Running title: The associations of oxidized lipoprotein lipids with lipoprotein subclass particle concentrations and their lipid compositions.

The Cardiovascular Risk in Young Finns Study.

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Abbreviations: oxHDL lipids=oxidized HDL lipids, oxLDL lipids=oxidized LDL lipids, Apo-B=Apolipoprotein-B, Apo-A1=Apolipoprotein-A1, NMR=Nuclear magnetic resonance, CVD=cardiovascular disease, L=lipids, C=cholesterol, FC= Free cholesterol, CE=Cholesterol esters, PL=phospholipids, TG=triglycerides, HDL=high-density lipoprotein, LDL=low-density lipoprotein, IDL=intermediate-density lipoprotein, VLDL=very low-density lipoprotein.
**Abstract**

**Objective:** Oxidation of low-density lipoprotein (LDL) may promote atherosclerosis, whereas the reverse transport of oxidized lipids by high-density lipoprotein (HDL) may contribute to atheroprotection. To provide insights into the associations of lipoprotein lipid oxidation markers with lipoprotein subclasses at the population level, we investigated the associations of oxidized HDL lipids (oxHDL\textsubscript{lipids}) and oxidized LDL lipids (oxLDL\textsubscript{lipids}) with lipoprotein subclasses in a population-based cross-sectional study of 1395 Finnish adults ages 24-39 years.

**Methods:** The analysis of oxidized lipids was based on the determination of the baseline level of conjugated dienes in lipoprotein lipids. A high-throughput nuclear magnetic resonance (NMR) platform was used to quantify circulating lipoprotein subclass concentrations and analyze their lipid compositions.

**Results:** OxHDL\textsubscript{lipids} were mainly not associated with lipoprotein subclass lipid concentrations and lipid composition after adjustment for Apolipoprotein-A1 (Apo-A1), waist circumference and age. OxLDL\textsubscript{lipids} were associated with several markers of lipoprotein subclass lipid concentrations and composition after adjustment for Apolipoprotein-B (Apo-B), age and waist circumference. Several measures of HDL and LDL subclasses, including phospholipid and triglyceride composition, associated directly with oxLDL\textsubscript{lipids}. Cholesterol ester and free cholesterol composition in HDL and LDL associated inversely with oxLDL\textsubscript{lipids}.

**Conclusion:** We conclude that these results do not support the idea that HDL’s particle size or composition would reflect its functional capacity in the reverse transport of oxidized lipids. On the contrary, oxLDL\textsubscript{lipids} were associated with the entire lipoprotein subclass profile, including numerous associations with the compositional descriptors of the particles. This is in line with the suggested role of LDL oxidation in atherogenesis.

**Key words:** HDL, LDL, Oxidized lipids, Atherosclerosis
Introduction

Low high-density lipoprotein (HDL) cholesterol levels and high low-density lipoprotein (LDL) levels are risk factors for cardiovascular diseases (CVDs)\(^1\). The main possible atheroprotective functions of HDL are unclear. HDL has been suggested to play an important role in the reverse cholesterol transport\(^2\). In addition, it may have anti-inflammatory\(^3\), antioxidant\(^4,5\), and antidiabetic\(^6\) effects. According to the oxidation hypothesis of atherosclerosis, oxidized LDL plays an important role in the pathogenesis of atherosclerosis\(^7\). Oxidized LDL lipids (oxLDL\(_{lipids}\)) are associated with several risk factors for atherosclerosis, including hypertension\(^8\), waist circumference\(^9\) and impaired insulin sensitivity\(^10\) and oxLDL\(_{lipids}\) are also associated with coronary atherosclerosis\(^11\). The role of LDL is to transport oxidized lipids toward peripheral tissues. It has been hypothesized that the oxidized lipid transporting capacity of HDL is an independent protective factor for CVDs\(^12\). Moreover, it has been speculated that the ratio of oxidized HDL lipids (oxHDL\(_{lipids}\))/oxLDL\(_{lipids}\) could be a marker of HDL’s capacity to transport oxidized lipids\(^12\). However, it is controversial, whether oxidized HDL or LDL could be used as a risk factor for CVDs\(^12\). Therefore, there has been recently increased interest to understand the functional properties of HDL in attempt to develop new antiatherogenic therapies\(^13,14\).

Lipoproteins’ main function is to transport lipids in circulation. HDL is a heterogeneous particle with various subpopulations, which differ in density, shape, size, composition, surface lipid and apolipoprotein composition\(^15,16\). Phospholipids constitute the major lipid class of HDL accounting for 30 % of total HDL mass. Commonly is known that phospholipids cover the surface of HDL together with free cholesterol and apolipoproteins. Cholesteryl esters and triglycerides form the hydrophobic lipid core of HDL.\(^17\) However, cholesterol esters and triglycerides may also locate in the surface of lipoprotein particles\(^18\). The amount of these “core lipids” that locate in the surface of lipoproteins is higher in the smaller particles\(^18\). The clinical importance of HDL subpopulations is unclear, but distinct HDL subpopulations show different associations with the risk of CVD\(^15\). Evidence suggests that large, phospholipid-rich HDL particles promote reverse cholesterol transport\(^19\). It is moreover suggested that large HDL particles are atheroprotective, because increasing HDL particle size was associated with lower coronary artery disease risk\(^20\). However, after adjustment for markers
associated with metabolic syndrome, the significant association between HDL particle size and coronary artery disease was diluted. HDL particle profile may therefore play a role in the cardioprotective effects of HDL.

To investigate interrelationships between lipoprotein lipid oxidation markers and lipoprotein composition and size, we studied the associations of oxidized HDL and LDL lipids with lipoprotein subclasses measured by nuclear magnetic resonance (NMR) spectroscopy in the Cardiovascular Risk in Young Finns Study. The aim was to gain information of the role of compositional descriptors of lipoprotein particles in the putative reverse transport of oxidized lipids.
Methods

The Cardiovascular Risk in Young Finns Study is a multicenter follow-up study in five cities and their rural surroundings in Finland to evaluate atherosclerotic risk factors from childhood into adulthood. The study began in 1980 and a total of 2284 subjects aged 24-39 years participated in 2001 follow-up. Participants were randomly selected from the national register and they gave written informed consent. The study was approved by local ethics committees. Details of the study design have been presented earlier.

Venous blood samples were collected after fasting. The analysis of oxidized HDL and LDL lipids was based on the determination of the baseline level of conjugated dienes in lipoprotein lipids. The serum HDL fraction (oxHDL) was isolated with phosphotungstic acid precipitation and serum LDL fraction (oxLDL) with buffered heparin. Lipids were extracted from the isolated lipoproteins by chloroform-methanol (2:1), dried under nitrogen and redissolved in cyclohexane. The amount of oxidized lipids was assessed spectrophotometrically at 234 nm in the supernatant fraction to measure oxHDL, and in the precipitate fraction to measure oxLDL. The isolation procedures were validated for the purpose and did not affect the level of oxidized lipids.

Apolipoproteins A-1 (Apo-A1) and B (Apo-B) were analyzed immunoturbidometrically (Orion Diagnostica, Espoo, Finland). A high-throughput NMR platform was used to quantify serum HDL and LDL subclasses. NMR-based metabolic profiling has been used in various epidemiological studies. Details of the method have been presented earlier. Waist circumference was measured at the level of umbilicus to an accuracy of 0.1 cm.

Statistical analyses

The normality assumptions were evaluated by examining histograms and normal probability plots. Variables with skewed distributions were log-transformed. T-test was used to examine differences in main characteristics between sexes. Because of significant characteristic differences between sexes, subsequent analyses were done sex wise (Table 1). Statistical significance was inferred at a two-tailed P<0.05. Multivariable mixed models for oxHDL and NMR variables were adjusted for Apo-A1,
waist circumference and age, and models for oxLDL-lipids were adjusted for Apo-B, waist
circumference and age. Mixed models for oxHDL-lipids/oxLDL-lipids ratio were adjusted for Apo-
A1/Apo-B ratio, waist circumference and age. Covariates in the multivariable mixed models were
selected based on the earlier findings regarding the associations of oxidized lipoprotein lipids with
risk factors for atherosclerosis. Regression coefficients are reported in standardized units of 1-SD
difference in oxidized HDL or LDL lipoprotein lipids per 1-SD difference in outcome variable.
Statistical analyses were performed to subjects who had data on oxHDL-lipids measured in the 2001
follow-up. Subjects who were pregnant were excluded. A total of 1395 subjects of 2001 follow-up
were included in the final analyses. All statistical analyses were performed using Statistical Analysis
System (SAS, version 9.4). Multiple testing corrections were performed using the Bonferroni method,
with $P < 0.0004$ considered statistically significant.
Results

Main characteristics of the study subjects in 2001 are presented in Table 1. Women had higher levels of oxHDL-lipids, Apo-A1 and total lipids in all HDL particles except for small HDL particles than in men. Also in women, diameter for HDL was larger than in men. Accordingly, women had lower levels of oxLDL-lipids, total lipids in all Apo-B containing particles, and smaller VLDL and LDL mean diameters than men. The rest of NMR variable characteristics of the study subjects are presented in the Supplement Table 1.

To gain insights into the associations between lipoprotein oxidation and lipoprotein subclass particle and lipid concentrations and composition, we studied the associations of oxHDL-lipids and oxLDL-lipids and their ratio (oxHDL-lipids/oxLDL-lipids) with HDL, VLDL, IDL, and LDL subclass particle and lipid concentrations (Figure 1, Supplement Tables 2 and 3), and also with lipid composition of the lipoprotein subclasses (Figure 2, Supplement Tables 4 and 5). The unadjusted results are presented in the Supplemental materials (Figures 1 and 2, Supplement Tables 6, 7, 8 and 9).

The associations of oxHDL-lipids with lipoprotein subclass particle and lipid concentrations (Figure 1).

OxHDL-lipids were mainly not associated with lipoprotein subclass particle and lipid concentrations (Figure 1 and Supplement Tables 2 and 3).

The associations of oxLDL-lipids with lipoprotein subclass particle and lipid concentrations (Figure 1).

Associations with HDL. In both sexes, oxLDL-lipids were directly associated with concentration, total lipids, triglycerides, phospholipids and phospholipids/total cholesterol ratio in medium and small HDL particles (Figure 1 and Supplement Tables 2 and 3). Also in both sexes phospholipids in very large HDL particles associated inversely with oxLDL-lipids. There were additionally several inverse significant associations for oxLDL-lipids in men including mean HDL size, total lipids in very large HDL particles, free cholesterol in very large and large HDL particles, and also total HDL cholesterol.
Associations with Apo-B containing particles (VLDL, IDL and LDL). There was a clear tendency that concentrations of VLDL subclass particles; and total lipid, total cholesterol, free cholesterol, cholesterol esters, triglycerides, phospholipids and phospholipid/total cholesterol ratio concentrations were directly associated with oxLDL_lipids, except for small and very small VLDL particles. These associations were mainly similar in both sexes. Mean diameter for VLDL associated directly with oxLDL_lipids in both sexes. There was additionally a significant inverse association between oxLDL_lipids and mean diameter for HDL and LDL in men (Figure 1).

The associations of oxHDL_lipids/oxLDL_lipids ratio with lipoprotein subclass particle and lipid concentrations (Figure 1).

Associations with HDL. The trend was that concentrations of free cholesterol, cholesterol esters and phospholipids in very large and large HDL particles associated directly with oxHDL_lipids/oxLDL_lipids ratio (Figure 1 and Supplement Tables 2 and 3). On the contrary, free cholesterol, cholesterol esters and phospholipids in medium and small HDL particles associated inversely with oxHDL_lipids/oxLDL_lipids ratio. Only concentrations of triglycerides in all HDL particle subclasses associated inversely with oxHDL_lipids/oxLDL_lipids ratio. These results were similar in both sexes.

Associations with Apo-B containing particles. Concentrations of Apo-B containing particles were mostly inversely associated with oxHDL_lipids/oxLDL_lipids ratio in both sexes.

The associations of oxHDL_lipids with lipid composition of lipoprotein subclass particles (Figure 2).

Associations with HDL. In men, total cholesterol and cholesterol esters in very large HDL particles associated inversely with oxHDL_lipids, and phospholipids in very large HDL particles associated directly with oxHDL_lipids. In women, only free cholesterol in very large HDL particles had an inverse association with oxHDL_lipids.

Associations with Apo-B containing particles. Lipid composition in Apo-B containing particles was not significantly associated with oxHDL_lipids in men. In women, triglyceride composition in all LDL
particles associated directly, and total cholesterol in all LDL particles, free cholesterol in very small VLDL and IDL, and cholesterol esters in large LDL associated inversely with oxHDL-lipids.

The associations of oxLDL-lipids with lipid composition of lipoprotein subclass particles (Figure 2).

Associations with HDL. There was a trend for inverse association of oxLDL-lipids with total cholesterol, free cholesterol and cholesterol esters in HDL particle subclasses. Triglyceride and phospholipid composition in HDL particle subclasses were direct correlates of oxLDL-lipids. The associations were mostly similar between sexes.

Associations with Apo-B containing particles. There was a trend that oxLDL-lipids associated inversely with total cholesterol, free cholesterol and cholesterol esters; and directly with triglycerides in Apo-B containing particles. Phospholipid composition in VLDL subclasses associated inversely and in LDL subclasses directly with oxLDL-lipids. These results were mainly similar in both sexes.

The associations of oxHDL-lipids/oxLDL-lipids ratio with lipid composition of lipoprotein subclass particles (Figure 2).

Associations with HDL. There was a clear tendency in both sexes that total cholesterol and cholesterol ester compositions in HDL particle subclasses associated directly with oxHDL-lipids/oxLDL-lipids ratio and triglyceride composition associated inversely. In men, large HDL phospholipid composition associated inversely with oxHDL-lipids/oxLDL-lipids ratio and free cholesterol composition in large HDL particles associated directly with the oxidized lipid ratio.

Associations with Apo-B containing particles. The associations between oxHDL-lipids/oxLDL-lipids ratio and lipid composition of lipoprotein subclass particles were quite similar between sexes. Trend was that total cholesterol composition was a direct and triglyceride composition was an inverse correlate for oxidized lipid ratio.
Discussion

The possible atheroprotective functions of HDL and the speculative atheroprotective significance of different HDL subpopulations are unknown. We observed in this study that oxHDL-lipids are not associated with lipoprotein lipid subclass concentration and composition after adjustment for Apo-A1, age and waist circumference. It seems therefore that oxidized lipids in HDL are associated with HDL particle amount, but not with HDL subclass composition and concentration. Oxidized lipids in LDL particles are however associated with lipoprotein subclasses after adjustment for Apo-B, waist circumference and age.

HDL cholesterol is considered as an independent risk factor for CVD. However, therapies raising HDL cholesterol levels have not been beneficial in clinical trials. In addition, genetically determined high serum HDL cholesterol levels are not associated with reduced CVD risk. Therefore, the current view is that HDL cholesterol levels per se are not causally associated with CVDs. HDL is a heterogeneous particle varying in its density, shape, size, surface and apolipoprotein composition. It may have numerous atheroprotective functions. Interest has therefore shifted from HDL cholesterol concentration into the functional properties of HDL. The central hypothesis states that HDL is active in the reverse transport of atherogenic oxidized lipids, and this capacity is speculated as an important mechanism in atheroprotection. Moreover, it has been suggested that the level of oxHDL-lipids may be an indicator of HDL’s capacity to remove oxidized lipids from the body. Earlier findings indicate that large HDL particles are inversely associated with CVD risk. Therefore, we hypothesized that larger HDL particle size and lipid composition would be associated with higher oxHDL-lipid levels. However, we found no evidence for such relations in the present study. Thus, these data do not support the idea that HDL’s particle size would reflect its functional capacity in the reverse transport of oxidized lipids. This may also be partly explained by the fact that HDL cholesterol levels are not causally associated with reduced CVD risk. However, this study was cross-sectional and therefore these results should be taken with caution. A possible functional role for the HDL oxidation was suggested in an earlier intervention study that demonstrated that the intensity of physical exercise was associated with the accumulation of oxidized lipids in HDL.
Large HDL particles containing high amounts of lipids, particularly phospholipids, are shown to enhance scavenger receptor-B1 mediated free cholesterol flux from cells compared with small lipid-poor HDL particles. We observed in this study that in men phospholipid composition in very large HDL particles is associated with higher levels of oxHDL lipids. Higher phospholipid composition in HDL particle results in greater lipid surface area and may consequently explain the direct association between oxHDL lipids and phospholipid composition of HDL particle. It is possible that such HDL composition could promote the ability of HDL to transport oxidized lipids. In addition, large lipid-rich HDL particles are suggested to promote cholesterol efflux via adenosine triphosphate-binding cassette transporter G1. In line with this, we have earlier observed that higher HDL cholesterol levels are directly associated with higher levels of oxHDL lipids. We additionally found that triglycerides in medium HDL particles are associated with oxHDL lipids in women. In line with this, we have earlier detected a significant association between triglycerides and oxHDL lipids in women. There was additionally a strong direct association between oxLDL lipids and triglyceride composition in all lipoproteins. This may be explained due to the fact that triglycerides contain three fatty acids, which are vulnerable for oxidative modifications. In comparison, cholesterol esters contain only one fatty acid and phospholipids two fatty acids. We have previously shown that oxLDL lipids are indirectly associated with serum polyunsaturated fatty acids and directly with serum saturated fatty acids.

High LDL cholesterol is a well-known risk factor for CVDs and oxLDL lipids are shown to be associated with an increased risk for atherosclerosis. The trend for the associations of oxLDL lipids with the markers of lipoprotein subclasses were apparently different than the associations of oxHDL lipids with the same markers. The associations between oxLDL lipids and lipoprotein subclass variables were mostly significant and oxHDL lipids were not associated with LDL subclasses. The lack of associations between oxHDL lipids and characteristics of LDL particles suggests that there is no close interrelation between these two in vivo. In line with this, it has been shown that in vitro HDL do not protect LDL from oxidation. It seems, however, that oxLDL lipids are associated with lipoprotein particle size and composition. This finding may partly explain why oxLDL lipids are associated with an increased CVD risk. However, based on the present cross-sectional study, we are not able to discuss
about the potential role of oxLDL-lipids to act as a cardiovascular risk factor. We found additionally some differences, when results were compared between sexes. For example, men but not women show a consistent relationship between oxLDL-lipids and phospholipid concentrations in LDL and IDL subclass particles. It is difficult to explain these results, but it might be related to the fact that women have higher HDL cholesterol levels and lower LDL cholesterol levels than men \(^{12}\), which may be reflected to the associations between oxidized lipoprotein lipids and lipoprotein subclass particle concentrations.

We have earlier detected that higher levels of oxHDL-lipids are associated with higher levels of oxLDL-lipids \(^{12}\). One possible explanation for this observation is that oxHDL-lipids may be an indicator of HDL´s capacity to remove oxidized lipids from LDL particles \(^{12}\). This is in accordance with the oxidized lipid removing function of HDL. OxHDL-lipids/oxLDL-lipids ratio is moreover speculated to be a better marker of HDL´s capacity to transport oxidized lipids than oxHDL-lipids alone \(^{12}\). In the present study, oxHDL-lipids/oxLDL-lipids Ratio associated widely with lipoprotein subclass concentration and composition markers. It is highly likely that the associations between oxHDL-lipids/oxLDL-lipids ratio and lipoprotein subclasses are due to effect of oxLDL-lipids. The effect of oxHDL-lipids seems to be non-significant. These findings are in line with the suggestion that Apo-B plays a key role in the chain leading to atherosclerosis \(^{39}\).

**Limitations**

Lipoproteins are molecular complexes. Determination of oxidized lipoproteins is challenging due to the heterogeneous nature of the chemistry of HDL and LDL oxidation. Consequently, the results on lipid oxidation should be taken with caution. Important strength of the study is that the baseline diene conjugation method is validated in detail \(^{23}\). The conjugated diene measurement provides a general measure of fatty acid oxidation, but exclude analysis of oxysterols not isoprostanes, which may contribute e.g. to inflammation. In addition, some oxidized phospholipids may exert anti-inflammatory properties. Therefore, a global measure of conjugated dienes used here does not comprehensively report on the potential range of functions from oxidized lipids. However, since the present study, to our knowledge, is the first to investigate lipoprotein oxidation and lipoprotein...
particle concentrations/lipid compositions in a population-based study, a general measure of lipid oxidation was considered most adequate. With this method, oxidative modifications in all lipid classes, including phospholipids, are measured. This study was cross-sectional. Therefore, this data do not allow assessing the causality of the observed associations. However, complete lack of cross-sectional links between oxHDL\textsubscript{lipid} levels and HDL’s particle size and composition indicate that these parameters do not reflect HDL’s functional capacity in the reverse transport of oxidized lipids. The Young Finns Study participants are still relatively young. Therefore, we are at this point unable to examine what is the role of the measured lipid markers in predicting atherosclerotic events. However, in the future, it would be important to study the role of lipoprotein oxidation markers with the cardiovascular risk factors in the prospective setting.

**Conclusion**

Our results in the present study show that higher oxHDL\textsubscript{lipid} levels are not associated with lipoprotein subclass lipid concentration and composition. These findings do not support the idea that HDL’s particle size or composition would reflect its functional capacity in the reverse transport of oxidized lipids. Lipid oxidation in LDL particles is however associated with lipoprotein subclass lipid composition and concentration.

**Conflict of interest**

No conflict of interest was declared.

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References


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<td>Large HDL*</td>
<td>0.473</td>
<td>0.210</td>
<td>0.262</td>
<td>0.180</td>
</tr>
<tr>
<td>Medium HDL*</td>
<td>0.567</td>
<td>0.148</td>
<td>0.497</td>
<td>0.123</td>
</tr>
<tr>
<td>Small HDL</td>
<td>0.520</td>
<td>0.100</td>
<td>0.529</td>
<td>0.106</td>
</tr>
<tr>
<td>HDL*</td>
<td>1.775</td>
<td>0.415</td>
<td>1.439</td>
<td>0.341</td>
</tr>
<tr>
<td>HDL2*</td>
<td>1.256</td>
<td>0.383</td>
<td>0.929</td>
<td>0.319</td>
</tr>
<tr>
<td>Lipoprotein</td>
<td>Size (nm)</td>
<td>SD</td>
<td>Size (nm)</td>
<td>SD</td>
</tr>
<tr>
<td>------------</td>
<td>----------</td>
<td>-----</td>
<td>-----------</td>
<td>-----</td>
</tr>
<tr>
<td>HDL3*</td>
<td>0.519</td>
<td>0.045</td>
<td>0.510</td>
<td>0.043</td>
</tr>
<tr>
<td>VLDL*</td>
<td>35.926</td>
<td>1.139</td>
<td>35.791</td>
<td>1.455</td>
</tr>
<tr>
<td>LDL*</td>
<td>23.653</td>
<td>0.145</td>
<td>23.584</td>
<td>0.153</td>
</tr>
<tr>
<td>HDL*</td>
<td>10.048</td>
<td>0.235</td>
<td>10.798</td>
<td>0.235</td>
</tr>
</tbody>
</table>

*P<0.05 between sexes. SD=standard deviation, HDL=high-density lipoprotein, CM=chylomicron, VLDL=very low-density lipoprotein, IDL=intermediate-density lipoprotein, LDL=low-density lipoprotein, oxLDLlipids=oxidized LDL lipids, oxHDLlipids=oxidized HDL lipids, Apo-B=apolipoprotein-B, Apo-A1=apolipoprotein-A1.
Figure 1. The adjusted associations of oxidized lipoprotein lipids with lipoprotein subclass particle and lipid concentrations.

Abbreviations as in Table 1. N=766 in women and N=629 in men. L., lipids; C, cholesterol; FC, Free cholesterol. Linear regression models for oxHDL lipids were adjusted with Apo-A1, waist circumference and age and models for oxLDL lipids were adjusted for Apo-B, waist circumference and age. Multivariable models for oxHDL lipids / oxLDL lipids ratio were adjusted for Apo-A1/Apo-B ratio, waist circumference and age. Regression coefficients are reported in standardized units of 1-SD difference in oxidized HDL or LDL lipoprotein lipids per 1-SD difference in outcome variable.
Figure 1 (continued). The adjusted associations of oxidized lipoprotein lipids with lipoprotein subclass particle and lipid concentrations.

Abbreviations as in Table 1. N=766 in women and N=629 in men. CE, Cholesterol esters; PL, phospholipids; TG, triglycerides. Linear regression models for oxHDL<sub>lipids</sub> were adjusted with Apo-A1, waist circumference and age, and models for oxLDL<sub>lipids</sub> were adjusted for Apo-B, waist circumference and age. Multivariable models for oxHDL<sub>lipids</sub> / oxLDL<sub>lipids</sub> ratio were adjusted for Apo-A1/Apo-B ratio, waist circumference and age. Regression coefficients are reported in standardized units of 1-SD difference in oxidized HDL or LDL lipoprotein lipids per 1-SD difference in outcome variable.
Figure 2. The adjusted associations of oxidized lipoprotein lipids with lipid composition of lipoprotein subclass particles.

Abbreviations as in Table 1 and in Figures 1a and 1b. N=766 in women and N=629 in men. Linear regression models for oxHDL
lipids were adjusted with Apo-A1, waist circumference and age, and models for oxLDL
lipids were adjusted for Apo-B, waist circumference and age. Multivariable models for oxHDL
lipids / oxLDL
lipids ratio were adjusted for Apo-A1/Apo-B ratio, waist circumference and age. Regression coefficients are reported in standardized units of 1-SD difference in oxidized HDL or LDL lipoprotein lipids per 1-SD difference in outcome variable.