Women have a lower risk of cardiovascular disease (CVD) and coronary heart disease compared to age-matched men (~half the CVD risk and ~10-year delay in first myocardial infarction event).

Sex differences in serum lipids could contribute to this CVD risk through driving atherosclerosis, the build-up of lipids in the sub-endothelial intimal layer of medium-sized to large arteries.

These lipids include low, intermediate and very low-density lipoproteins (LDL, IDL and VLDL, typically atherogenic) and high density lipoproteins (HDL, typically atheroprotective).

Investigating the relationship between sex hormones and lipid metabolism is therefore important for understanding CVD risk.

We aimed to investigate the role of sex hormones in systemic lipid metabolism and consequential atherosclerotic/CVD risk in young pre- and post-pubertal cis-gendered boys/girls and men/women as well as in young transgender individuals under cross-sex hormone treatment (trans-men/trans-women) using NMR-based serum metabolomics.

HDL-associated metabolites, including ApoA1, were significantly influenced by all sex hormone changes and oestriol increases ApoA1 (HDL) in a dose dependent and chromosome independent manner.

CONCLUSIONS

- Oestradiol increases atheroprotective HDL/ApoA1 in cis- and trans-women
- Differences in HDL/ApoA1 are induced in a dose dependent manner by oestradiol
- Sex differences are not identified pre-puberty in children
- Serum lipid metabolites could inform sex-tailored strategies for CVD risk management

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