CEP Group Meeting

Update on *paper 3* of my PhD

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Overview

- **Aim**: to research the *short-term* effects of childhood exposures to non-persistent EDCs on neurodevelopment in childhood, and how the metabolome **might** *mediate* these effects.
- **How**: by making use of the principles and criteria of triangulation.
- **Population**: the HELIX sub-cohort, consisting of N $= 1200$ mother-child pairs.
- **Exposures**: non-persistent EDCs (phenols, phthalates, and organophosphate compounds), measured in childhood in a pool of two urine samples.
- **Outcome**: Attention Network Test, to provide a measure of the efficiency of three different functions of attention.
- ***Mediators***: urine metabolites (focus on corticosteroids).

The Research Questions

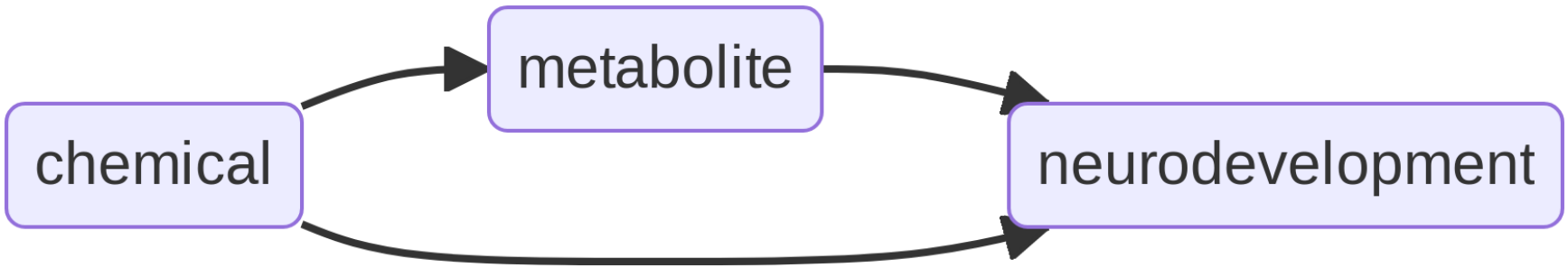


Figure 1: Simplified *DAG*.

Issues and limitations:

- The effect of exposure to these chemicals on neurodevelopment has been studied already, although there are clear issues with that study (e.g., wrong model, DAG **not** tailored to the exposures of interest).
- The effect of exposure to these chemicals on these **newly** measured metabolites could be identifiable, although they were measured in the same samples. This question poses some challenges since they were all measured in urine (inter-individual variability in urine dilution).
- The effect of these **newly** measured metabolites on neurodevelopment could be identifiable, since they were measure in the urine samples (which aliquot?) collected before the visit.

Triangulation

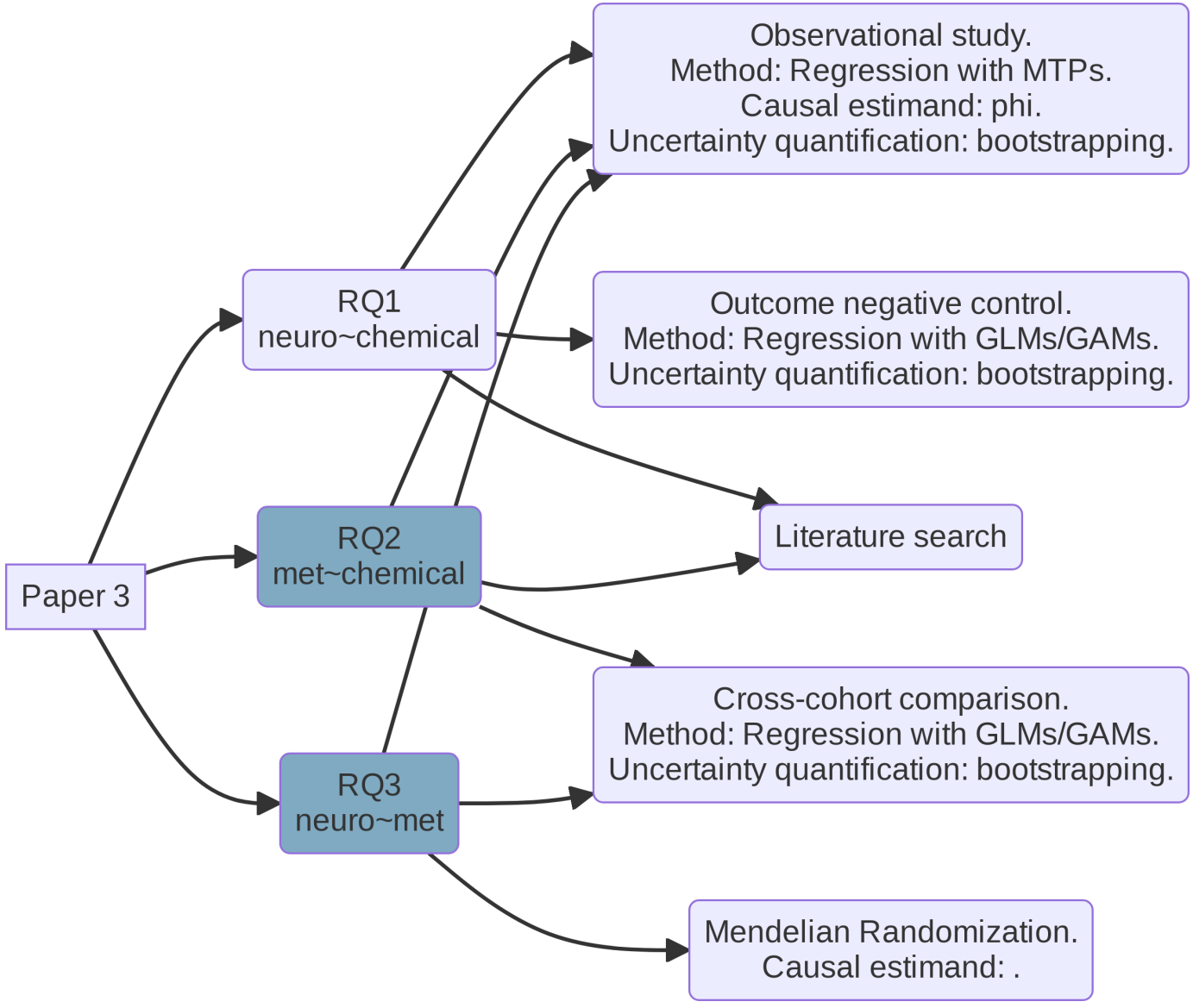


Figure 2: Diagram summarizing research questions and methods.

myphd R package

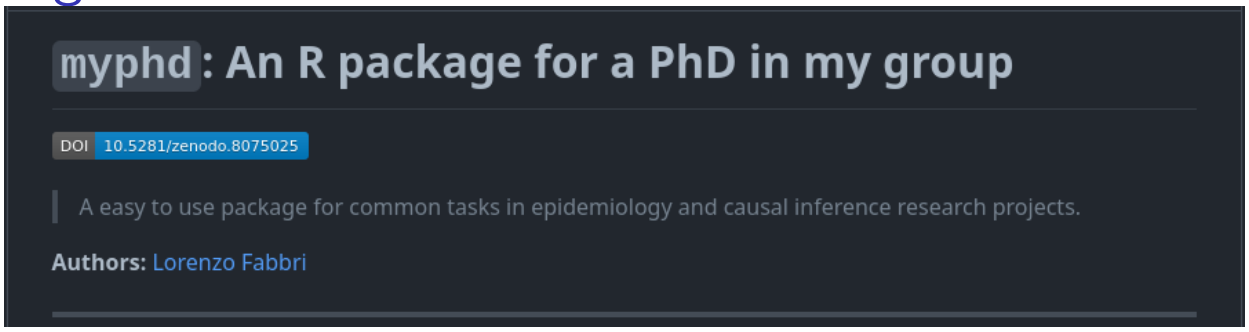


Figure 3: myphd

- URL manual: https://isglobal-cep.github.io/myphd/
- To install it: `remotes::install_github("isglobal-cep/myphd")`.

```
myphd::create_formula(
  dat,
  outcome,
  exposure,
  covariates,
  method,
  add_inter_exposure,
  add_splines_exposure,
  df_splines,
  threshold_smooth,
  threshold_k
)
```

```
myphd::describe_data(
  dat,
  id_var,
  grouping_var
)
```

```
myphd::preproc_data(
  dat,
  outcome = NULL,
  dic_steps,
  id_var,
  by_var
)
```

Current setup

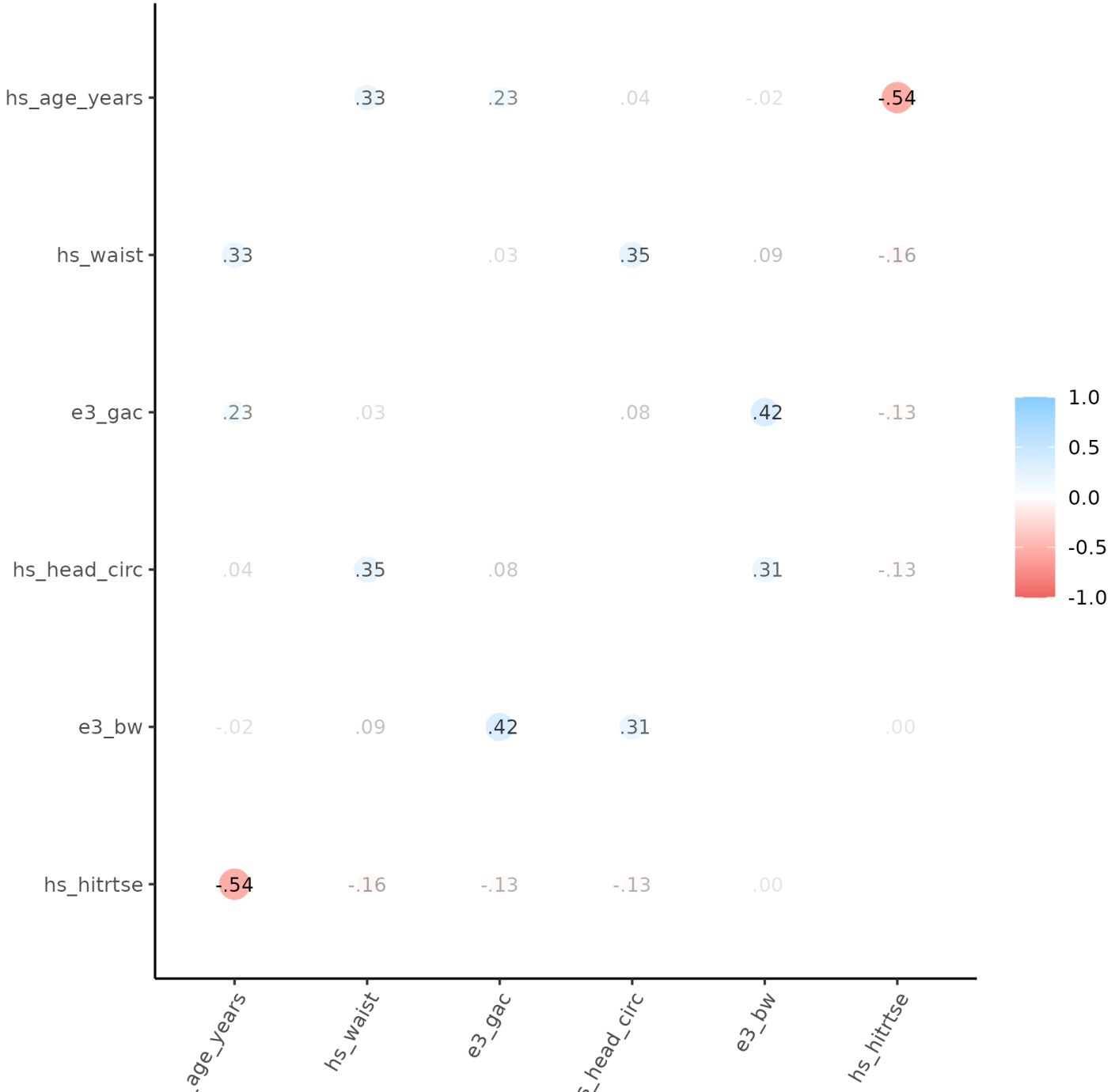
Variables:

- Clinical outcome: Attention Network Test (`hs_hitrtse`, Hit Reaction Time Standard Error).

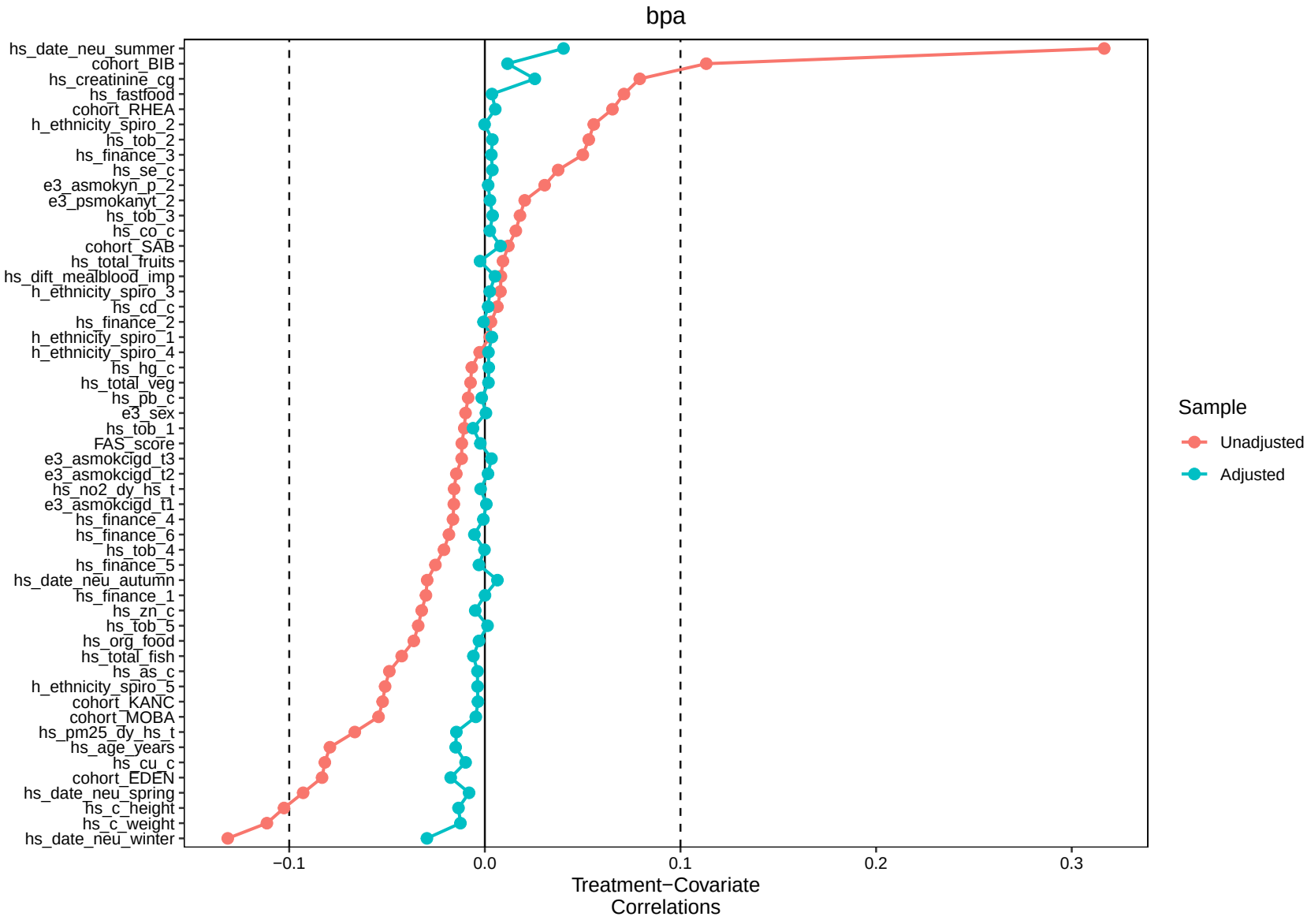
Methods:

- Weights estimation (`chemical ~ covariates`): energy balancing.
- Effect estimation (`outcome ~ chemical + covariates`): `glm` with natural splines for exposure.

Population description: correlations



Preliminary results: weights



Preliminary results: weighted G-computation

- Marginal effects of exposure to non-persistent EDCs on Cortisone: comparison `Q3 - Q1`.

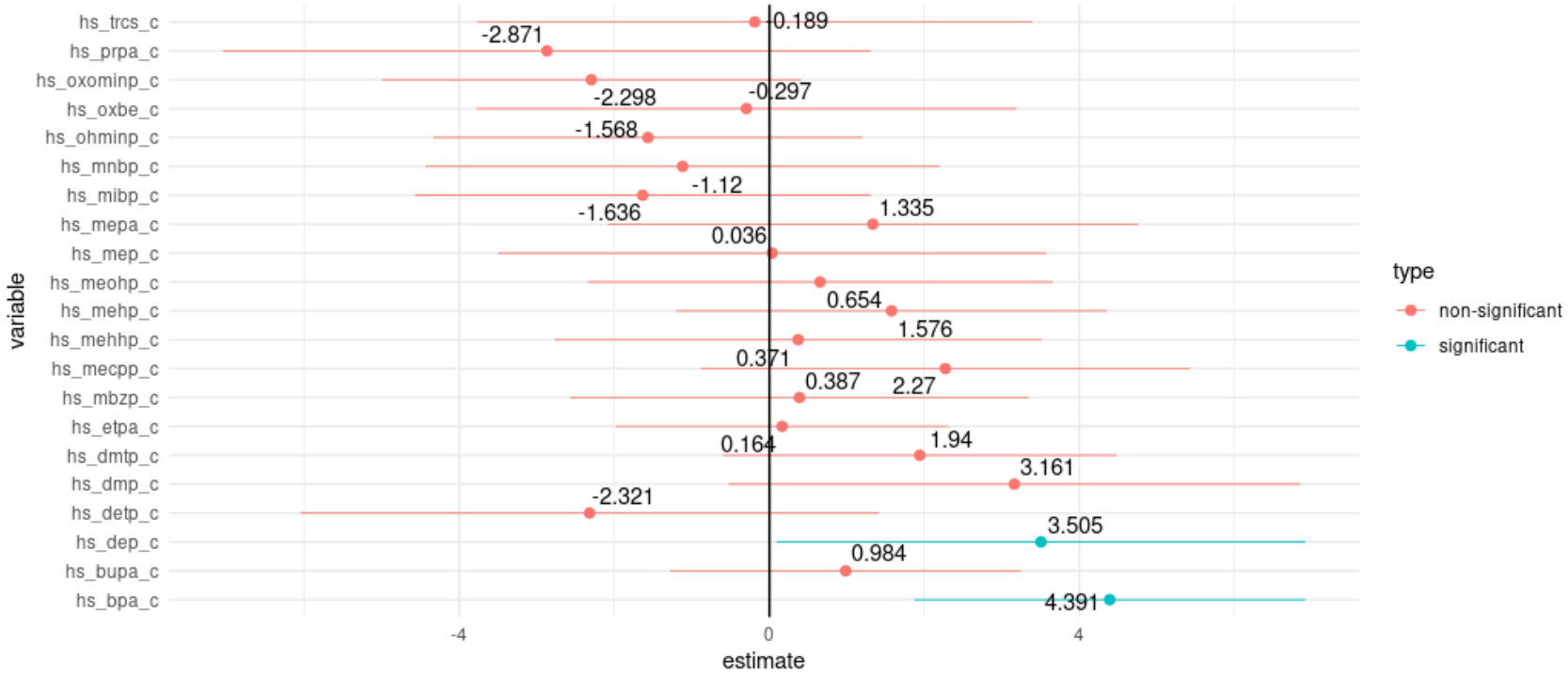
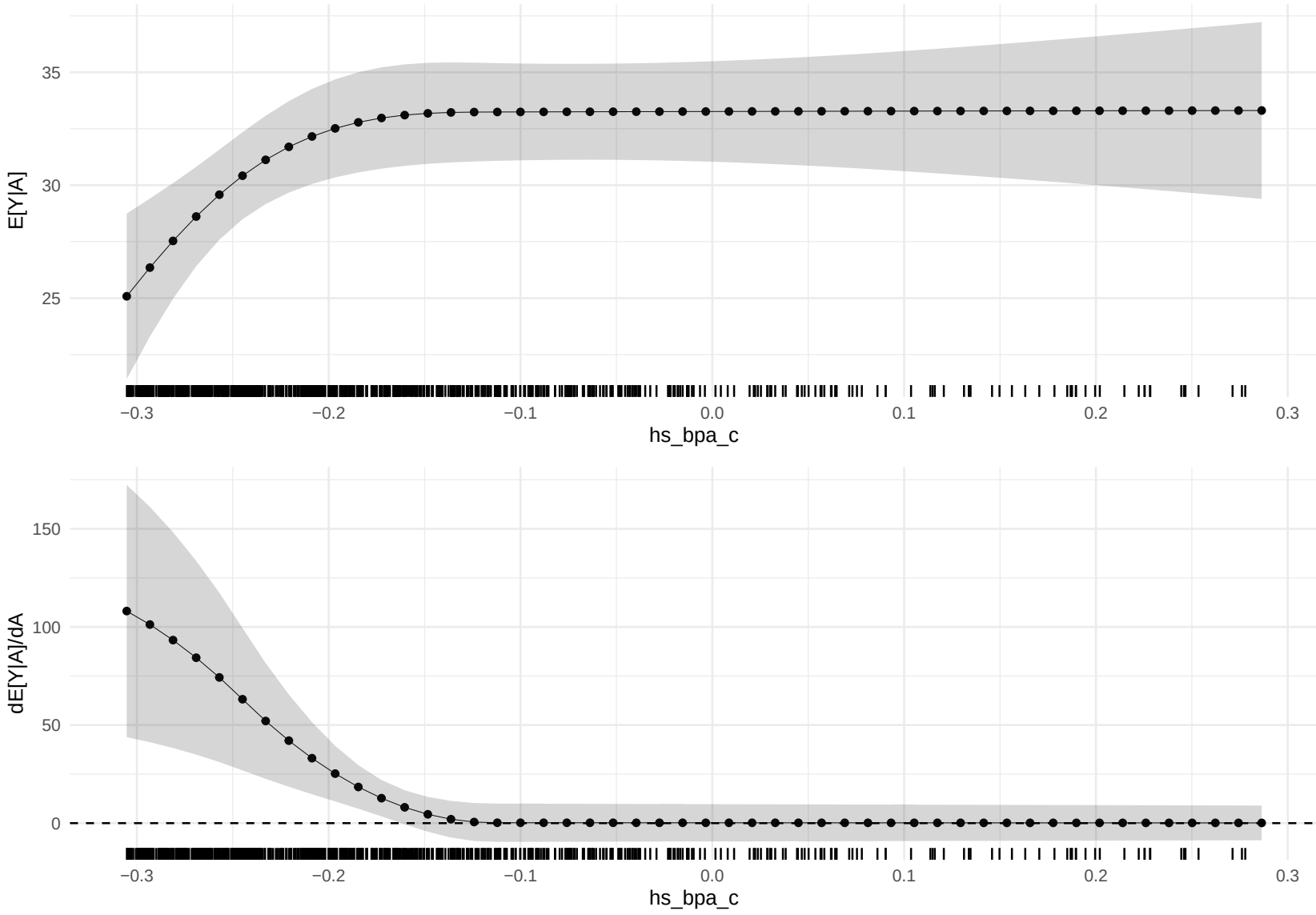


Figure 5: Effect estimates for EDCs and Cortisone.

Characteristic	**Overall**, N = 832	**BIB**, N = 130	**EDEN**, N = 134	**KANC**, N = 143	**MOBA**, N = 122	**RHEA**, N = 128	**SAB**, N = 175
BPA	-0.19 (-0.27, -0.06)	-0.13 (-0.26, 0.15)	-0.24 (-0.29, -0.17)	-0.20 (-0.27, -0.08)	-0.18 (-0.24, -0.08)	-0.18 (-0.25, -0.04)	-0.18 (-0.27, -0.04)
cortisone	23 (12, 39)	26 (14, 42)	28 (14, 42)	21 (12, 32)	23 (12, 39)	29 (19, 59)	16 (10, 27)

[1] Median (IQR)

Preliminary results: ADRF and AMEF



Next steps

- Dealing with creatinine.

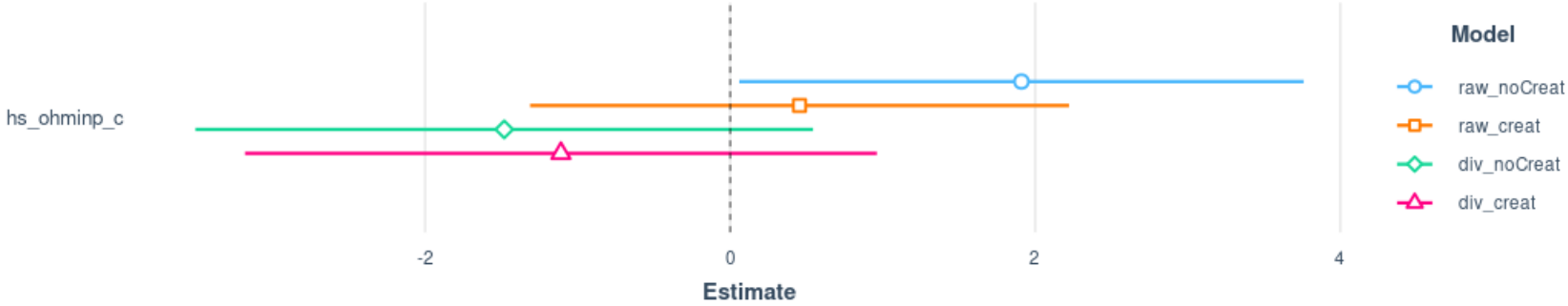


Figure 6: Comparison of effect estimation.

- Developing a more appropriate pipeline to deal with censored exposures and metabolites.
- Dealing with more appropriate modeling strategies?
  - `lmtp` will be the focus of my research stay (*Mixtures done right*) under the supervision of Prof. Jessica G. Young and Prof. Ivan Diaz (who formalized causal identification of interventions that depend on the natural value of treatment).