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Discordance of LDL-C with ApoB and the presence of cardiovascular disease

Context

This project aims to investigate the impact of different lipoprotein-related cardiovascular risk factors on cardiovascular disease. For example, the factors can be LDL-C, apoB, or nonHDL-C levels. LDL-C has been a major cardiovascular risk factor for decades. However, it might not fully capture cardiovascular risk. In this line, other lipid-related risk factors have been suggested to improve cardiovascular risk assessment beyond LDL-C.
For instance, it has been shown that the number of LDL particles, instead of their cholesterol cargo, can be a better predictor of cardiovascular disease. Moreover, LDL-C does not take into account other atherogenic lipoprotein classes such as VLDL. Because each atherogenic lipoprotein particle (VLDL, IDL, and LDL) transports one molecule of ApoB, apoB is a good indicator of the total number of atherogenic particles. In addition, VLDL-C has also been shown to be a causal marker of CVD. In this regard, nonHDL-C literally means Non-High-Density-Lipoprotein-Cholesterol. It is the cholesterol that is transported by all the lipoproteins that are not high-density lipoproteins, that is all the atherogenic lipoproteins from VLDLs to LDLs. Overall, what literature tells us is that if LDL-C levels are normal but either apoB or nonHDL-C levels are high, the risk of CVD events increases.

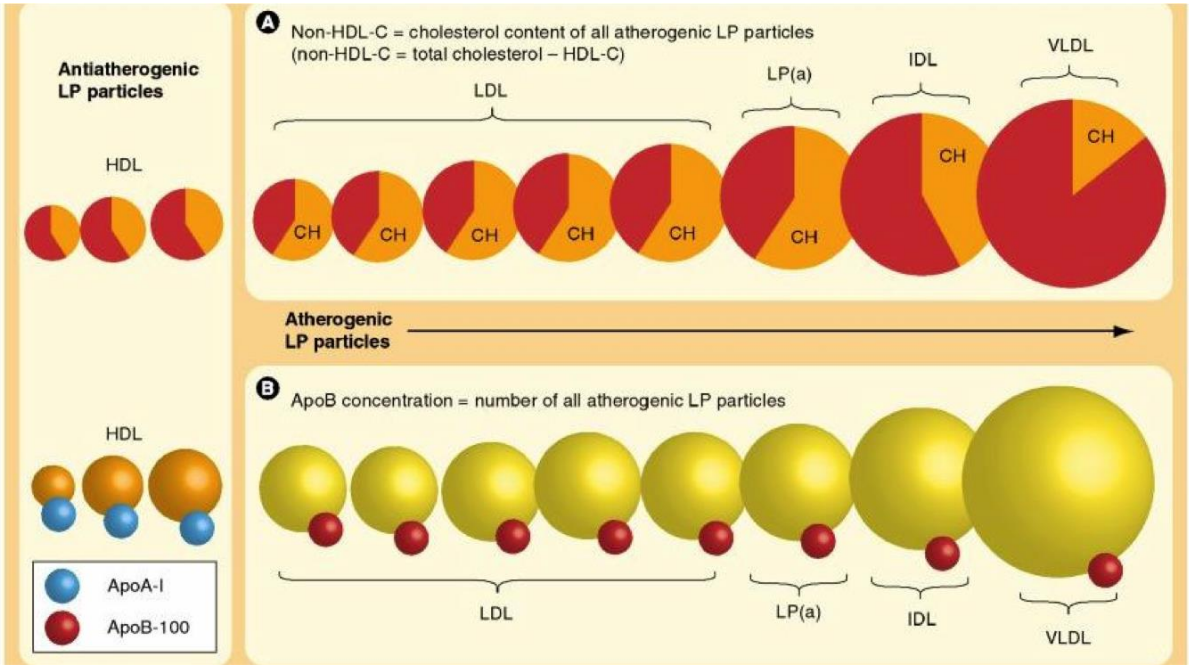

Figure 1 Representation of the different antiatherogenic and atherogenic LP particles

Aim of the project

The aim of the project is to assess the risk of cardiovascular diseases by studying the discordance in apoB and LDL-C levels. To do so, three questions were stated. The first one is to confirm or infirm what literature tells us, namely, we want to know if apoB and LDL-C are good indicators of CVD. The second one, also related to literature, is to confirm or infirm that apoB is a better CVD factor than LDL-C. Concerning the last question we want to see if there are other better markers of CVD.

To answer these questions, we studied a population sample of 4680 individuals from the CoLaus study. The main statistical analysis method we used was logistic regression:

- Linear regression is used to predict an outcome according to one or multiple variables. In our case, we want to predict an increase or decrease of CVD.
- Since we want to repressent this in probabilities, we need to use a function that, by default, ranges from 0 to 1.
- We implement our linear regression function in that function, and transformn it to obtain a linear relationship between the logarithm of the ods and the predictors

Results

ApoB and LDL-C:

We found no significant association between apoB levels and CVD events, which is not coherent with literature. Our trouble is with the correlation between apoB and LDL-C levels, which was not as high as observed in literature.

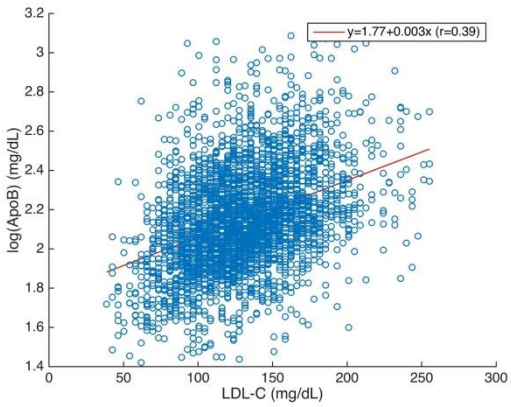

Figure 2: Correlation between LDL-C and apoB levels

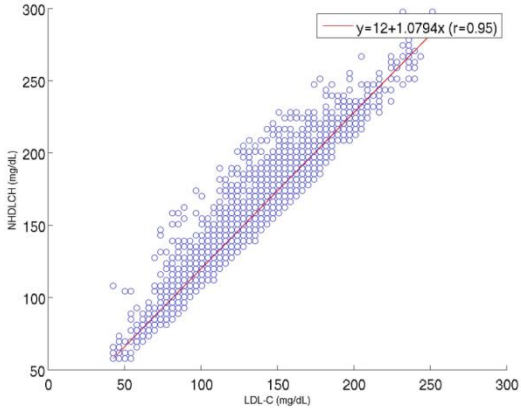

Figure 3: Correlation between LDL-C and NHDL-C levels

NHDL-C and LDL-C:

When studying the correlation between NHDL-C and LDL-C however, we found a much better relation. This allowed us to divide the population into discordant (high ldl-c with low nhdl-c or low ldl-c and high nhdl-c) and concordant (high ldl-c and nhdl-c or low ldl-c and nhdl-c) groups. At this point we encountered a problem in group sizes: the discordant groups had too little individuals to obtain conclusive results. This made us consider other possibilities of distributing our population.

An other method of creating discordant groups was also tested. To do so, we did a transformation of our data to percentage. Additionally, we checked for a proper interval defining the concordant group in order to get more fitting group sizes.

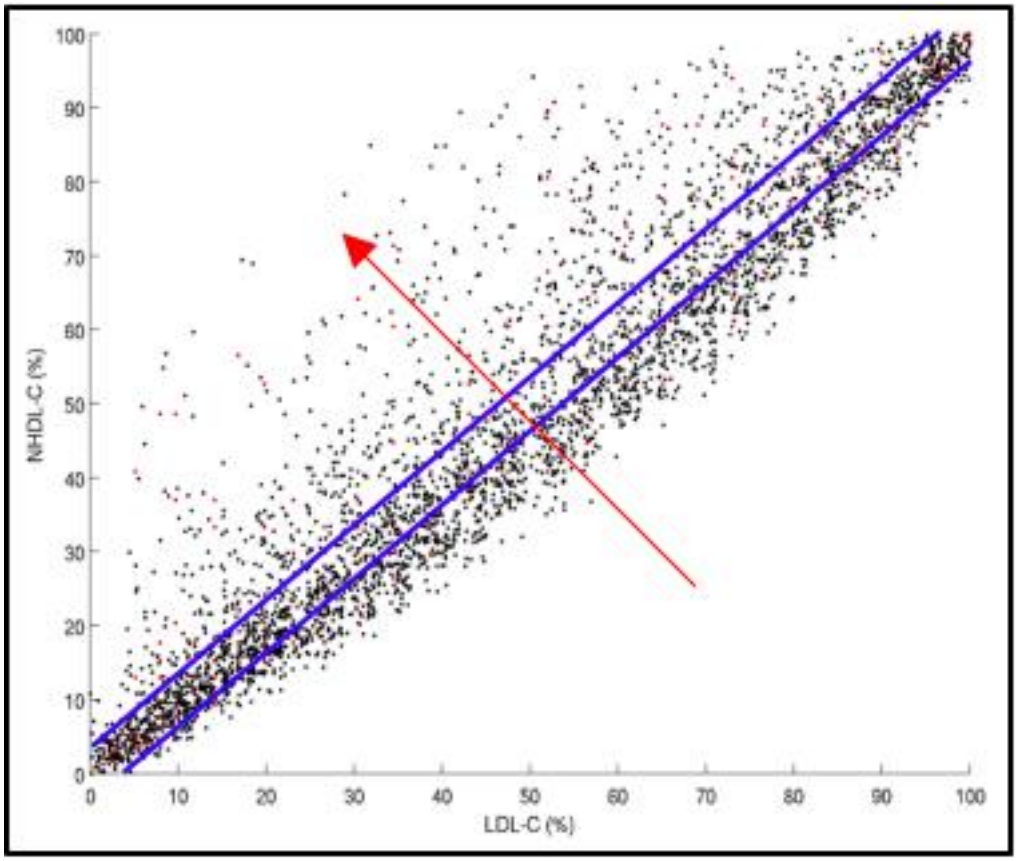

Figure 4 Correlation between LDL-C and nonHDL-C (percentile)

The principle is the following; we have one concordant group in the middle and 2 discordant groups on each side (Figure 2). The first discordant group is with high NHDL-C and low LDL-C and the second one is the contrary, low NHDL-C and high LDL-C. Moreover, on figure 2 we can observe a tendency in CVD events (represented with the red dots): We have more CVD events as we move from the second discordant group towards the first one (represented with the arrow). But this model is a bit shaky as we can obtain completely different results depending on the threshold we choose. So a more stable method is the discordance score.

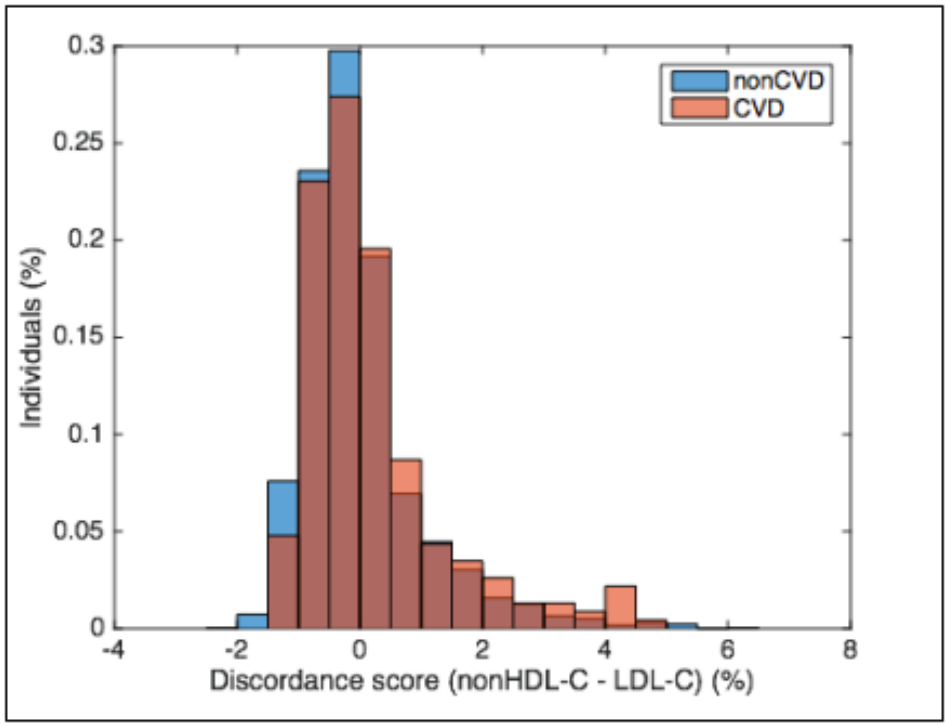

Figure 5 Histogram of th discordance score (nonHDL-C - LDL-C) in %

Figure 5 is a histogram of the discordance score, which is a percentile of NHDL-C - LDL-C. We can see that the individuals with CVD are more present on the right side of the histogram. This is where we have high nonHDL-C and low LDL-C. And the individuals with no CVD are more present on the left side, where we have low nonHDL-C and high LDL-C.

Table 1 is where we used the logistic regression to define an increase or a decrease in CVD events according to the discordant groups. We used the concordant group as a reference. On the one hand, we can see that the odds ratio is higher for the first discordance group (high nonHDL-C and low LDL-C), than the one of the reference. This means that we have a higher tendency for CVD in this group and by looking at the p-value, we can see that the difference is significant. On the other hand, the odds ratio of the second discordant group is decreasing compared to the reference and it is not significant.

Disc. groups	Odds Ratio	95% IC	p-value
D1	1.508	[1.19 ; 1.82]	0.012
C	1	-	-
D2	0.847	[0.51 ; 1.18]	0.33

Table 1 This table show the odds ratio, the 95% IC and the p-value for the discordant groups obtained after transformation of the data to percentage. D1 is with high nonHDL-C and low LDL-C and D2 represents the group of individuals with low nonHDL-C and high LDL-C.

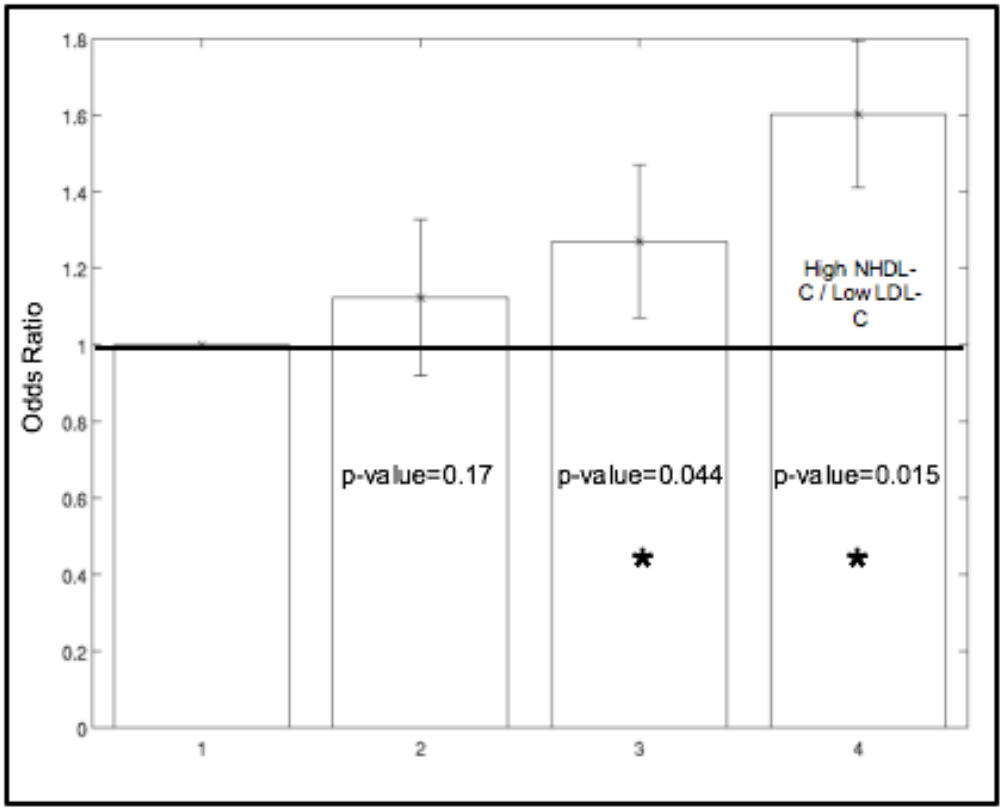

Figure 6 Discordance score (quartiles)

Concerning the figure 4, the boxes are beta coefficient of the discordance score, and the moustaches are the standard error of the beta-coefficient. The first box is our group of reference which is the one with low nonHDL-C and high LDL-C. In order to have a better view of the difference between the reference group and the other groups, we have this black line that is the level of the reference group. In this data analysis, we managed to get an increase in the odds ratio in each quartile according to the reference. Additionally, we can see that we have a significant difference for the third and the fourth group.

Conclusion

To answer the first and second question, we found no significant increase or decrease of CVD events associated with apoB and LDL-C levels. For the third one, concerning other markers for CVD, we found that discordance in NHDL-C and LDL-C levels show a significant increase in CVD events in the case of high NHDLC and low LDL-C levels.