

Childhood exposure to non-persistent endocrine disrupting chemicals and multi-omic profiles: a panel study

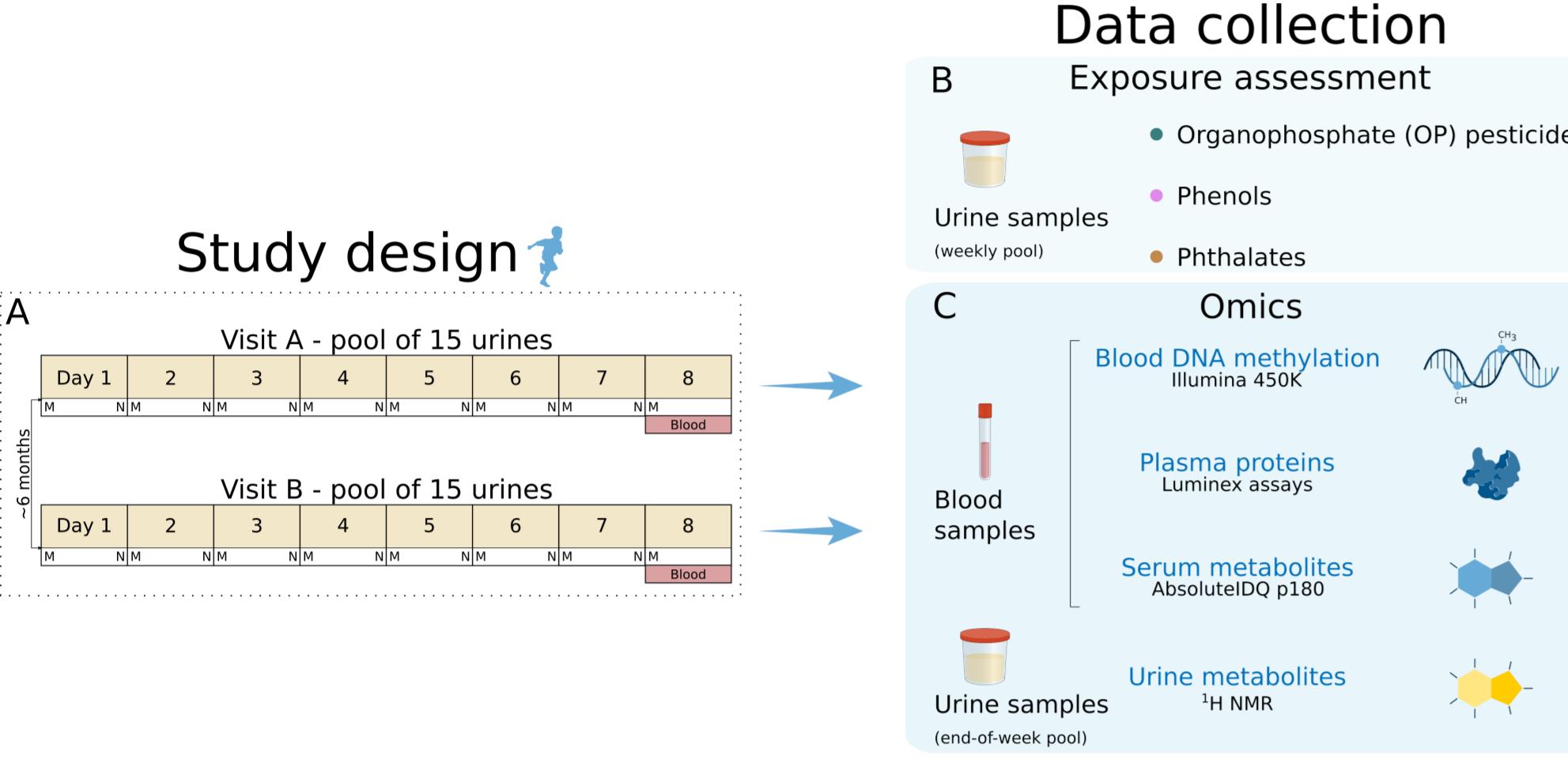
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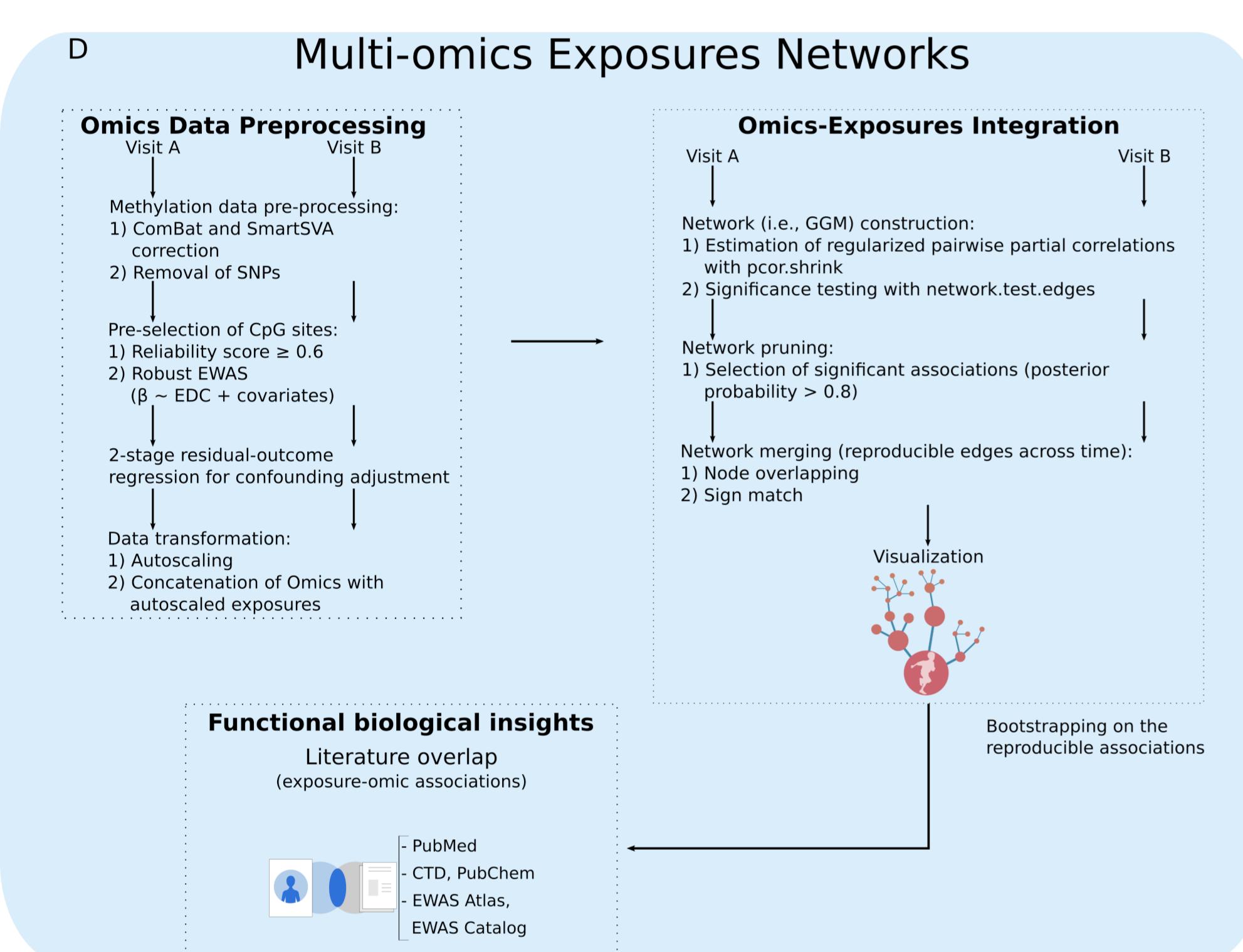
Background & Objectives

- Individuals are exposed to multiple environmental pollutants with endocrine disrupting activity (endocrine disruptors, EDCs)
- Few studies have integrated multiple omic layers, especially in a child cohort
- We aimed to identify multi-omic signatures associated with childhood exposure to non-persistent EDCs using a network approach

Methods



- Data: HELIX (Human Early-Life Exposome) Child Panel Study
- Exposures: 22 non-persistent EDCs (10 phthalate, 7 phenol, and 5 organophosphate pesticide metabolites) with repeated measures
- Multi-omic profiles: methylome, serum and urinary metabolome, proteome



- We developed Gaussian Graphical Models (GGMs) based on shrinkage estimates of pairwise partial correlations between EDCs and molecular features in each week
- The obtained networks for the two visits were merged in order to identify reproducible associations
- We corroborated the associations between EDCs and omic features with
 - Manual literature review (PubMed)
 - Adverse health effects associated with the EDCs (PubChem)
 - Traits associated with the CpG sites (EWAS Atlas)
 - Genes mapped to the CpG sites (EWAS Atlas, EWAS Catalog)

Results

Study population

Characteristic Visit A, N = 140 Visit B, N = 143

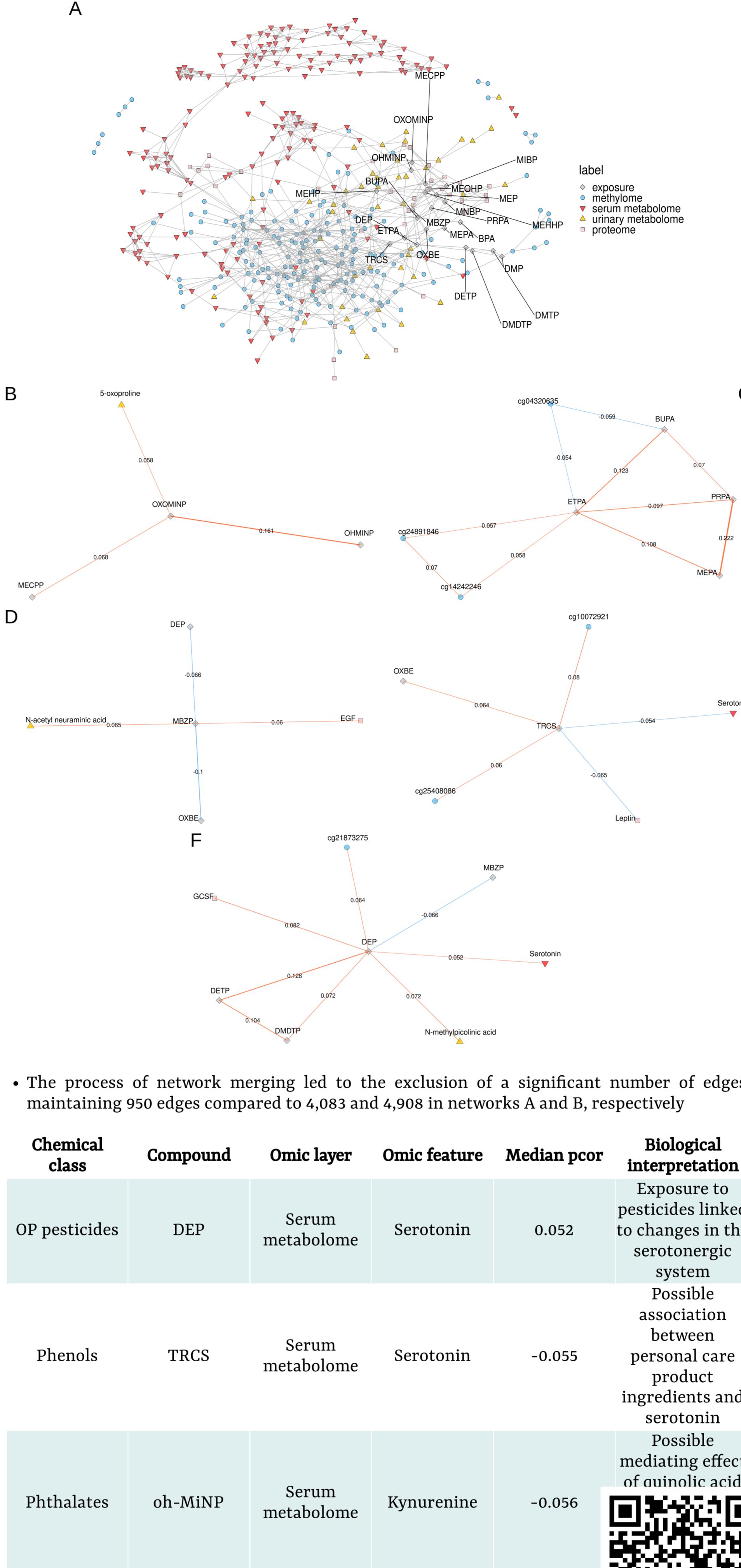
Characteristic	Visit A, N = 140	Visit B, N = 143
Cohort		
BIB	27 (19%)	27 (19%)
EDEN	23 (16%)	23 (16%)
KANC	27 (19%)	26 (18%)
RHEA	29 (21%)	29 (20%)
SAB	34 (24%)	38 (27%)
Sex		
female	60 (43%)	61 (43%)
male	80 (57%)	82 (57%)
Age	6.97 (6.44, 8.85)	7.55 (6.93, 9.62)
Ethnicity		
Caucasian	129 (92%)	132 (92%)
Pakistani	10 (7.1%)	10 (7.0%)
Other	1 (0.7%)	1 (0.7%)
zBMI	0.28 (-0.34, 1.09)	0.26 (-0.34, 1.09)
Season		
autumn	35 (25%)	38 (27%)
spring	50 (36%)	49 (34%)
summer	20 (14%)	8 (5.6%)
winter	35 (25%)	48 (34%)

Chemical class	Compound	Omic layer	Omic feature	Median pcor	Biological interpretation
Phenols	TRCS	Proteome	Leptin	-0.066	Effect of mixtures of phenols and parabens

Conclusions

- We employed an integrative method to investigate reproducible associations across time points between non-persistent EDCs and multi-omic profiles in a child cohort
- Strengths: repeated pooled samples of urines across each week; reproducible and quantifiable measurements of the metabolome
- Limitations: relatively small sample size; residual confounding
- Some of these biological signatures point towards the potential biological effects of OP pesticide and phthalate metabolites on the nervous system
- Among the most significant, we found associations between diethyl phosphate and serotonin, triclosan and serotonin, mono-4-methyl-7-hydroxyoctyl phthalate and kynurenone, triclosan and leptin

Merged network: reproducible associations across visits



Chemical class	Compound	Omic layer	Omic feature	Median pcor	Biological interpretation
OP pesticides	DEP	Serum metabolome	Serotonin	0.052	Exposure to pesticides linked to changes in the serotonergic system
Phenols	TRCS	Serum metabolome	Serotonin	-0.055	Possible association between personal care product ingredients and serotonin
Phthalates	oh-MiNP	Serum metabolome	Kynurenone	-0.056	Possible mediating effect of o-nitrophenol

