

## **Assessing the causal role of adiposity on early markers of cardiovascular disease: increases in blood pressure, but not metabolic risk factors, are related to arterial stiffness in young adults**

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### **Background:**

Elevated BMI is associated with a clustering of cardiometabolic risk factors in young adulthood which may cause early arterial stiffening and an increased risk of cardiovascular disease in later life. Whilst numerous studies have strongly suggested a role for increased BMI in the development of an adverse cardiometabolic profile, the causal role of adiposity on these changes and its impact on arterial stiffness at this age have yet to be determined.

### **Purpose:**

To determine the causal role of BMI on numerous cardiometabolic risk factors in young adults and investigate their relationship to arterial stiffness.

### **Methods:**

Within the Avon Longitudinal Study of Parents and Children (ALSPAC), 436 young adults ( $23.4 \pm 0.5$  years; 272 female) were recruited using a recall-by-genotype study design before undergoing detailed cardiovascular phenotyping. Participants were selected from the lower (low risk;  $n=190$ ) and higher (high risk;  $n=225$ ) tails of a genome wide risk score, and the causal effect of BMI on numerous cardiovascular risk factors was assessed by comparing the two recalled groups. Individual components of the metabolic syndrome (waist circumference, blood pressure, triglycerides, high-density lipoprotein, glucose, and insulin) were measured and a continuous clustered cardiometabolic risk score (CRS), comprised of age- and sex-standardised measures (z-scores) of each of these components, was calculated to assess clustering of cardiometabolic risk. Arterial stiffness was measured using carotid-femoral pulse wave velocity (PWV). Observational and causal relationships were determined using multiple linear regression and low/high risk genetic groups, respectively.

### **Results:**

BMI was  $3.57\text{kg/m}^2$  higher in the high risk group and caused a higher CRS (mean difference 1.21; 95%CI 0.53,1.88;  $p<0.001$ ). PWV in the high risk group was also increased (mean difference 0.17m/s; 95%CI 0.02,0.31;  $p=0.022$ ), although this effect was abolished after adjusting for blood pressure. With the exception of glucose which appeared unrelated to adiposity, both observational and genetic studies showed similar effects of BMI on all individual components of the metabolic syndrome ( $p = 0.001$  to  $0.025$ ). After adjusting for age, sex, height, and BMI; multiple linear regression showed only a weak association between CRS and PWV (0.03 m/s per 1-SD increase CRS; 95%CI 0.01, 0.05;  $p=0.018$ ), and when assessed as individual components, waist circumference and blood pressure were the only risk factors correlated with PWV.

### **Conclusions:**

BMI causes adverse changes in multiple components of the metabolic syndrome in young adulthood and results in a clustering of cardiometabolic risk factors. Increases in arterial stiffness at this age, however, appear to be predominantly driven by increases in blood pressure. These findings suggest that interventions in the young to reduce adiposity will also reduce blood pressure and lower arterial stiffness at this age.