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## Comparison of the effects of three healthy diets on the 112 lipoprotein subclass profiles using a nuclear magnetic resonance-based metabolomics approach

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Diet is a key modifiable factor for improving suboptimal lipoprotein profiles and reducing cardiovascular disease (CVD) risk<sup>(1)</sup>. Dietary patterns like the Dietary Approaches to Stop Hypertension (DASH) or the Mediterranean Diet, with varying macronutrient components, have shown positive effects on total cholesterol and low-density lipoproteins (LDL)<sup>(2)</sup>. However, limited research exists on the impact of different healthy diets on lipoprotein subclass profiles, which are increasingly known to influence CVD risk. This study aims to compare the nuclear magnetic resonance (NMR)-measured 112 lipoprotein profiles across three healthy dietary patterns: a carbohydrate-rich diet (CARB), similar to the DASH diet; a protein-rich diet (PROT); and an unsaturated fat-rich diet (USFA), similar to the Mediterranean diet. Lipoprotein parameters were generated using the Bruker IVDr Lipoprotein Subclass Analysis (B.I.LISA) method<sup>(3)</sup>. The lipoprotein subclasses included different molecular components of very low-density lipoprotein (VLDL, 0.950–1.006 kg/L), low-density lipoprotein (LDL, density 1.09–1.63 kg/L), intermediate-density lipoprotein (IDL, density 1.006–1.019 kg/L), and high-density lipoprotein (HDL, density 1.063–1.210 kg/L). The LDL subfraction was further divided into six density classes, and the HDL subfractions were divided into four different density classes. Plasma samples from a randomised cross-over intervention study involving 156 individuals who completed more than two dietary patterns were included for the NMR analysis (registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) as NCT00051350 and NCT03369535). The Friedman's test with post-hoc analysis, corrected for multiple testing, showed that all healthy dietary patterns led to a reduction in overall lipoprotein subclasses known to be associated with atherogenic risk. This reduction included large and medium-sized LDL subclasses, all intermediate-density IDL subclasses, as well as total plasma cholesterol, triglycerides, apolipoprotein-B100, apo-B100/apo-A1 ratio, and LDL-cholesterol ( $p < 0.05$ ). Additional variations in lipoprotein subclasses specific to each diet were also observed. The PROT diet showed a decrease in small-sized and dense LDL, large to medium VLDL subclasses, and large-sized HDL subclasses. Conversely, the CARB diet exhibited an increase in smaller-sized and denser LDL, along with a decrease in large-sized HDL and an increase in smaller-sized HDL subclasses. The USFA diet led to decreases in LDL and overall VLDL subclasses, while increasing LDL and HDL subclasses ( $p < 0.05$ ). The impact of different healthy diets with differential effects on lipoproteins suggests the possibility of targeting the cholesterol status of individuals to optimise lipoprotein profiles and thereby reduce CVD risk. Preliminary exploratory analyses based on linear mixed-effect models coupled with a latent profile analysis, adjusted for cholesterol status, showed that individual lipoprotein responses to specific diets varied. Inter-individual variations in lipoprotein responses to healthy diets were evident. A small proportion of individuals only responded to specific diets, suggesting potential of personalised nutrition based on individual lipoprotein profiles. These observed variations highlight the complexity of individual responses to dietary interventions.

### References

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