Supplementary Material

DNA Methylation as a Potential Mediator of the Association Between Prenatal Tobacco and Alcohol Exposure and Child Neurodevelopment in a South African Birth Cohort

Supplementary Methods

Socioeconomic status (SES) composite variable

The SES composite variable was calculated as follows:

INPUTS

STEP 1: RESPONSE CODING

- **a.** Maternal employment
  - **i.** Employment = 1 vs Unemployment = 0
- **b.** Maternal education
  - **i.** Primary education = 0
  - **ii.** Some secondary = 1
  - **iii.** Completed secondary = 2
  - **iv.** Any tertiary = 3
- **c.** Household income
  - **i.** <R1000/m = 0
  - **ii.** R1000 – 5000/m = 1
  - **iii.** >R5000/m =2
- **d.** Household assets and financial activities
  - **i.** Sum over 10 items (each checked item counts as 1):
    1. Electricity
    2. Tap or running water
    3. Domestic worker
    4. A flush toilet inside
    5. A built-in kitchen sink
    6. An electric stove or hotplate
    7. A working telephone (this includes a cell phone)
    8. At least one motor car or truck
    9. A motorcycle or scooter
    10. A bicycle
  - **ii.** Sum over 3 items (each checked item counts as 1)
    1. Shop at supermarkets

2. Use any financial services (such as bank account, ATM card or credit card)
3. Have an account at a retail store (e.g. Pep, Jet, etc)

STEP 2: STANDARDIZATION OF INPUTS

a. Standardize the sum of household asset/financial activities (variable name: ***"stdassetsum"***)

b. Standardize income (variable name: ***"stdincome"***)

c. Standardize education (variable name: ***"stdeducation"***)

OUTPUTS

STEP 1: DERIVING A *CONTINUOUS* SOCIOECONOMIC COMPOSITE

a. Continuous socioeconomic status composite (variable name: *"**sessumscore**"*)

Sessumscore = **stdassetsum** + **stdeducation** + **stdincome** + **(employment*0.5)**

STEP 2: DERIVING A *CATEGORICAL* SOCIOECONOMIC COMPOSITE

b. Categorical socioeconomic status composite (variable name: *"**sesquartile**"*)

Sesquartile is derived from **sessumscore** composite split into **quartiles**:

1. Lowest SES
2. Low-mod SES
3. Mod-high SES
4. High SES

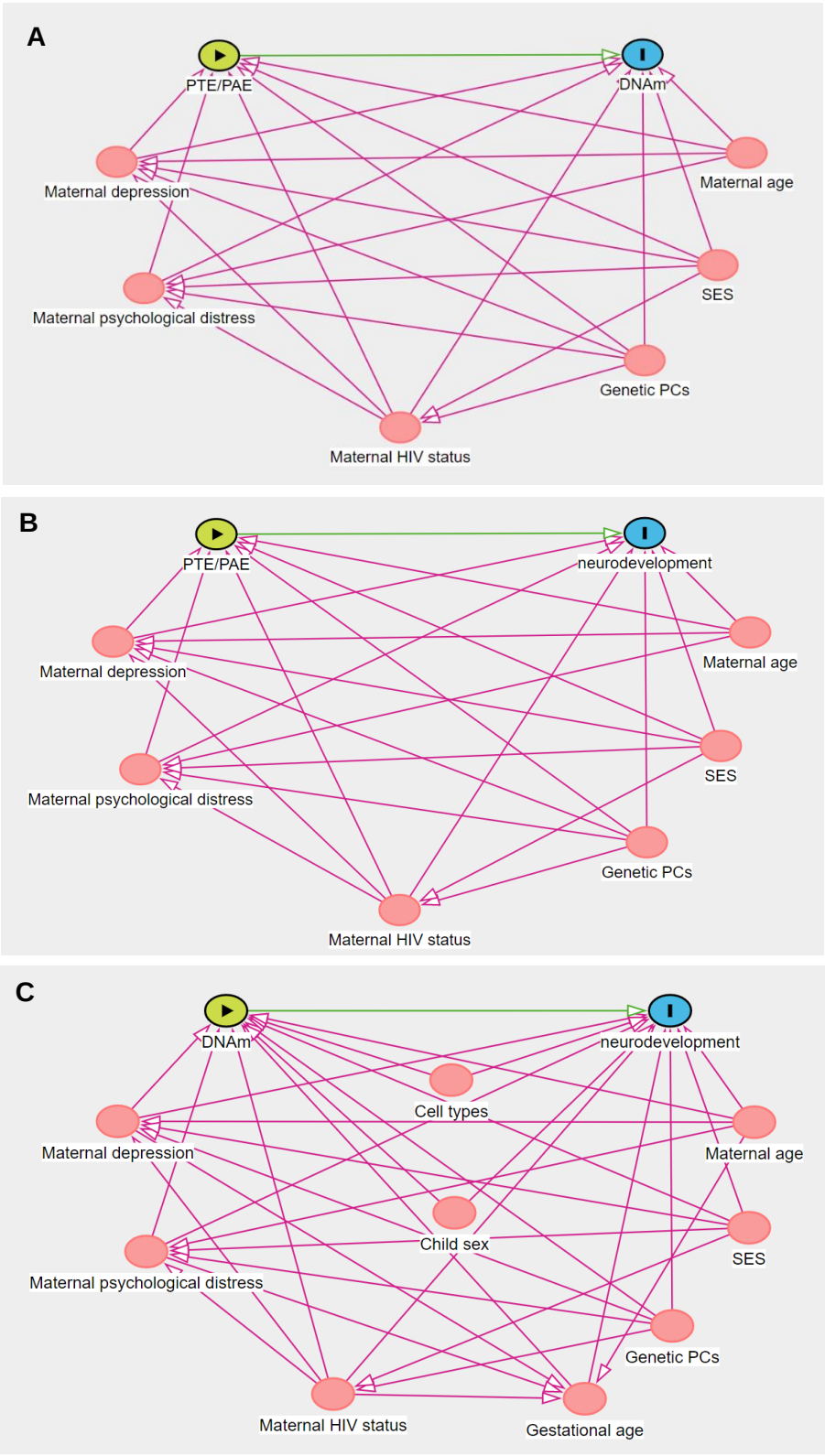

Figure S1: **Directed acyclic graphs (DAGs) used for confounding assessment. S1A)** Exposure-mediator DAG. **S1B)** Exposure-outcome DAG. **S1C)** Mediator-outcome DAG

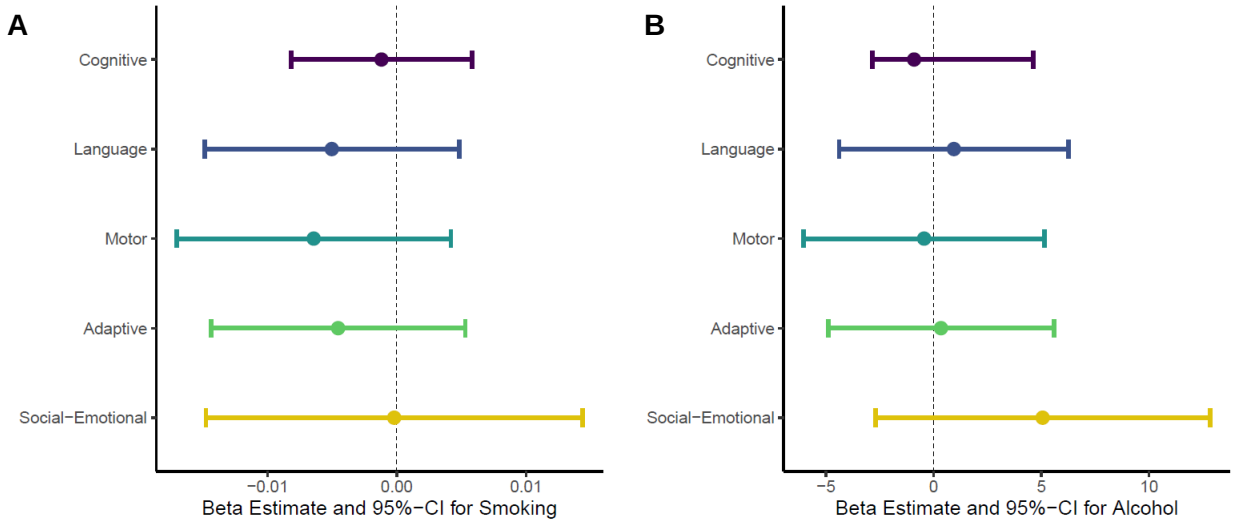

Figure S2: **Association of PTE and PAE on neurodevelopment domains at 24 months.** Models were adjusted for paternal SES, maternal depression, maternal psychological distress, gestational age, maternal age, maternal HIV status, cell-type proportions, and the first 5 genetic principal components. **S2A)** Association of PTE on neurodevelopment domains, additionally adjusted for PAE. **S2B)** Association of PAE on neurodevelopment domains, additionally adjusted for PTE.