OP68 **PROSPECTIVE SEX-SPECIFIC TRANS-GENERATIONAL ASSOCIATION BETWEEN CARDIOVASCULAR RISK FACTORS OF MATERNAL AND PATERNAL GRANDPARENTS AND THEIR GRANDCHILDREN'S BIRTH WEIGHTS IN THE LIFEWAYS CROSS GENERATION COHORT STUDY**

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Purpose The association between infants' birth-weight (BW) and cardiovascular (CVD) morbidity or mortality of their grandparents has been reported by only three studies, but has not been investigated with antenatally measured CVD risk clinical parameters. Such antenatal clinical parameters studies are rare even with parents' data. We prospectively examined the relationship between measured CVD risk profile of grandparents and their grandchild's (proband's) measured BW. As sex differences have been documented in inheritance of diseases and individual's association of BW with CVD risk, we further examined the risk association by grandparent-grandchild's gender.

Methods This cross-generation birth cohort study was established at antenatal stage. At baseline, grandparents of expected probands participated in a CVD risk examination (European Health Risk Monitoring protocol) inclusive of anthropometric, blood pressure (mm Hg) and serum lipid profile (mmol/l) assessments. 931 grandparents (359 maternal-grandmothers (MGM), 215 maternal-grandfathers (MGF), 213 paternal-grandmothers (PGM) and 144 paternal-grandfathers (PGF)) were eligible for analyses at birth of the proband infant. Initially, clinical predictors of probands' BW (gms) were examined (partial correlations) with all grandparents clustered together, followed by separate examination for grandparent-grandchild dyad. Statistically significant parameters were re-examined in multivariable linear regression models, adjusted for child's characteristics (gestational age, gender), grandparent's characteristics (age, smoking, measured height and waist-hip ratio), and maternal prenatal characteristics (age, parity, smoking, body mass index). Significant predictors were further explored by grandchild's gender. Adjusted regression results displayed as (unstandardised β-coefficient; 95% CI; p-value).

Results Initial analyses suggested only a weakly negative correlation with all grandparents' high density lipoprotein cholesterol (HDL-C) and probands' BW (r=-0.1; p<0.01), not attenuated by adjustments. However, grandparent-grandchild dyad examination revealed that MGMs' diastolic blood pressure (DBP) (5.9; 0.0-11.9; 0.05); PGMs' triglyceride (TG) (70.1; 3.5-136.7; 0.04); PGFs' systolic blood pressure (SBP) (6.2; 0.8-11.5; 0.02) were predictive of grandchild's BW. No pattern was seen for MGFs. The MGM risk (DBP=(8.3; 0.2-16; 0.04)) associations were stronger and statistically significant for granddaughters than grandsons. Associations attenuated for MGM with adjustments, particularly height. Gender-specific analyses further established strong association for PGM risk (HDL-C=(-401; -700 to -102; <0.01), TG=(103; 18–189; 0.02)) with granddaughters, which was not found for grandsons. The PGF risk (SBP=(8; 0.1-16; <0.05)) associations were statistically significant only with boys and became evident after adjustment for grandparents' height.

Conclusions Infant grandchildren's birth-weight relates to their grandparents' CVD profile, but by different pathways. The MGM-granddaughters' association is lost with adjustment for factors related to intrauterine development, whereas the association in particular between PGM lipid profile and granddaughters' birth-weight suggests a heritable X-chromosome related mechanism.