

Exposome Data Challenge Event

28-30 April 2021

Topic 4: Causal modelling, mediation and triangulation

Meet-in-the-middle meets multi-omics

A strategy to identify molecular signatures of environmental drivers of childhood BMI

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29th April, 2021

Study design

Objectives

Objective 1: Integration of high-dimensional heterogeneous data

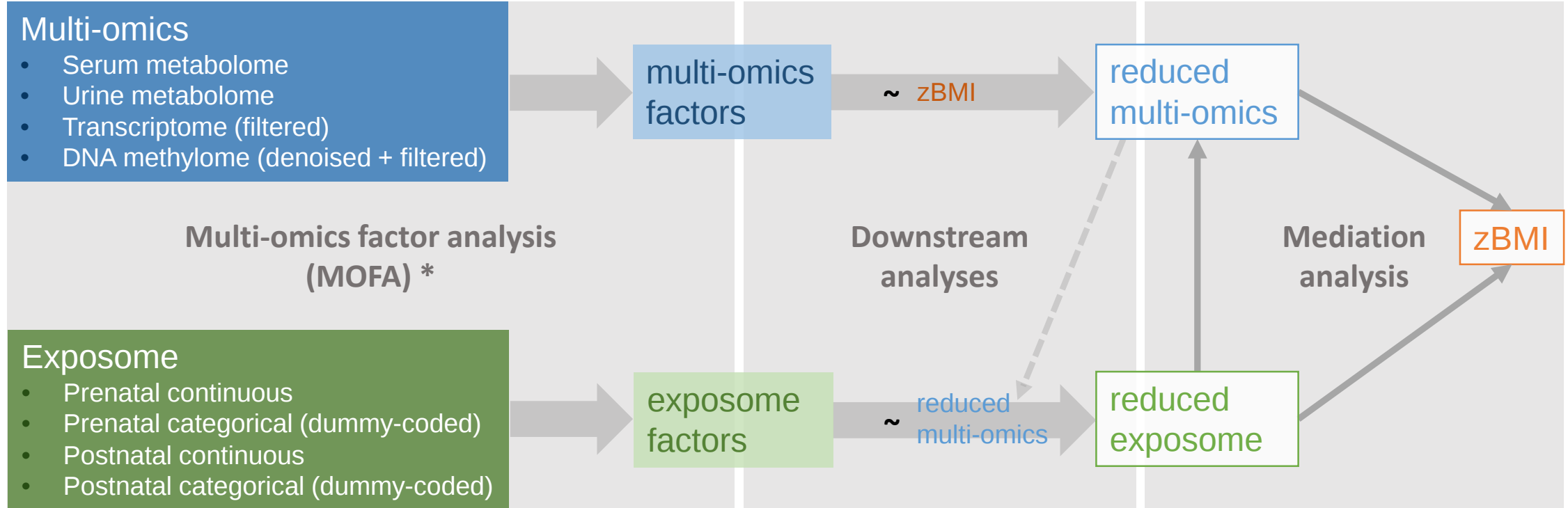
- Exposome (p=223, N=1301)
 - pre- and postnatal
 - outdoor exposures, chemicals, lifestyles
- Multi-omics
 - serum metabolome (p=177, N=1198)
 - urine metabolome (p=44, N=1192)
 - whole blood gene expression (p=28738, N=1007)
 - buffy coat DNA methylome (p=299221, N=918)

Objective 2: Causal inference with mediation analysis

- Exposure = exposome
- Mediator = multi-omics
- Outcome = childhood zBMI

Study design

Meet-in-the-middle

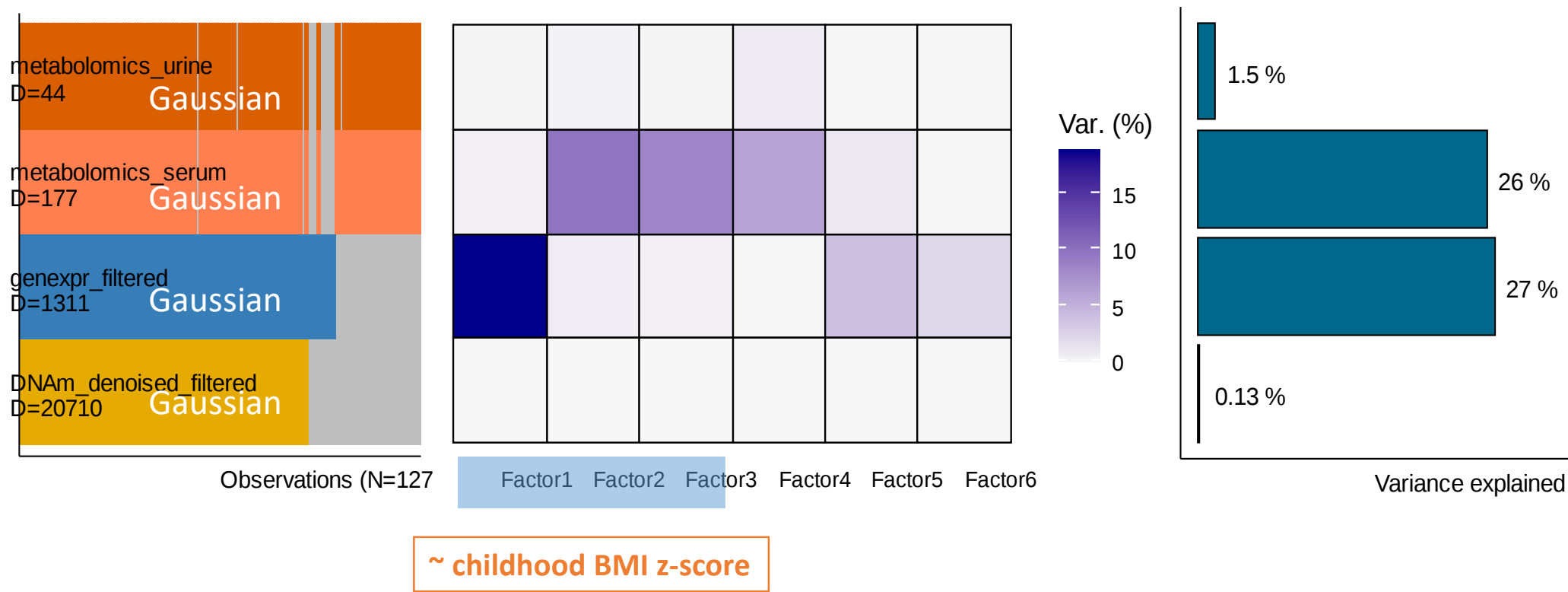


Objective 1: Integration of high-dimensional and heterogeneous data

Objective 2: Causal inference

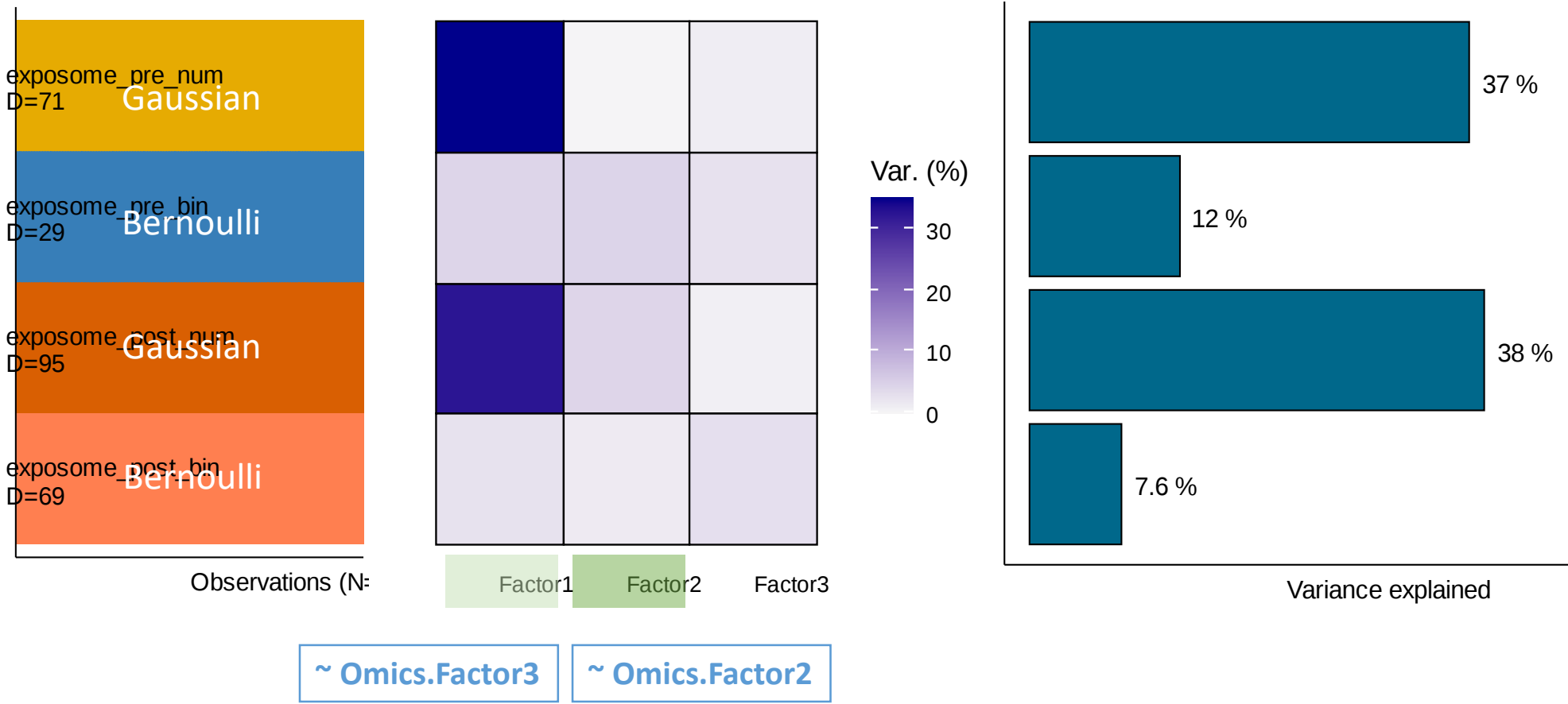
MOFA on multi-omics

Data modality and variance decomposition



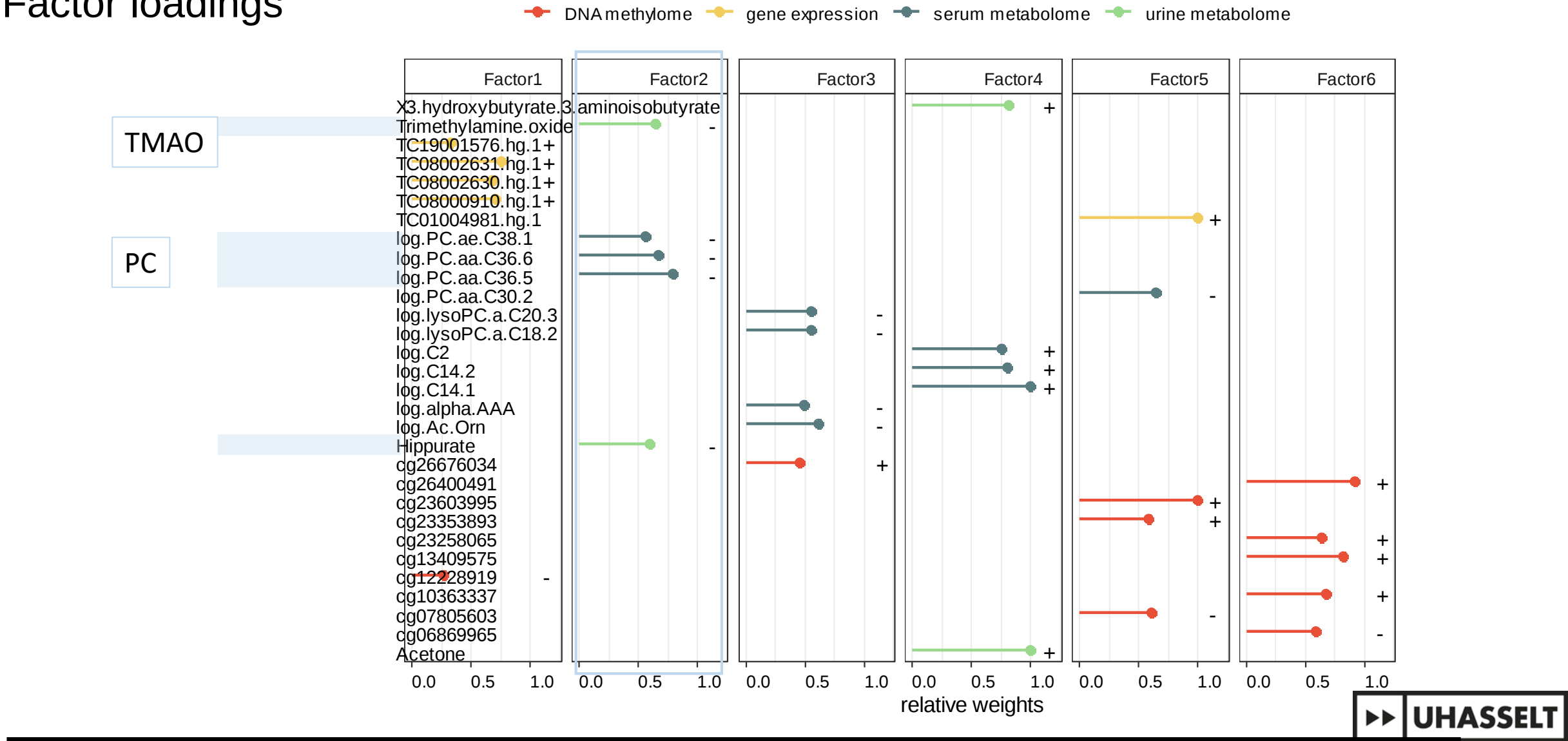
■ MOFA on exposome

Data modality and variance decomposition



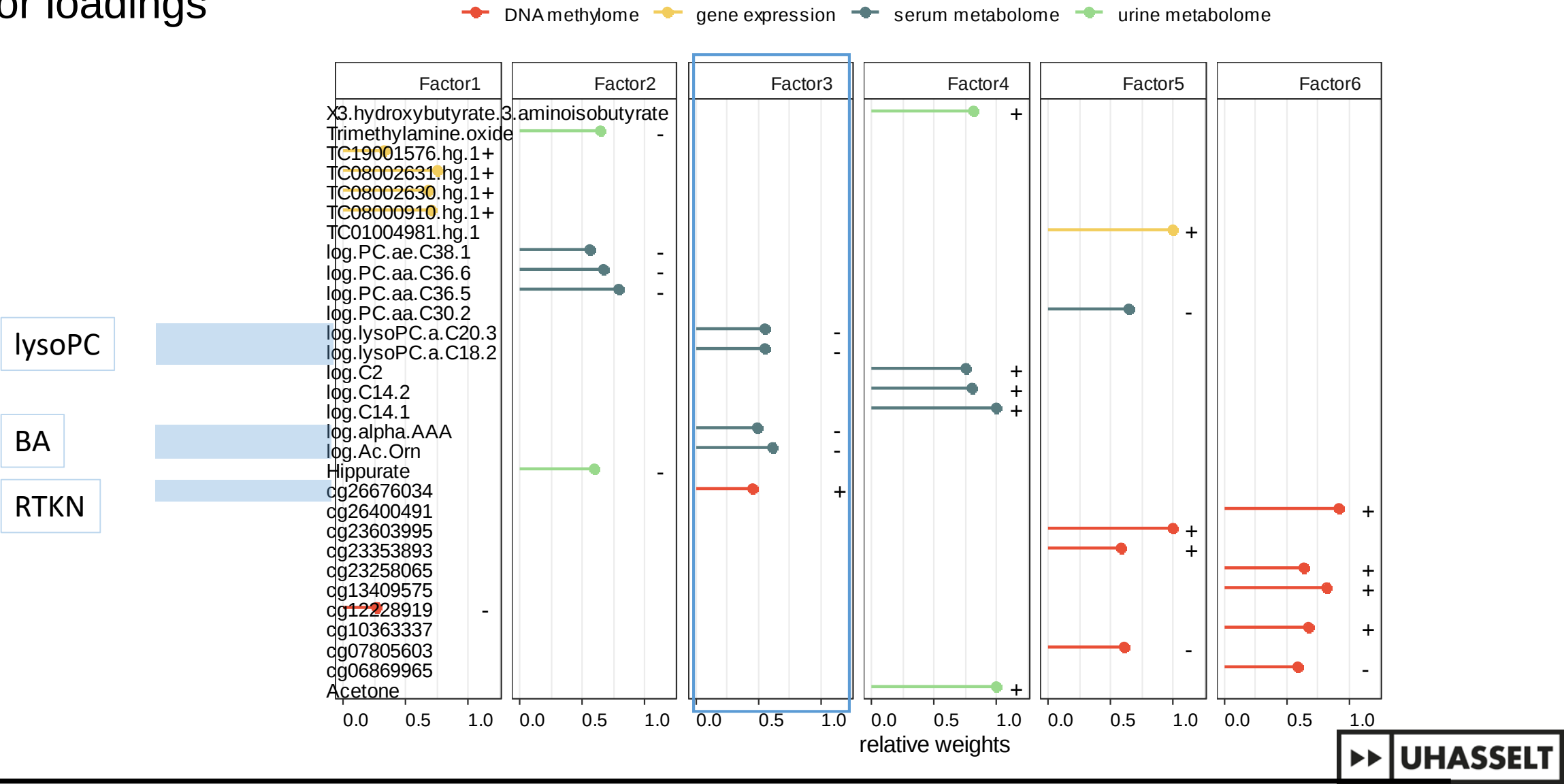
MOFA on multi-omics

Factor loadings



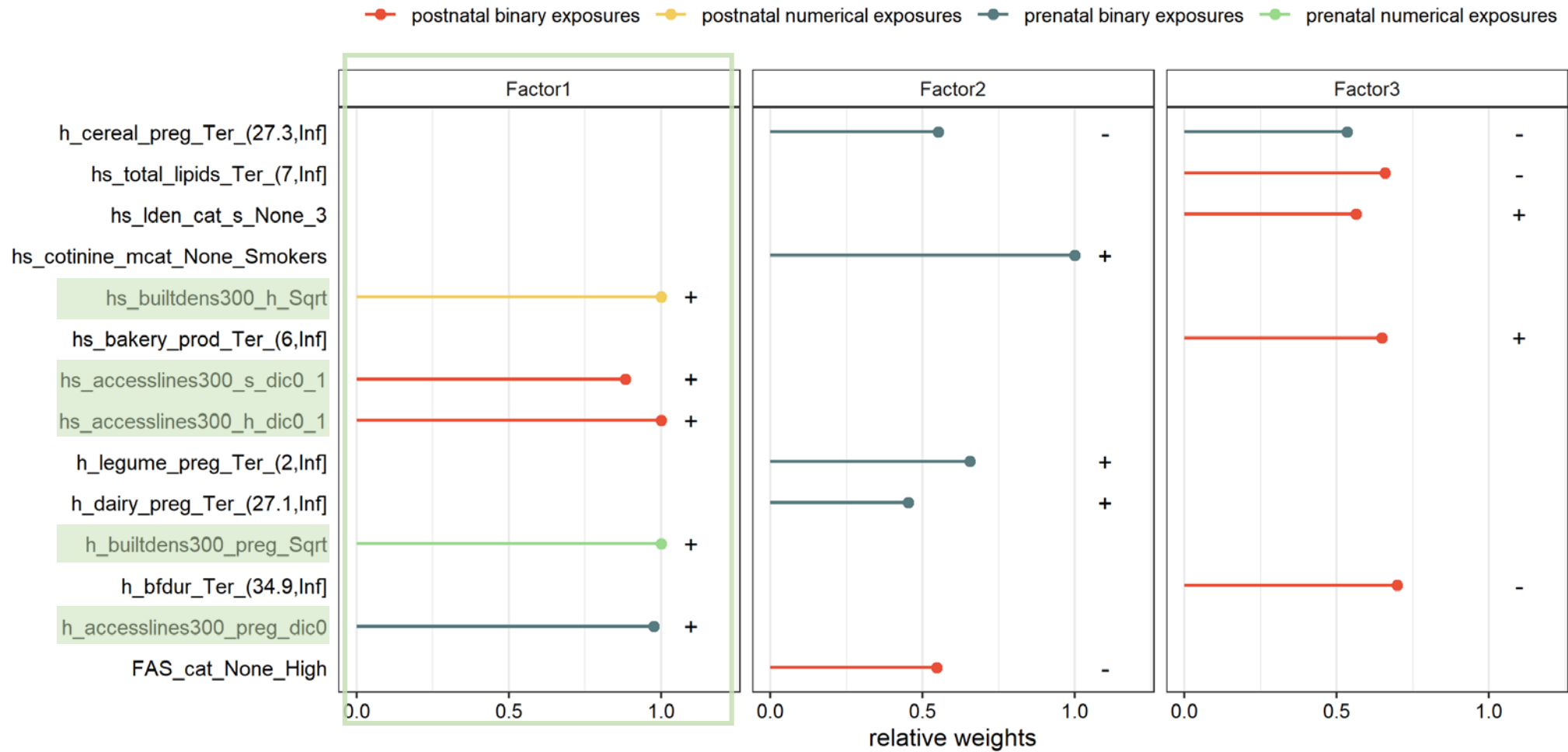
MOFA on multi-omics

Factor loadings



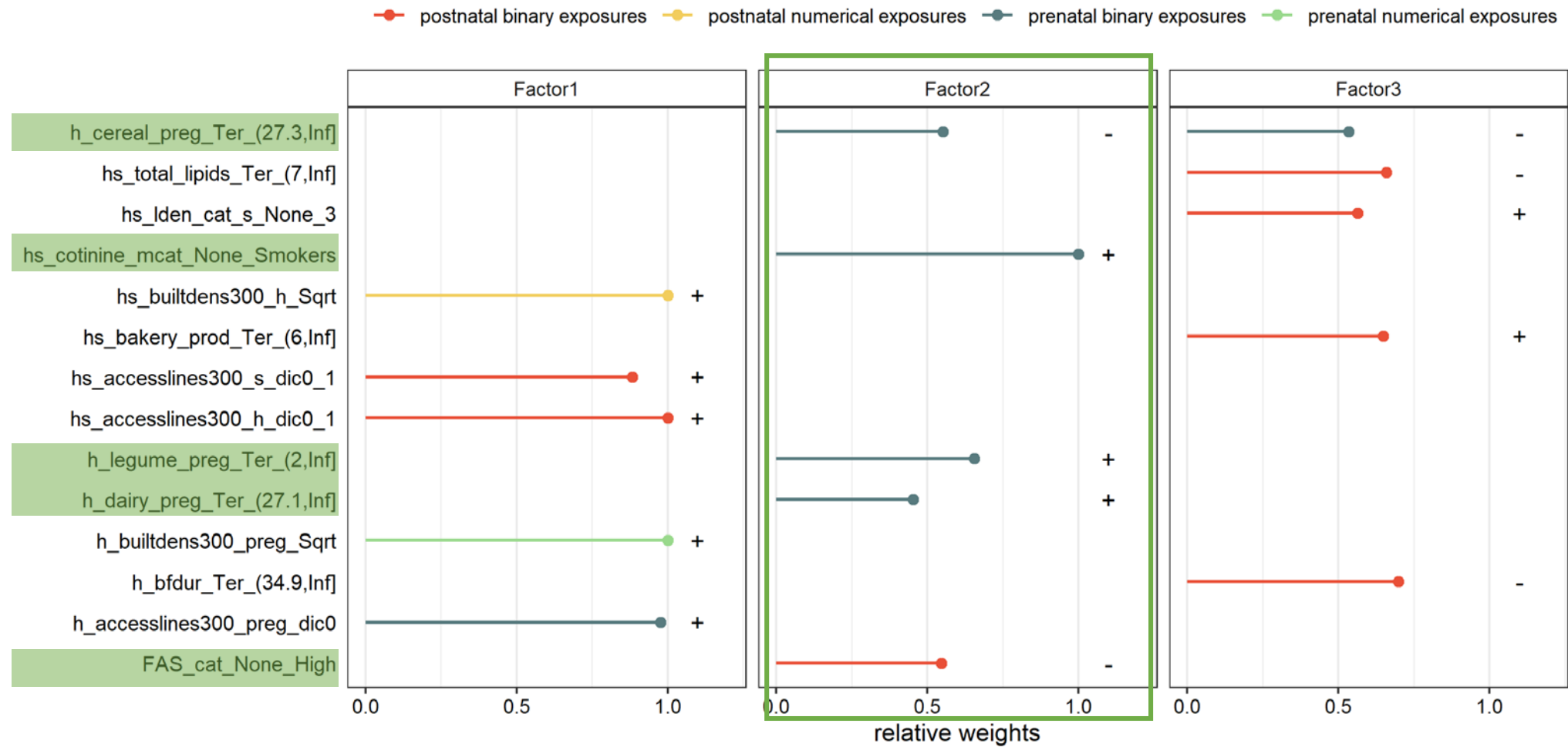
■ MOFA on exposome

Factor loadings

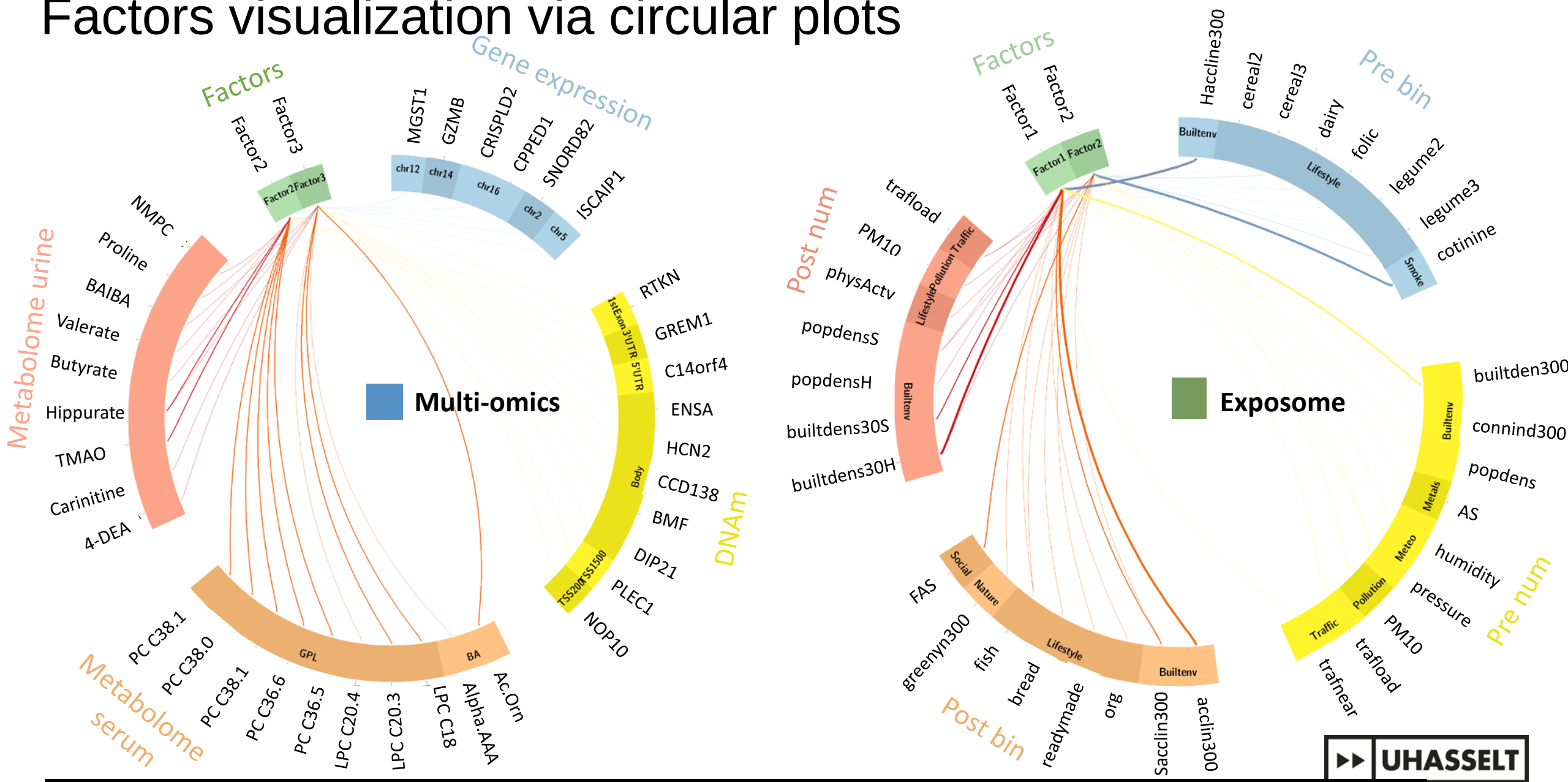


■ MOFA on exposome

Factor loadings

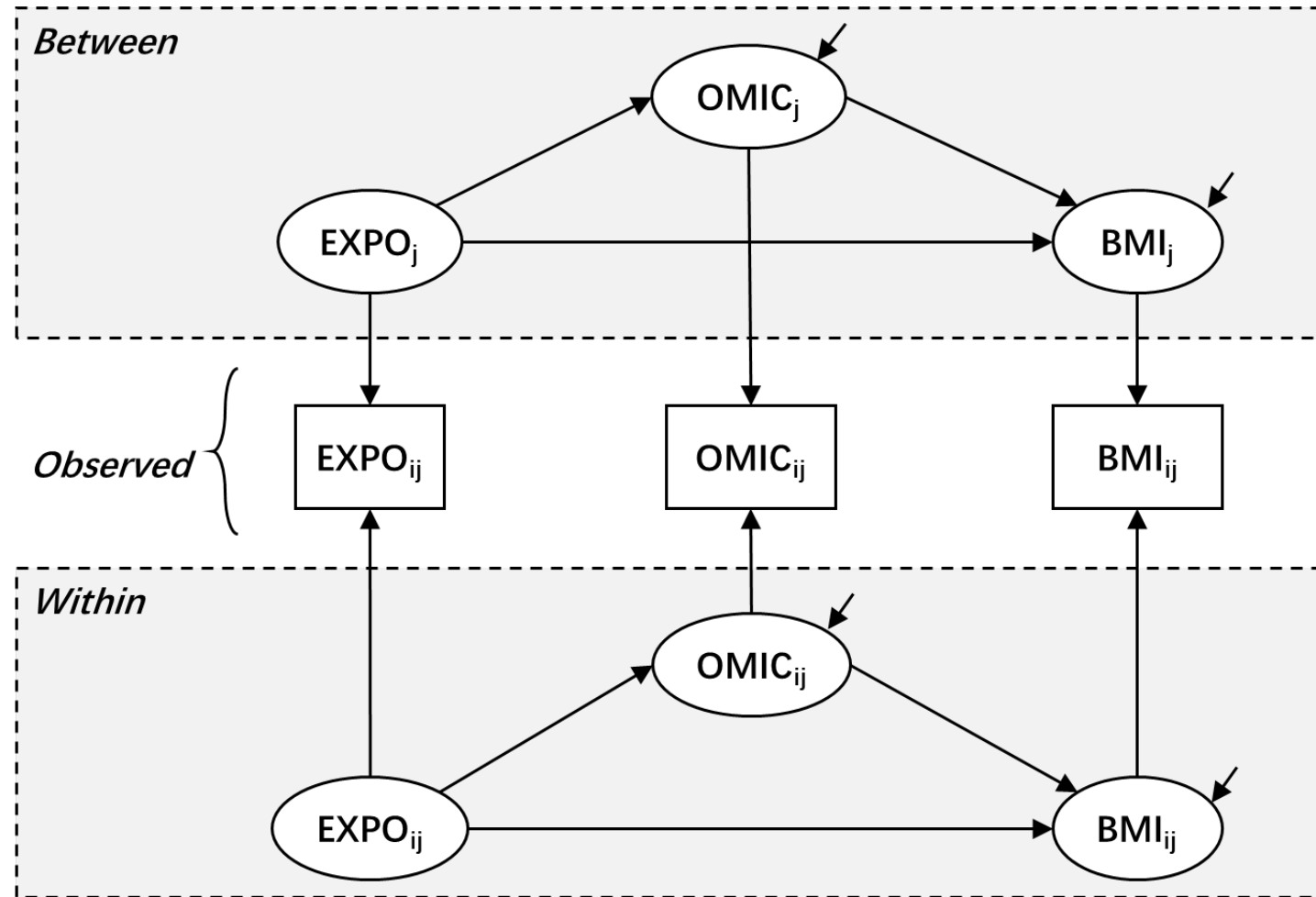


Factors visualization via circular plots



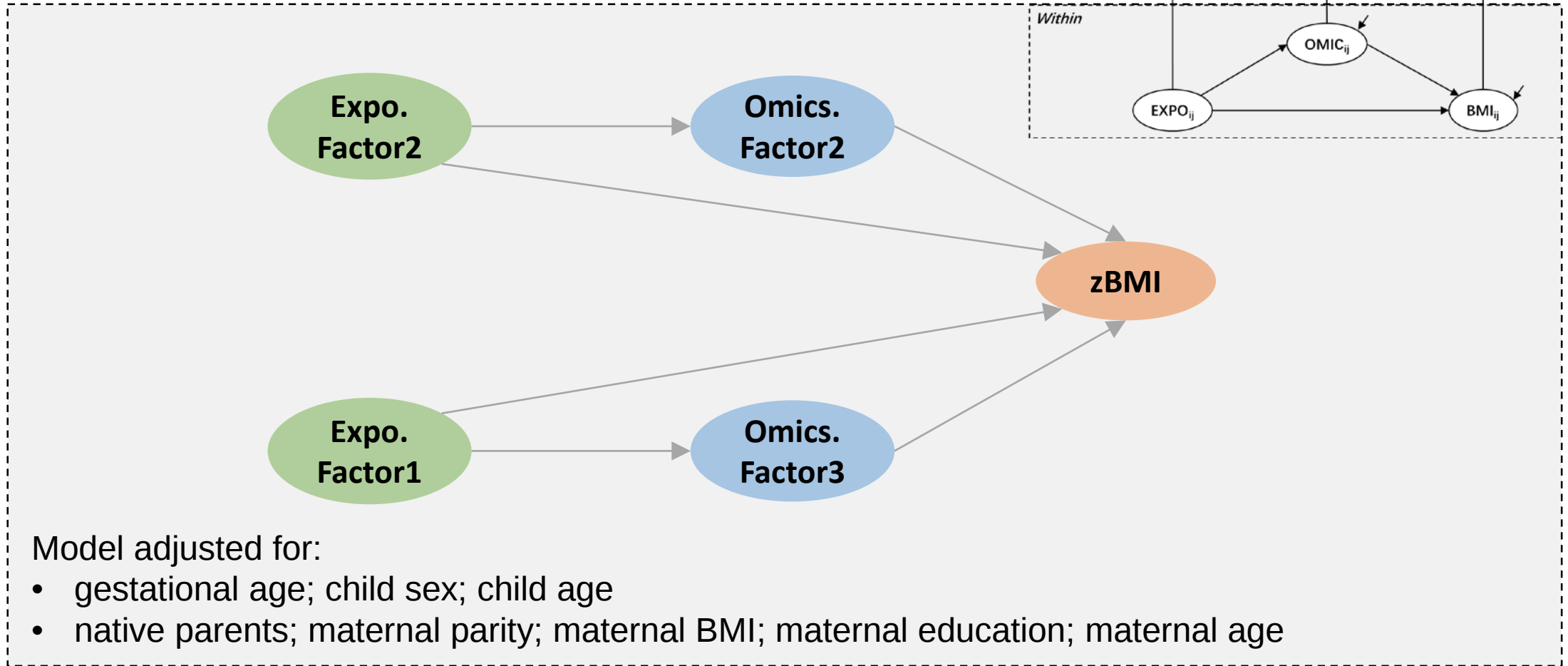
Mediation analysis

Multi-level structural equation modelling



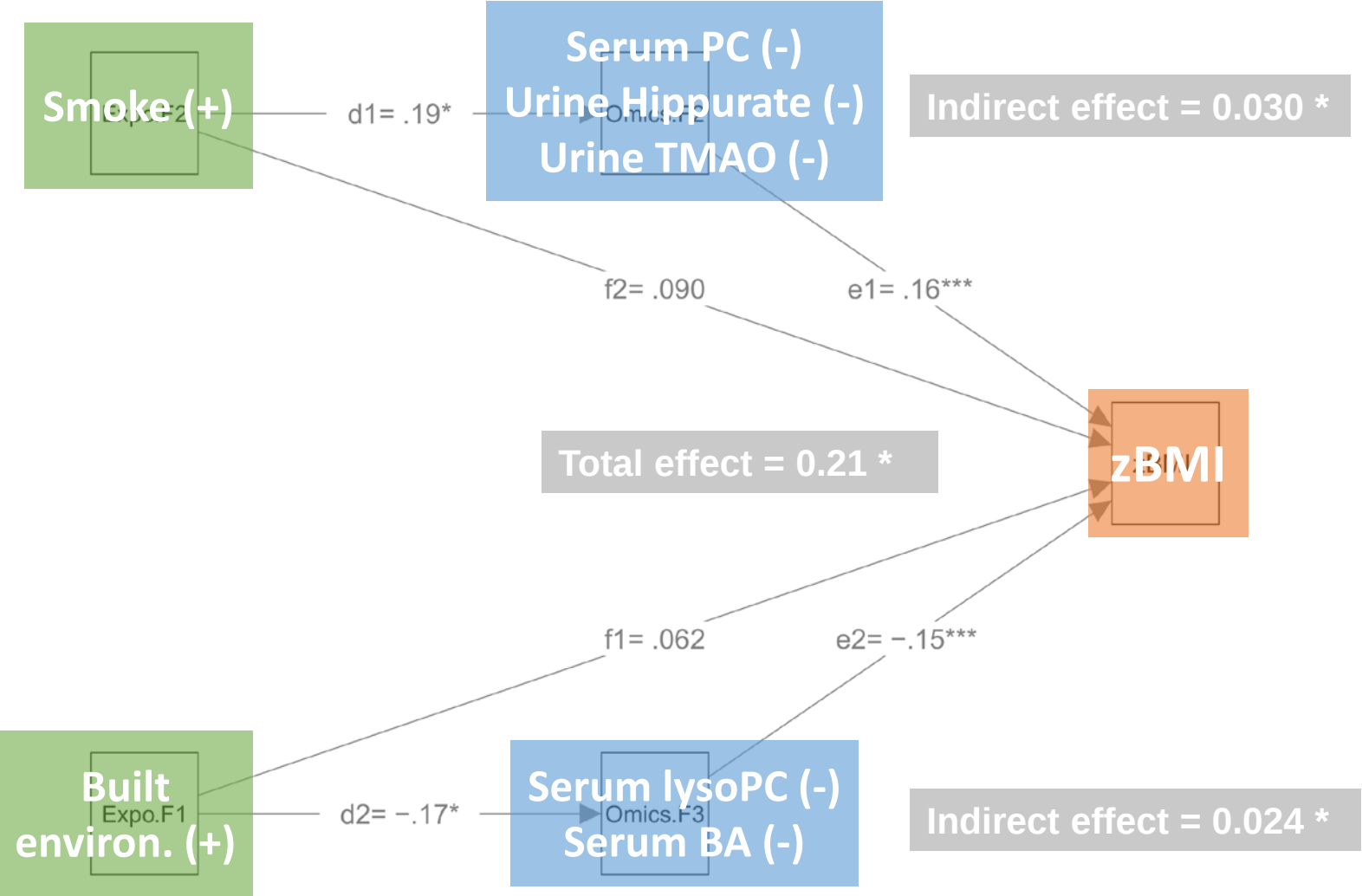
Mediation analysis

Within-cohort mediation effects



Mediation analysis

Model estimates



Conclusions

Achievements:

- Novel in combining multi-omics factorization with meet-in-the-middle
- Integrated high-dimensional and heterogeneous data
- Identified the main drivers of the variation
- Omics factors (metabolites) mediates the effect of exposome factors (built env. & smoke) on childhood zBMI

Strength:

- A simple and efficient strategy for causal inference
- Missing value is allowed

Limitations:

- Explorative analysis – validation using sub-samples

Thank you for your attention!

Q & A



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