SAT-LB132: 3-Generation Study of Metabolic Disruption by Pregnancy Serum PFASs: Associations with Abdominal and Whole-Body Obesity in Granddaughters in a 60-Year Follow-Up of the Child Health and Development Studies Cohort

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Introduction: We previously found a 3.6-fold increased risk of breast cancer in daughters associated with high maternal (F0) early postpartum serum EtFOSAA combined with high F0 cholesterol (https://doi.org/10.1016/j.reprotox.2019.06.012). Here we test the hypothesis that F0 early postpartum EtFOSAA, in combination with F0 serum cholesterol predicts abdominal obesity (waist circumference > 88cm) and/or whole-body obesity (body mass index > 30 kg/m2) in daughters (F1) at age 30 and granddaughters (F2) at age 20.

Methods: We measured F1 and F2 weight, height, waist circumference and blood pressure when F1 were an average age of 50 years and adult F2 were an average age of 20 years (N=219 dyads). F1 also reported their weight at age 30, near the mean age of their pregnancies with their daughters (F2) to allow control for obesity during F2 gestation. EtFOSAA, PFOS, and cholesterol were assayed in archived early postpartum F0 serum samples collected within 3 days of delivery.

Results: F0 cholesterol significantly ($p<0.05$) modified the association of F0 EtFOSAA with self-reported obesity at age 30 in F1 and measured abdominal and whole-body obesity, and blood pressure at age 20 in F2. Association patterns were similar for all outcomes: F0 EtFOSAA was associated with high metabolic risk when F0 serum cholesterol was low (Quartile 1): e.g. 20-year-old F2 had an estimated 2.3 fold increase in the joint risk of abdominal and whole-body obesity over the inter-quartile range of F0 ETFOSAA , 95% Confidence Interval= 1.1, 4.8. F0 EtFOSAA associations with F2 metabolic risk were independent of F0 race, early pregnancy overweight (BMI >25 kg/m2), and serum PFOS. F1 obesity at age 30 did not mediate F0 EtFOSAA associations with F2 outcomes, but additionally predicted high metabolic F2 risk.

Conclusions: Findings support the hypothesis that in utero exposure to EtFOSAA impacts metabolic risk factors in female F2 exposed as germline and also independently via promotion of overweight in F1 (their mothers) during F2 gestation.