as early as after the first 2 weeks of intervention (Table 1, Fig. 1). In contrast to plasma total- and LDL-C values, TG values did not reach the minimum after the first 2 weeks, and there was a trend (albeit nonlinear) toward a further slight lowering of values.

Finally, the most interesting results pertained to HDL-C. In contrast to other plasma lipids, where changes in expected positive directions were observed almost immediately after the start of the intervention (at the first examination), HDL-C values did not follow this trend. In contrast, there was a significant drop in plasma HDL-C of 5.7% ( $p < 0.0001$ ). For all subsequent measurements,

HDL-C values remained lower than those recorded at baseline. We did, however, note a slight increase beginning in week 8, with HDL-C almost reaching baseline levels after 10 weeks (but still 1.3% lower).

## Discussion

In this study, we found that a short-term intensive lifestyle modification regime involving an increase in physical activity and optimization of energy intake in metabolically healthy overweight females led to a rapid decrease (within 2 weeks) in all plasma lipid parameters, including HDL-C levels.

The results of our study highlight the different trajectories of plasma lipids when analyzed over short intensive periods of intervention. We observed rapid and dramatic changes in plasma TC, LDL-C and TG concentrations in desirable directions. However, subsequent weeks of increased physical activity did not result in further decreases in these values.

Unexpectedly, plasma HDL-C concentrations decreased in the same manner (albeit not as dramatically) as other plasma counterparts. Even after 10 weeks of intervention, no HDL-C increases, in comparison to baseline values, were detected.

Our findings are in contrast to similar studies on the topic. In a study examining the short-term (20 min of physical exercise for 4 days) effect of physical activity among males ( $n = 10$ ), Sabaka et al.<sup>16</sup> observed no effect on plasma HDL-C concentrations but a significant decrease in small dense HDL particles, with the effects disappearing after 2 days of rest. In a study using a similar protocol to ours (physical activity 3 times per week for 16 weeks), no effect on HDL-C was observed in patients with chronic kidney disease ( $n = 25$ , both males and females).<sup>17</sup> Similarly, the authors of another study involving 20 subjects (10 males and 10 females) with metabolic syndrome found that 3 months of moderately intensive exercise training (on cycle ergometers) did not lead to changes in HDL-C levels.<sup>15</sup> In their study of 14 young healthy men, Bounds et al.<sup>14</sup> reported a significant increase in HDL-C concentrations and a decrease in TG after only 2 weeks of aerobic exercise. Finally, the authors of the large interethnic HERITAGE study, which involved more than 600 adult males and females, documented a 3% increase in HDL-C with huge inter-individual variability in response to 20 weeks of supervised cycle ergometer exercise.<sup>21</sup> It is important to note that most of these studies were performed among males and recruited significantly lower numbers of participants (max. 25) in comparison to our study ( $n = 202$ ).

Our study is also in contrast with results from a meta-analysis performed by Dattilo and Kris-Etherton.<sup>22</sup> They suggest that HDL-C decreases are linearly associated with the amount of body weight lost. However, the trajectories we observed show that maximal HDL-C decrease is achieved very quickly – specifically, just after 2 weeks of intervention. At this time point, the mean body weight loss was only 1.5 kg.

Importantly, further body weight reduction was not accompanied by HDL-C decrease, but rather with slight return to baseline. Thus, there was no linear decrease in HDL-C concentrations in subjects that were actively losing weight.

Interestingly, it has been reported (in a review by März et al.<sup>23</sup>) that pharmacological treatment used to increase HDL-C concentrations is not accompanied by adequate reductions in cardiovascular outcomes. However, increasing HDL-C through lifestyle changes (not only increased physical activity, but also smoking cessation, for example) has positive effects on CVD outcomes.

Generally, it is recommended that physical activity be increased to improve plasma concentrations of HDL-C.<sup>12</sup> Our short-term study involving overweight, but otherwise healthy, female subjects shows that within about the first 2 months of starting exercise, plasma concentrations of HDL-C decreased in line with the same trajectories as other plasma lipids. Even after 10 weeks of intervention, plasma HDL-C values remained slightly below the baseline values found before the start of the intervention.

## Limitations


Besides the strengths of our study – namely it being the first study of its kind to focus exclusively on females, and involving a well-controlled intensive lifestyle intervention boasting of a large number of highly motivated subjects, as well as ethnic homogeneity – our study also had some limitations. Unfortunately, the protocol of our study did not allow us to detect the time point at which HDL-C levels may have achieved significant improvement (i.e., a significant increase). And as our study only involved relatively healthy females, short-term lipid trajectories may be different in males and in individuals suffering from metabolic disease.

## Conclusions


In conclusion, our short-term intervention involving physical activity and dietary intake optimization in overweight females led to reductions in HDL-C levels.

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