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# Association between APOE genotype with body composition and cardiovascular disease risk markers is modulated By BMI in healthy adults: findings from the BODYCON study

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The relationship between *APOLIPOPROTEIN (APO)E* genotype and cardiovascular disease (CVD) risk is extensively studied due to its effect on the plasma lipid profile[(1)]. However, studies investigating the associations between *APOE* genotype with CVD risk markers have generated inconsistent results, with a small number of human studies suggesting that BMI might play an important role in this relationship[(2, 3)].Therefore, we assessed the association between *APOE* genotype with body composition and CVD risk markers, with further examination of the role of BMI on this association.

BODYCON (impact of physiological and lifestyle factors on body composition) was a cross-sectional observational study in which 360 healthy men and women aged 18–70 y with a BMI of 18.5–39.9 kg/m$^2$ underwent a measure of body composition by dual energy x-ray absorptiometry, assessment of physical activity level using a tri-axial accelerometer and habitual dietary intake using a 4-day weighed food diary. Circulating lipid CVD risk markers were measured in a fasting blood sample and participants were genotyped retrospectively for *APOE* (rs429358 and rs7412). A general linear model was used to determine the impact of genotype on body composition measures and CVD risk markers, and interaction between *APOE* and BMI on these outcome measures.

In the study cohort, n = 46 participants were *APOE2/E3*, n = 228 the wild type *APOE3/E3* group and n = 81 *E4* carriers (*APOE3/E4* and *APOE4/E4*). The *APOE2/E3* group had on average 9%–18% lower fasting total, low-density lipoprotein and non-high density lipoprotein cholesterol concentrations compared to the *APOE4* carrier and *APOE3/E3* groups ($p \leq 0.01$). Significant *APOE* x BMI interactions were observed for body weight and android fat mass ($p \leq 0.01$). When the group were stratified into normal-weight and overweight/obese BMI groups, lean body mass was 6.4% lower in the *APOE3/E3* group (mean ± SE,45.2 ± 0.5 kg) compared to the *APOE4* carriers (48.1 ± 0.9 kg) in the normal BMI group ($p \leq 0.02$), while in the overweight/obese BMI group, the android:gynoid fat ratio was 7.6% lower in the *APOE4* carriers (1.10 ± 0.03) compared to the *APOE3/E3* group (1.19 ± 0.02)($p = 0.04$).Differences in fasting lipid concentrations between the *APOE2/E3* and other genotype groups was only found within the normal weight ($p \leq 0.04$) but not overweight/obese BMI subgroup. Moreover, the *APOE2/E3* participants within the normal-weight BMI group had a lower dietary fibre and trans-fat intake compared to the *APOE4* carriers and lower carbohydrate intake compared to the *APOE3/E3* group while there were no differences between genotypes in the overweight/obese BMI group. Physical activity levels were similar between genotype groups within each BMI group.

Our findings confirm previous studies suggesting that the impact of *APOE* genotype on CVD risk markers is modulated by BMI but indicate that diet may also play a role in this relationship. Further research is needed to draw a firm conclusion on the underlying mechanisms.

## References

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