Supplemental Material

Prenatal Exposure to DDT and Pyrethroids for Malaria Control and Child Neurodevelopment: The VHEMBE Cohort, South Africa

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Table S1. Wet weight (ug/L) and creatinine-adjusted (g/L) maternal urinary concentrations of pyrethroid metabolites, VHEMBE study, Limpopo South Africa.

| Pyrethroid metabolite | n   | % Detected | % Quantifiable | Geo. Mean ± GSD | Min   | 10     | 25     | 50     | 75     | 90     | Max     |
|-----------------------|-----|------------|----------------|-----------------|-------|--------|--------|--------|--------|--------|---------|
| **Wet Weight Concentrations** |     |            |                |                 |       |        |        |        |        |        |         |
| cis-DBCA              | 695 | 100        | 99.6           | 0.227 ± 3.42    | 0.005 | 0.050  | 0.099  | 0.226  | 0.483  | 1.141  | 18.416  |
| cis-DCCA              | 695 | 100        | 99.9           | 0.312 ± 2.96    | 0.015 | 0.085  | 0.154  | 0.305  | 0.611  | 1.058  | 104.744 |
| trans-DCCA            | 695 | 100        | 99.6           | 0.364 ± 3.44    | 0.008 | 0.079  | 0.161  | 0.347  | 0.805  | 1.526  | 134.473 |
| 3-PBA                 | 694 | 100        | 100            | 0.724 ± 2.81    | 0.022 | 0.215  | 0.380  | 0.711  | 1.397  | 2.434  | 59.724  |
| 4-F-3 PBA             | 672 | 12.5       | 7.7            | N/A             | <LOD  <LOD <LOD <LOD <LOD 0.008 | 0.293  |
| **Creatinine-Adjusted Concentrations** |     |            |                |                 |       |        |        |        |        |        |         |
| cis-DBCA              | 695 | 100        | 99.6           | 0.181 ± 3.08    | 0.008 | 0.044  | 0.075  | 0.167  | 0.377  | 0.834  | 8.213   |
| cis-DCCA              | 695 | 100        | 99.9           | 0.248 ± 2.51    | 0.034 | 0.086  | 0.137  | 0.234  | 0.400  | 0.726  | 171.788 |
| trans-DCCA            | 695 | 100        | 99.6           | 0.289 ± 3.04    | 0.017 | 0.074  | 0.142  | 0.272  | 0.527  | 1.098  | 220.545 |
| 3-PBA                 | 694 | 100        | 100            | 0.576 ± 2.35    | 0.047 | 0.211  | 0.339  | 0.541  | 0.937  | 1.559  | 74.151  |
| 4-F-3 PBA             | 672 | 12.5       | 7.7            | N/A             | <LOD  <LOD <LOD <LOD <LOD 0.009 | 0.293  |

GSD = Geometric Standard Deviation

aDetection limits are 0.0025 ug/L for cis-DBCA, 0.0045 ug/L for cis-DCCA, 0.0038 ug/L for trans-DCCA, 0.0047 ug/L for 3-PBA, and 0.005 ug/L for 4-F-3 PBA.

bQuantification limits are 0.0082 ug/L for cis-DBCA, 0.015 ug/L for cis-DCCA, 0.013 ug/L for trans-DCCA, 0.016 ug/L for 3-PBA, and 0.011ug/L for 4-F-3 PBA.
Table S2. Pearson correlation coefficients for maternal serum concentrations of \( p,p'-\text{DDT} \) and \( p,p'-\text{DDE} \) (\( \log_{10} \) transformed; lipid-adjusted), and urinary concentrations of pyrethroid metabolites (\( \log_{10} \) transformed; specific-gravity adjusted), VHEMBE study (n=705), Limpopo South Africa.

| Compound   | \( p,p'-\text{DDT} \) | \( p,p'-\text{DDE} \) | \( \text{cis-DBCA} \) | \( \text{cis-DCCA} \) | \( \text{trans-DCCA} \) | \( 3\text{PBA} \) |
|------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------------|
| \( p,p'-\text{DDT} \) | -                     | 0.85 (p<0.001)        | 0.02 (p=0.54)         | 0.04 (p=0.29)         | 0.02 (p=0.53)       | 0.04 (p=0.24)    |
| \( p,p'-\text{DDE} \) | -                     | -                     | -0.03 (p=0.48)        | 0.03 (p=0.49)         | 0.02 (p=0.65)       | 0.03 (p=0.48)    |
| \( \text{cis-DBCA} \) | -                     | -                     | -                     | 0.46 (p<0.001)        | 0.47 (p<0.001)      | 0.62 (p<0.001)   |
| \( \text{cis-DCCA} \) | -                     | -                     | -                     | -                     | 0.90 (p<0.001)      | 0.88 (p<0.001)   |
| \( \text{trans-DCCA} \) | -                     | -                     | -                     | -                     | -                     | 0.87 (p<0.001)   |
Table S3. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal urinary pyrethroid metabolite concentrations measured before delivery only (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

| BSID Measure                  | cis-DBCA β (95% CI) | cis-DCCA β (95% CI) | trans-DCCA β (95% CI) | 3PBA β (95% CI) |
|-------------------------------|---------------------|---------------------|-----------------------|-----------------|
| **At 1 Year (n=425)**         |                     |                     |                       |                 |
| Cognitive                     | -0.02 (-0.41, 0.38) | -0.23 (-0.60, 0.14) | -0.19 (-0.51, 0.12)  | -0.21 (-0.59, 0.17) |
| Receptive Communication      | 0.13 (-0.17, 0.43)  | -0.03 (-0.36, 0.29) | -0.11 (-0.41, 0.20)  | -0.06 (-0.41, 0.30) |
| Expressive Communication     | -0.23 (-0.61, 0.15) | -0.20 (-0.56, 0.17) | -0.20 (-0.51, 0.11)  | -0.19 (-0.55, 0.18) |
| Fine Motor                   | -0.13 (-0.54, 0.28) | -0.47 (-0.86, -0.07) | -0.42 (-0.80, -0.04) | -0.43 (-0.84, -0.01) |
| Gross Motor                  | 0.07 (-0.43, 0.57)  | 0.03 (-0.46, 0.53)  | 0.03 (-0.42, 0.48)   | 0.06 (-0.46, 0.58) |
| Language Composite           | -0.32 (-1.84, 1.20) | -0.70 (-2.23, 0.84) | -0.87 (-2.21, 0.47)  | -0.72 (-2.31, 0.87) |
| Motor Composite              | -0.19 (-2.28, 1.91) | -1.30 (-3.39, 0.80) | -1.15 (-3.14, 0.84)  | -1.09 (-3.30, 1.12) |
| Social-Emotional             | -0.11 (-0.68, 0.46) | -0.52 (-1.18, 0.13) | -0.45 (-1.02, 0.12)  | -0.53 (-1.20, 0.13) |
| **At 2 Years (n=418)**       |                     |                     |                       |                 |
| Cognitive                     | -0.20 (-0.47, 0.07) | -0.29 (-0.64, 0.06) | -0.28 (-0.58, 0.03)  | -0.29 (-0.61, 0.04) |
| Receptive Communication      | -0.31 (-0.62, -0.01) | -0.10 (-0.45, 0.25) | -0.24 (-0.54, 0.06)  | -0.18 (-0.53, 0.18) |
| Expressive Communication     | -0.61 (-1.04, -0.17) | -0.31 (-0.81, 0.19) | -0.53 (-0.96, -0.10) | -0.42 (-0.95, 0.10) |
| Fine Motor                   | -0.05 (-0.36, 0.26) | 0.13 (-0.23, 0.48)  | 0.10 (-0.22, 0.42)   | 0.12 (-0.26, 0.49) |
| Gross Motor                  | -0.32 (-0.61, -0.04) | -0.06 (-0.42, 0.29) | -0.11 (-0.42, 0.19)  | -0.05 (-0.42, 0.32) |
| Language Composite           | -2.64 (-4.57, -0.71) | -1.19 (-3.46, 1.08) | -2.23 (-4.17, -0.29) | -1.74 (-4.08, 0.61) |
| Motor Composite              | -1.15 (-2.55, 0.26) | 0.18 (-1.50, 1.86)  | -0.04 (-1.54, 1.47)  | 0.19 (-1.59, 1.97) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal urinary pyrethroid metabolite concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; psychometrician at the time of exam; and urine sample collection before or after delivery.

*p<0.05
Table S4. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal \( p,p' \)-DDT and \( p,p' \)-DDE serum concentrations (log\(_{10}\) transformed; lipid-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (BSID) (3\(^{rd}\) edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Preterm births removed as a covariate in the models.

| BSID Measure            | \( p,p' \)-DDT \( \beta \) (95% CI) | \( p,p' \)-DDE \( \beta \) (95% CI) |
|------------------------|-------------------------------------|-------------------------------------|
| At 1 Year (n=689)       |                                     |                                     |
| Cognitive              | 0.15 (-0.02, 0.33)                  | 0.24 (0.05, 0.43)*                  |
| Receptive Communication| -0.02 (-0.17, 0.13)                 | 0.00 (-0.19, 0.19)                 |
| Expressive Communication| -0.09 (-0.26, 0.09)                | -0.04 (-0.25, 0.18)                |
| Fine Motor             | -0.02 (-0.24, 0.19)                 | 0.04 (-0.19, 0.27)                 |
| Gross Motor            | 0.11 (-0.12, 0.35)                  | 0.08 (-0.20, 0.36)                 |
| Language Composite     | -0.33 (-1.11, 0.45)                 | -0.12 (-1.09, 0.85)                |
| Motor Composite        | 0.24 (-0.83, 1.31)                  | 0.35 (-0.89, 1.59)                 |
| Social-Emotional\( ^a \)| 0.08 (-0.21, 0.36)                  | 0.25 (-0.09, 0.59)                 |
| At 2 years (n=681)      |                                     |                                     |
| Cognitive              | -0.04 (-0.19, 0.10)                 | 0.05 (-0.13, 0.24)                 |
| Receptive Communication| 0.00 (-0.14, 0.15)                  | 0.03 (-0.15, 0.22)                 |
| Expressive Communication| -0.05 (-0.27, 0.17)                | 0.06 (-0.23, 0.35)                 |
| Fine Motor             | -0.08 (-0.24, 0.09)                 | 0.02 (-0.19, 0.22)                 |
| Gross Motor            | 0.02 (-0.11, 0.16)                  | 0.06 (-0.10, 0.23)                 |
| Language Composite     | -0.12 (-1.07, 0.83)                 | 0.30 (-0.92, 1.52)                 |
| Motor Composite        | -0.16 (-0.91, 0.58)                 | 0.23 (-0.68, 1.13)                 |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven’s Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; and psychometrician.

\( ^a \)Models include 696 participants.

\( ^* \)p<0.05
Table S5. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal urinary pyrethroid metabolite concentration (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Preterm births removed as a covariate in the models.

| BSID Measure       | cis-DBCA (β (95% CI)) | cis-DCCA (β (95% CI)) | trans-DCCA (β (95% CI)) | 3PBAa (β (95% CI)) |
|--------------------|-----------------------|-----------------------|-------------------------|--------------------|
| At 1 year (n=681)  |                       |                       |                         |                    |
| Cognitive          | 0.05 (-0.26, 0.36)    | 0.01 (-0.30, 0.33)    | 0.02 (-0.25, 0.30)      | 0.03 (-0.31, 0.37) |
| Receptive Communication | 0.13 (-0.12, 0.38) | 0.04 (-0.24, 0.33)    | -0.02 (-0.28, 0.24)     | 0.09 (-0.22, 0.41) |
| Expressive Communication | -0.21 (-0.50, 0.08) | -0.06 (-0.35, 0.23)  | -0.09 (-0.34, 0.16)     | -0.10 (-0.41, 0.20) |
| Fine Motor         | 0.09 (-0.25, 0.42)    | -0.08 (-0.47, 0.30)   | -0.07 (-0.42, 0.27)     | -0.01 (-0.41, 0.40) |
| Gross Motor        | 0.10 (-0.29, 0.50)    | 0.36 (-0.10, 0.81)    | 0.24 (-0.17, 0.64)      | 0.27 (-0.21, 0.76)  |
| Language Composite | -0.26 (-1.50, 0.99)   | -0.08 (-1.39, 1.23)   | -0.31 (-1.47, 0.85)     | -0.06 (-1.47, 1.35) |
| Motor Composite    | 0.59 (-1.15, 2.33)    | 0.84 (-1.22, 2.90)    | 0.52 (-1.33, 2.36)      | 0.82 (-1.35, 2.98)  |
| Social-Emotionalb  | -0.19 (-0.64, 0.26)   | -0.63 (-1.14, -0.12)  | -0.48 (-0.92, -0.04)    | -0.58 (-1.10, -0.05) |
| At 2 years (n=671) |                       |                       |                         |                    |
| Cognitive          | -0.01 (-0.24, 0.22)   | 0.03 (-0.27, 0.34)    | -0.03 (-0.29, 0.24)     | 0.04 (-0.26, 0.33)  |
| Receptive Communication | -0.21 (-0.45, 0.03) | 0.07 (-0.21, 0.35)    | -0.10 (-0.34, 0.15)     | -0.07 (-0.36, 0.23) |
| Expressive Communication | -0.40 (-0.76, -0.03)  | 0.00 (-0.41, 0.41)   | -0.24 (-0.59, 0.12)     | -0.23 (-0.67, 0.21) |
| Fine Motor         | 0.16 (-0.12, 0.43)    | 0.31 (-0.02, 0.64)    | 0.18 (-0.12, 0.47)      | 0.31 (-0.04, 0.65)  |
| Gross Motor        | -0.19 (-0.43, 0.05)   | 0.08 (-0.22, 0.38)    | -0.05 (-0.31, 0.22)     | 0.03 (-0.30, 0.36)  |
| Language Composite | -1.72 (-3.33, -0.11)  | 0.23 (-1.62, 2.07)    | -0.95 (-2.55, 0.65)     | -0.82 (-2.78, 1.15) |
| Motor Composite    | -0.11 (-1.38, 1.16)   | 1.19 (-0.38, 2.76)    | 0.39 (-1.02, 1.80)      | 0.99 (-0.68, 2.66)  |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal urinary pyrethroid metabolite concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven’s Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; psychometrician; and time of urine collection (before or after delivery).

a Due to 1 missing value, models with 3PBA had 680 participants at 1 year and 670 participants at 2 years.

b Social-Emotional outcome models had 688 participants for cis-DBCA, cis-DCCA, and trans-DCCA exposures, and 687 participants for 3PBA.

*p<0.05
Table S6. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal \( p,p' \)-DDT and \( p,p' \)-DDE serum concentrations (log\(_{10}\) transformed; lipid-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (BSID) (3\(^{rd}\) edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Maternal HIV status included in models.

| BSID Measure                  | \( p,p' \)-DDT β (95% CI) | \( p,p' \)-DDE β (95% CI) |
|-------------------------------|-----------------------------|---------------------------|
| At 1 Year (n=687)             |                             |                           |
| Cognitive                     | 0.16 (-0.02, 0.33)          | 0.24 (0.05, 0.43)         |
| Receptive Communication       | -0.02 (-0.17, 0.13)         | 0.00 (-0.19, 0.19)        |
| Expressive Communication      | -0.09 (-0.27, 0.09)         | -0.04 (-0.26, 0.17)       |
| Fine Motor                    | -0.02 (-0.23, 0.20)         | 0.05 (-0.19, 0.28)        |
| Gross Motor                   | 0.11 (-0.12, 0.35)          | 0.08 (-0.20, 0.36)        |
| Language Composite            | -0.32 (-1.11, 0.46)         | -0.13 (-1.10, 0.84)       |
| Motor Composite               | 0.26 (-0.82, 1.33)          | 0.37 (-0.87, 1.62)        |
| Social-Emotional\(^a\)        | 0.08 (-0.20, 0.37)          | 0.25 (-0.09, 0.59)        |
| At 2 years (n=678)            |                             |                           |
| Cognitive                     | -0.04 (-0.19, 0.10)         | 0.05 (-0.13, 0.23)        |
| Receptive Communication       | 0.00 (-0.14, 0.15)          | 0.03 (-0.15, 0.22)        |
| Expressive Communication      | -0.06 (-0.28, 0.16)         | 0.06 (-0.23, 0.34)        |
| Fine Motor                    | -0.07 (-0.24, 0.10)         | 0.02 (-0.19, 0.23)        |
| Gross Motor                   | 0.03 (-0.11, 0.16)          | 0.06 (-0.11, 0.23)        |
| Language Composite            | -0.15 (-1.10, 0.80)         | 0.28 (-0.94, 1.51)        |
| Motor Composite               | -0.14 (-0.88, 0.60)         | 0.23 (-0.68, 1.14)        |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, HIV status, and poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; and psychometrician.

\(^a\) Models include 646 participants.

\(^*\) p<0.05
Table S7. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal urinary pyrethroid metabolite concentration (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Maternal HIV status included in models.

| BSID Measure                  | cis-DBCA          | cis-DCCA          | trans-DCCA         | 3PBA\(^a\)         |
|-------------------------------|-------------------|-------------------|--------------------|--------------------|
|                               | β (95% CI)        | β (95% CI)        | β (95% CI)         | β (95% CI)         |
| At 1 year (n=679)             |                   |                   |                    |                    |
| Cognitive                     | 0.05 (-0.26, 0.36)| 0.01 (-0.30, 0.33)| 0.02 (-0.26, 0.30)| 0.03 (-0.31, 0.38) |
| Receptive Communication       | 0.13 (-0.12, 0.38)| 0.04 (-0.24, 0.32)| -0.03 (-0.29, 0.23)| 0.08 (-0.24, 0.39) |
| Expressive Communication      | -0.20 (-0.50, 0.10)| -0.06 (-0.36, 0.23)| -0.09 (-0.34, 0.16)| -0.11 (-0.41, 0.20) |
| Fine Motor                    | 0.08 (-0.26, 0.42)| -0.08 (-0.46, 0.31)| -0.07 (-0.42, 0.27)| 0.00 (-0.40, 0.41) |
| Gross Motor                   | 0.13 (-0.27, 0.52)| 0.35 (-0.11, 0.81)| 0.23 (-0.17, 0.64)| 0.27 (-0.22, 0.75) |
| Language Composite            | -0.23 (-1.48, 1.02)| -0.09 (-1.39, 1.22)| -0.34 (-1.49, 0.82)| -0.12 (-1.52, 1.29) |
| Motor Composite               | 0.63 (-1.12, 2.39)| 0.83 (-1.23, 2.89)| 0.50 (-1.35, 2.34)| 0.83 (-1.34, 2.99) |
| Social-Emotional\(^b\)        | -0.17 (-0.61, 0.28)| -0.64 (-1.14, -0.13)*| -0.49 (-0.93, -0.06)*| -0.60 (-1.13, -0.08)* |
| At 2 years (n=669)            |                   |                   |                    |                    |
| Cognitive                     | 0.00 (-0.23, 0.23)| 0.04 (-0.27, 0.34)| -0.02 (-0.29, 0.24)| 0.05 (-0.25, 0.35) |
| Receptive Communication       | -0.21 (-0.45, 0.04)| 0.07 (-0.21, 0.36)| -0.09 (-0.34, 0.15)| -0.05 (-0.35, 0.25) |
| Expressive Communication      | -0.41 (-0.77, -0.04)*| 0.01 (-0.40, 0.42)| -0.22 (-0.58, 0.13)| -0.22 (-0.66, 0.22) |
| Fine Motor                    | 0.16 (-0.12, 0.44)| 0.31 (-0.02, 0.64)| 0.17 (-0.13, 0.47)| 0.30 (-0.05, 0.65) |
| Gross Motor                   | -0.17 (-0.42, 0.07)| 0.08 (-0.22, 0.38)| -0.05 (-0.31, 0.22)| 0.03 (-0.30, 0.36) |
| Language Composite            | -1.74 (-3.35, -0.12)*| 0.24 (-1.61, 2.09)| -0.90 (-2.50, 0.70)| -0.75 (-2.72, 1.21) |
| Motor Composite               | -0.07 (-1.35, 1.21)| 1.18 (-0.39, 2.75)| 0.36 (-1.04, 1.76)| 0.98 (-0.69, 2.65) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal urinary pyrethroid metabolite concentrations. Models adjusted for maternal education, age, marital status, HIV status, and poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; psychometrician; and time of urine collection (before or after delivery).

\(^a\) Due to 1 missing value, models with 3PBA had 678 participants at 1 year and 668 participants at 2 years.

\(^b\) Social-Emotional outcome models had 688 participants for cis-DBCA, cis-DCCA, and trans-DCCA exposures, and 687 participants for 3PBA.

\(*p<0.05\)
Table S8. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal \( p,p' \)-DDT and \( p,p' \)-DDE serum concentrations (log\(_{10}\) transformed; lipid-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (BSID) (3rd edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with blood lead measurements; child blood lead controlled for in models.

| BSID Measure                  | \( p,p' \)-DDT \( \beta \) (95% CI) | \( p,p' \)-DDE \( \beta \) (95% CI) |
|-------------------------------|-------------------------------------|-------------------------------------|
| At 1 Year (n=494)             |                                     |                                     |
| Cognitive                     | 0.25 (0.04, 0.45)*                  | 0.23 (-0.01, 0.46)                 |
| Receptive Communication       | -0.08 (-0.26, 0.11)                 | -0.03 (-0.26, 0.19)                |
| Expressive Communication      | -0.10 (-0.32, 0.11)                 | -0.05 (-0.32, 0.22)                |
| Fine Motor                    | -0.01 (-0.29, 0.27)                 | 0.07 (-0.23, 0.36)                 |
| Gross Motor                   | 0.19 (-0.08, 0.47)                  | 0.15 (-0.19, 0.49)                 |
| Language Composite            | -0.52 (-1.44, 0.39)                 | -0.24 (-1.40, 0.92)                |
| Motor Composite               | 0.52 (-0.78, 1.83)                  | 0.63 (-0.92, 2.19)                 |
| Social-Emotional\(^a\)        | 0.13 (-0.24, 0.50)                 | 0.25 (-0.19, 0.68)                 |
| At 2 years (n=480)            |                                     |                                     |
| Cognitive                     | -0.02 (-0.20, 0.15)                 | 0.07 (-0.15, 0.29)                 |
| Receptive Communication       | -0.06 (-0.24, 0.13)                 | -0.04 (-0.27, 0.18)                |
| Expressive Communication      | -0.20 (-0.46, 0.05)                 | -0.16 (-0.50, 0.18)                |
| Fine Motor                    | -0.08 (-0.29, 0.13)                 | 0.00 (-0.24, 0.25)                 |
| Gross Motor                   | -0.04 (-0.20, 0.12)                 | -0.05 (-0.26, 0.16)                |
| Language Composite            | -0.74 (-1.89, 0.42)                 | -0.57 (-2.04, 0.90)                |
| Motor Composite               | -0.36 (-1.28, 0.55)                 | -0.14 (-1.23, 0.95)                |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven’s Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; child’s blood lead at 1 year; and psychometrician.

\(^a\)Models include 497 participants.

\(^*\)\( p<0.05 \)
Table S9. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal \( p,p'\)-DDT and \( p,p'\)-DDE serum concentrations (log\(_{10}\) transformed; lipid-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (BSID) (3\(^{rd}\) edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with blood lead measurements; child blood lead levels are not controlled for in models.(for comparison with Table S8).

| BSID Measure              | \( p.p'\)-DDT | \( p,p'\)-DDE |
|---------------------------|----------------|---------------|
|                           | β (95% CI)     | β (95% CI)    |
| **At 1 Year (n=494)**    |                |               |
| Cognitive                 | 0.24 (0.04, 0.45)\(^*\) | 0.23 (-0.01, 0.46) |
| Receptive Communication   | -0.07 (-0.25, 0.11) | -0.03 (-0.25, 0.20) |
| Expressive Communication  | -0.10 (-0.31, 0.12) | -0.05 (-0.32, 0.22) |
| Fine Motor                | 0.01 (-0.27, 0.29) | 0.08 (-0.22, 0.37) |
| Gross Motor               | 0.22 (-0.05, 0.50) | 0.17 (-0.18, 0.51) |
| Language Composite        | -0.48 (-1.40, 0.44) | -0.22 (-1.39, 0.96) |
| Motor Composite           | 0.67 (-0.64, 1.97) | 0.71 (-0.85, 2.28) |
| Social-Emotional\(^a\)    | 0.12 (-0.25, 0.49) | 0.24 (-0.19, 0.67) |
| **At 2 years (n=480)**   |                |               |
| Cognitive                 | -0.02 (-0.19, 0.16) | 0.08 (-0.15, 0.30) |
| Receptive Communication   | -0.04 (-0.23, 0.14) | -0.04 (-0.26, 0.19) |
| Expressive Communication  | -0.20 (-0.45, 0.06) | -0.16 (-0.50, 0.18) |
| Fine Motor                | -0.08 (-0.29, 0.13) | 0.00 (-0.24, 0.25) |
| Gross Motor               | -0.03 (-0.19, 0.13) | -0.04 (-0.25, 0.16) |
| Language Composite        | -0.68 (-1.83, 0.46) | -0.55 (-2.01, 0.92) |
| Motor Composite           | -0.33 (-1.25, 0.59) | -0.13 (-1.22, 0.96) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; and psychometrician.

\(^a\)Models include 497 participants.

\(^*\)p<0.05
Table S10. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal urinary pyrethroid metabolite concentration (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with lead measurements; child lead level controlled for in models.

| BSID Measure          | cis-DBCA β (95% CI) | cis-DCCA β (95% CI) | trans-DCCA β (95% CI) | 3PBAa β (95% CI) |
|-----------------------|---------------------|---------------------|----------------------|------------------|
| **At 1 year (n=491)** |                     |                     |                      |                  |
| Cognitive             | 0.22 (-0.16, 0.59)  | 0.02 (-0.37, 0.41)  | 0.05 (-0.27, 0.38)  | 0.10 (-0.33, 0.52) |
| Receptive Communication| 0.16 (-0.15, 0.46)  | -0.07 (-0.43, 0.28) | -0.08 (-0.39, 0.24) | 0.05 (-0.35, 0.45) |
| Expressive Communication| -0.23 (-0.61, 0.15) | -0.10 (-0.45, 0.26) | -0.07 (-0.37, 0.23) | -0.07 (-0.46, 0.31) |
| Fine Motor            | 0.12 (-0.30, 0.54)  | 0.00 (-0.47, 0.47)  | 0.03 (-0.39, 0.44)  | 0.14 (-0.37, 0.65) |
| Gross Motor           | 0.33 (-0.16, 0.82)  | 0.59 (0.05, 1.14)   | 0.58 (0.10, 1.05)   | 0.63 (0.04, 1.21)  |
| Language Composite    | -0.22 (-1.76, 1.33) | -0.48 (-2.04, 1.08) | -0.36 (-1.74, 1.01) | -0.06 (-1.82, 1.69) |
| Motor Composite       | 1.39 (-0.79, 3.56)  | 1.82 (-0.70, 4.34)  | 1.86 (-0.32, 4.05)  | 2.35 (-0.33, 5.02) |
| Social-Emotionalb     | -0.24 (-0.77, 0.29) | -0.81 (-1.39, -0.24) | -0.62 (-1.12, -0.11) | -0.64 (-1.26, -0.01) |

| **At 2 years (n=477)** |                     |                     |                      |                  |
| Cognitive             | 0.03 (-0.26, 0.32)  | 0.11 (-0.27, 0.50)  | 0.08 (-0.23, 0.40)  | 0.10 (-0.27, 0.47) |
| Receptive Communication| -0.21 (-0.52, 0.09) | 0.11 (-0.23, 0.46)  | -0.04 (-0.34, 0.26) | -0.01 (-0.38, 0.37) |
| Expressive Communication| -0.23 (-0.67, 0.21) | 0.15 (-0.36, 0.66)  | -0.14 (-0.57, 0.29) | -0.07 (-0.61, 0.47) |
| Fine Motor            | 0.17 (-0.18, 0.51)  | 0.37 (-0.02, 0.76)  | 0.26 (-0.10, 0.61)  | 0.39 (-0.02, 0.80) |
| Gross Motor           | -0.21 (-0.49, 0.08) | 0.08 (-0.28, 0.44)  | 0.05 (-0.26, 0.37)  | 0.08 (-0.32, 0.48) |
| Language Composite    | -1.26 (-3.24, 0.72) | 0.78 (-1.51, 3.07)  | -0.51 (-2.49, 1.47) | -0.18 (-2.62, 2.27) |
| Motor Composite       | -0.12 (-1.67, 1.43) | 1.36 (-0.58, 3.30)  | 0.95 (-0.79, 2.70)  | 1.42 (-0.66, 3.49) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal urinary pyrethroid metabolite concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; child’s blood lead at 1 year; psychometrician; and time of urine collection (before or after delivery).

a Due to 1 missing value, models with 3PBA had 490 participants at 1 year and 476 participants at 2 years.

b Social-Emotional outcome models had 494 participants for cis-DBCA, cis-DCCA, and trans-DCCA exposures, and 493 participants for 3PBA.

p<0.05
Table S11. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal urinary pyrethroid metabolite concentration (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with lead measurements; child lead level not controlled for in models. (for comparison with Table S10).

| BSID Measure       | cis-DBCA β (95% CI) | cis-DCCA β (95% CI) | trans-DCCA β (95% CI) | 3PBA<sup>a</sup> β (95% CI) |
|--------------------|---------------------|---------------------|-----------------------|-----------------------------|
| At 1 year (n=491)  |                     |                     |                       |                             |
| Cognitive          | 0.22 (-0.16, 0.59)  | 0.02 (-0.37, 0.41)  | 0.05 (-0.28, 0.38)    | 0.09 (-0.33, 0.52)          |
| Receptive Communication | 0.16 (-0.15, 0.47) | -0.07 (-0.42, 0.29) | -0.07 (-0.39, 0.25)   | 0.05 (-0.35, 0.46)          |
| Expressive Communication | -0.23 (-0.61, 0.15) | -0.09 (-0.45, 0.26) | -0.06 (-0.36, 0.24)   | -0.07 (-0.45, 0.31)         |
| Fine Motor         | 0.13 (-0.30, 0.55)  | 0.01 (-0.46, 0.48)  | 0.04 (-0.37, 0.46)    | 0.15 (-0.36, 0.67)          |
| Gross Motor        | 0.34 (-0.15, 0.82)  | 0.62 (0.07, 1.16)<sup>*</sup> | 0.61 (0.13, 1.08)<sup>*</sup> | 0.65 (0.07, 1.23)<sup>*</sup> |
| Language Composite | -0.21 (-1.76, 1.34) | -0.44 (-2.01, 1.12) | -0.32 (-1.70, 1.06)   | -0.03 (-1.80, 1.73)         |
| Motor Composite    | 1.41 (-0.77, 3.59)  | 1.92 (-0.60, 4.45)  | 1.99 (-0.21, 4.19)    | 2.44 (-0.25, 5.13)          |
| Social-Emotional<sup>b</sup> | -0.24 (-0.78, 0.29) | -0.82 (-1.39, -0.24)<sup>*</sup> | -0.62 (-1.13, -0.12)<sup>*</sup> | -0.64 (-1.27, -0.02)<sup>*</sup> |
| At 2 years (n=477) |                     |                     |                       |                             |
| Cognitive          | 0.03 (-0.26, 0.32)  | 0.12 (-0.26, 0.50)  | 0.09 (-0.23, 0.41)    | 0.11 (-0.26, 0.48)          |
| Receptive Communication | -0.21 (-0.51, 0.10) | 0.12 (-0.22, 0.47)  | -0.03 (-0.33, 0.27)   | 0.01 (-0.37, 0.38)          |
| Expressive Communication | -0.23 (-0.67, 0.21) | 0.16 (-0.36, 0.67)  | -0.13 (-0.57, 0.30)   | -0.06 (-0.60, 0.48)         |
| Fine Motor         | 0.17 (-0.18, 0.51)  | 0.37 (-0.03, 0.76)  | 0.25 (-0.11, 0.61)    | 0.38 (-0.03, 0.80)          |
| Gross Motor        | -0.20 (-0.48, 0.08) | 0.09 (-0.27, 0.45)  | 0.07 (-0.25, 0.39)    | 0.09 (-0.31, 0.49)          |
| Language Composite | -1.23 (-3.22, 0.75) | 0.83 (-1.47, 3.12)  | -0.45 (-2.44, 1.53)   | -0.13 (-2.57, 2.32)         |
| Motor Composite    | -0.11 (-1.67, 1.45) | 1.38 (-0.56, 3.33)  | 0.98 (-0.78, 2.74)    | 1.44 (-0.64, 3.52)          |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal urinary pyrethroid metabolite concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; psychometrician; and time of urine collection (before or after delivery).

<sup>a</sup> Due to 1 missing value, models with 3PBA had 490 participants at 1 year and 476 participants at 2 years.

<sup>b</sup> Social-Emotional outcome models had 494 participants for cis-DBCA, cis-DCCA, and trans-DCCA exposures, and 493 participants for 3PBA.

<sup>*</sup>p<0.05
Table S12. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal p,p'-DDT and p,p'-DDE serum concentrations (log_{10} transformed; lipid-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (BSID) (3rd edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with hemoglobin measurements at 1-year; child hemoglobin level controlled for in models.

| BSID Measure               | p,p'-DDT  | p,p'-DDE  |
|----------------------------|-----------|-----------|
|                            | β (95% CI)| β (95% CI)|
| **At 1 Year (n=570)**      |           |           |
| Cognitive                  | 0.16 (-0.04, 0.35) | 0.19 (-0.02, 0.40) |
| Receptive Communication    | -0.05 (-0.21, 0.11) | -0.04 (-0.25, 0.16) |
| Expressive Communication   | -0.12 (-0.32, 0.08) | -0.08 (-0.33, 0.17) |
| Fine Motor                 | -0.04 (-0.29, 0.21) | -0.01 (-0.28, 0.26) |
| Gross Motor                | 0.17 (-0.10, 0.43) | 0.12 (-0.19, 0.43) |
| Language Composite         | -0.52 (-1.37, 0.33) | -0.36 (-1.43, 0.72) |
| Motor Composite            | 0.34 (-0.89, 1.58) | 0.33 (-1.11, 1.76) |
| Social-Emotional<sup>a</sup> | 0.02 (-0.30, 0.34) | 0.13 (-0.26, 0.51) |
| **At 2 years (n=553)**     |           |           |
| Cognitive                  | -0.07 (-0.24, 0.09) | 0.02 (-0.19, 0.23) |
| Receptive Communication    | -0.04 (-0.21, 0.12) | -0.04 (-0.24, 0.17) |
| Expressive Communication   | -0.20 (-0.44, 0.03) | -0.13 (-0.46, 0.20) |
| Fine Motor                 | -0.09 (-0.28, 0.10) | 0.00 (-0.24, 0.23) |
| Gross Motor                | 0.01 (-0.14, 0.16) | 0.02 (-0.16, 0.21) |
| Language Composite         | -0.70 (-1.75, 0.35) | -0.47 (-1.85, 0.92) |
| Motor Composite            | -0.24 (-1.06, 0.59) | 0.06 (-0.96, 1.07) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; child hemoglobin at 1 year; and psychometrician.

<sup>a</sup>Models include 573 participants.
Table S13. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal \( p,p' \)-DDT and \( p,p' \)-DDE serum concentrations (log_{10} transformed; lipid-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (BSID) (3rd edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with hemoglobin measurements at 1-year; child hemoglobin level not controlled for in models. (for comparison to Table S12).

| BSID Measure          | \( p,p' \)-DDT β (95% CI) | \( p,p' \)-DDE β (95% CI) |
|-----------------------|-----------------------------|-----------------------------|
| **At 1 Year (n=570)** |                             |                             |
| Cognitive             | 0.16 (-0.04, 0.35)          | 0.19 (-0.02, 0.40)          |
| Receptive Communication| -0.05 (-0.21, 0.11)         | -0.04 (-0.25, 0.16)         |
| Expressive Communication| -0.12 (-0.32, 0.08)       | -0.08 (-0.33, 0.17)         |
| Fine Motor            | -0.04 (-0.29, 0.21)         | -0.01 (-0.28, 0.26)         |
| Gross Motor           | 0.16 (-0.10, 0.43)          | 0.12 (-0.19, 0.43)          |
| Language Composite    | -0.52 (-1.37, 0.33)         | -0.36 (-1.44, 0.72)         |
| Motor Composite       | 0.34 (-0.89, 1.57)          | 0.32 (-1.12, 1.76)          |
| Social-Emotional\(^a\) | 0.02 (-0.30, 0.35)          | 0.13 (-0.26, 0.52)          |
| **At 2 years (n=553)**|                             |                             |
| Cognitive             | -0.08 (-0.24, 0.09)         | 0.02 (-0.19, 0.23)          |
| Receptive Communication| -0.04 (-0.21, 0.12)        | -0.04 (-0.24, 0.17)         |
| Expressive Communication| -0.20 (-0.44, 0.03)       | -0.13 (-0.46, 0.20)         |
| Fine Motor            | -0.09 (-0.28, 0.10)         | 0.00 (-0.23, 0.23)          |
| Gross Motor           | 0.01 (-0.14, 0.16)          | 0.02 (-0.17, 0.21)          |
| Language Composite    | -0.70 (-1.75, 0.34)         | -0.47 (-1.85, 0.92)         |
| Motor Composite       | -0.24 (-1.07, 0.59)         | 0.06 (-0.96, 1.07)          |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven's Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; and psychometrician.

\(^a\)Models include 573 participants.
Table S14. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal urinary pyrethroid metabolite concentration (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with hemoglobin measurements at 1-year; child hemoglobin level controlled for in models.

| BSID Measure         | cis-DBCA β (95% CI) | cis-DCCA β (95% CI) | trans-DCCA β (95% CI) | 3PBAa β (95% CI) |
|----------------------|---------------------|---------------------|-----------------------|------------------|
| At 1 year (n=567)    |                     |                     |                       |                  |
| Cognitive            | 0.14 (-0.21, 0.50)  | -0.02 (-0.37, 0.33) | 0.00 (-0.29, 0.30)   | 0.05 (-0.33, 0.44) |
| Receptive Communication | 0.18 (-0.10, 0.47)  | -0.01 (-0.33, 0.31) | -0.04 (-0.33, 0.25)  | 0.04 (-0.32, 0.41) |
| Expressive Communication | -0.20 (-0.56, 0.16) | -0.10 (-0.42, 0.22) | -0.10 (-0.37, 0.17) | -0.09 (-0.45, 0.26) |
| Fine Motor           | 0.10 (-0.30, 0.51)  | -0.10 (-0.54, 0.34) | -0.10 (-0.49, 0.29)  | 0.00 (-0.48, 0.48) |
| Gross Motor          | 0.27 (-0.18, 0.71)  | 0.41 (-0.09, 0.92)  | 0.39 (-0.06, 0.83)   | 0.44 (-0.10, 0.98) |
| Language Composite   | -0.06 (-1.53, 1.41) | -0.31 (-1.74, 1.12) | -0.38 (-1.64, 0.88)  | -0.14 (-1.76, 1.48) |
| Motor Composite      | 1.12 (-0.92, 3.17)  | 0.96 (-1.42, 3.33)  | 0.89 (-1.20, 2.98)   | 1.34 (-1.17, 3.85) |
| Social-Emotionalb    | -0.26 (-0.75, 0.24) | -0.80 (-1.35, -0.26) | -0.64 (-1.11, -0.17) | -0.75 (-1.32, -0.17) |
| At 2 years (n=550)   |                     |                     |                       |                  |
| Cognitive            | 0.02 (-0.26, 0.29)  | 0.06 (-0.28, 0.41)  | 0.03 (-0.27, 0.33)   | 0.09 (-0.25, 0.43) |
| Receptive Communication | -0.15 (-0.43, 0.13) | 0.17 (-0.14, 0.48)  | 0.04 (-0.23, 0.31)   | 0.07 (-0.26, 0.41) |
| Expressive Communication | -0.27 (-0.70, 0.15) | 0.13 (-0.32, 0.59)  | -0.10 (-0.49, 0.30)  | -0.09 (-0.59, 0.41) |
| Fine Motor           | 0.15 (-0.16, 0.46)  | 0.29 (-0.07, 0.65)  | 0.22 (-0.11, 0.55)   | 0.31 (-0.08, 0.69) |
| Gross Motor          | -0.14 (-0.41, 0.13) | 0.09 (-0.23, 0.42)  | 0.09 (-0.20, 0.38)   | 0.12 (-0.24, 0.48) |
| Language Composite   | -1.18 (-3.04, 0.68) | 0.90 (-1.14, 2.94)  | -0.15 (-1.95, 1.65)  | 0.00 (-2.22, 2.23) |
| Motor Composite      | 0.03 (-1.40, 1.45)  | 1.16 (-0.56, 2.88)  | 0.94 (-0.60, 2.49)   | 1.29 (-0.57, 3.14) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal urinary pyrethroid metabolite concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven’s Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; child hemoglobin at 1 year; psychometrician; and time of urine collection (before or after delivery).

a Due to 1 missing value, models with 3PBA had 566 participants at 1 year and 549 participants at 2 years.

b Social-Emotional outcome models had 570 participants for cis-DBCA, cis-DCCA, and trans-DCCA exposures, and 569 participants for 3PBA.

*p<0.05
Table S15. Adjusted linear regression β coefficient and 95% confidence interval (CI) for the association between maternal prenatal urinary pyrethroid metabolite concentration (specific gravity-adjusted) and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Restricted to subset of children with hemoglobin measurements at 1-year; child hemoglobin level not controlled for in models. (for comparison to Table S14).

| BSID Measure               | cis-DBCA β (95% CI) | cis-DCCA β (95% CI) | trans-DCCA β (95% CI) | 3PBA² β (95% CI) |
|----------------------------|---------------------|---------------------|-----------------------|------------------|
| Cognitive                  | 0.13 (-0.22, 0.49)  | -0.02 (-0.37, 0.33) | -0.01 (-0.31, 0.29)  | 0.03 (-0.36, 0.41) |
| Receptive Communication    | 0.18 (-0.11, 0.47)  | -0.01 (-0.33, 0.31) | -0.04 (-0.33, 0.25)  | 0.04 (-0.32, 0.40) |
| Expressive Communication   | -0.21 (-0.56, 0.15) | -0.10 (-0.42, 0.22) | -0.11 (-0.38, 0.16)  | -0.11 (-0.46, 0.24) |
| Fine Motor                 | 0.10 (-0.30, 0.51)  | -0.10 (-0.54, 0.34) | -0.10 (-0.49, 0.29)  | -0.01 (-0.49, 0.47) |
| Gross Motor                | 0.25 (-0.20, 0.71)  | 0.40 (-0.10, 0.91)  | 0.37 (-0.08, 0.81)   | 0.41 (-0.13, 0.94) |
| Language Composite         | -0.08 (-1.53, 1.38) | -0.32 (-1.75, 1.11) | -0.41 (-1.67, 0.85)  | -0.19 (-1.79, 1.42) |
| Motor Composite            | 1.08 (-0.99, 3.16)  | 0.93 (-1.43, 3.30)  | 0.83 (-1.25, 2.91)   | 1.22 (-1.28, 3.73) |
| Social-Emotionalb          | -0.25 (-0.75, 0.24) | -0.80 (-1.35, -0.25) | -0.63 (-1.11, -0.16) | -0.73 (-1.30, -0.15) |

At 2 years (n=550)

| BSID Measure               | cis-DBCA β (95% CI) | cis-DCCA β (95% CI) | trans-DCCA β (95% CI) | 3PBA² β (95% CI) |
|----------------------------|---------------------|---------------------|-----------------------|------------------|
| Cognitive                  | 0.01 (-0.26, 0.28)  | 0.06 (-0.28, 0.41)  | 0.03 (-0.27, 0.33)   | 0.08 (-0.26, 0.42) |
| Receptive Communication    | -0.15 (-0.43, 0.13) | 0.17 (-0.14, 0.48)  | 0.04 (-0.24, 0.31)   | 0.07 (-0.27, 0.41) |
| Expressive Communication   | -0.27 (-0.70, 0.15) | 0.13 (-0.32, 0.59)  | -0.10 (-0.49, 0.30)  | -0.09 (-0.59, 0.41) |
| Fine Motor                 | 0.15 (-0.16, 0.46)  | 0.29 (-0.07, 0.65)  | 0.22 (-0.11, 0.55)   | 0.31 (-0.08, 0.70) |
| Gross Motor                | -0.14 (-0.41, 0.13) | 0.09 (-0.23, 0.42)  | 0.08 (-0.20, 0.37)   | 0.11 (-0.25, 0.47) |
| Language Composite         | -1.19 (-3.05, 0.67) | 0.90 (-1.14, 2.94)  | -0.15 (-1.95, 1.64)  | -0.01 (-2.24, 2.22) |
| Motor Composite            | 0.02 (-1.41, 1.44)  | 1.16 (-0.55, 2.87)  | 0.93 (-0.61, 2.48)   | 1.26 (-0.60, 3.13) |

Coefficients show the change in scaled BSID score associated with a 10-fold increase in maternal DDT/E serum concentrations. Models adjusted for maternal education, age, marital status, poverty status at delivery, risk for depression (CES-D) and Raven’s Coloured Progressive Matrices score (at 1-year visit); food insecurity (USD food security survey); HOME score; preterm delivery; psychometrician; and time of urine collection (before or after delivery).

² Due to 1 missing value, models with 3PBA had 566 participants at 1 year and 549 participants at 2 years.

b Social-Emotional outcome models had 570 participants for cis-DBCA, cis-DCCA, and trans-DCCA exposures, and 569 participants for 3PBA.

p<0.05
Figure S1. Directed Acyclic Graph (DAG) of possible confounding in the relationship between DDT/pyrethroid insecticides and children’s performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Blue circles indicate ancestors of outcomes; green circles indicate ancestors of exposures; red circles indicate ancestors of exposures and outcomes; gray circles represent unobserved (latent) variables. Green arrows represent causal paths; red arrows represent biasing paths. Right-facing triangle represents the primary exposure; I symbol represents the outcome.

DAG based on Textor J, Hardt J, Knuppel S. 2011. DAGitty: a graphical tool for analyzing causal diagrams. Epidemiology 22:745, and produced at http://www.dagity.net
Figure S2. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Cognitive subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S2 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for p,p’-DDE with the Bayley score when p,p’-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S3. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Expressive Communication scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S3 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for \( p,p' \)-DDE with the Bayley score when \( p,p' \)-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S4. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Receptive Communication subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S4 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for \( p,p' \)-DDE with the Bayley score when \( p,p' \)-DDT is held at quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S5. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Fine Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S5 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for $p,p'$-DDE with the Bayley score when $p,p'$-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S6. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Gross Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S6 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for \( p,p' \)-DDE with the Bayley score when \( p,p' \)-DDT is held at quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S7. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Language Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S7 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for \( p,p' \)-DDE with the Bayley score when \( p,p' \)-DDT is held a quantiles of 10\%, 25\%, 50\%, 75\%, and 90\%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S8. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Motor Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

Figure S8 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for p,p'-DDE with the Bayley score when p,p'-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S9. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Bayley Social-Emotional subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa. Figure S9 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for p,p’-DDE with the Bayley score when p,p’-DDT is held at quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S10. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Cognitive subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

Figure S10 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for $p,p'$-DDE with the Bayley score when $p,p'$-DDT is held at quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S11. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Expressive Communication subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

Figure S11 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for p,p'-DDE with the Bayley score when p,p'-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S12. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Receptive Communication subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

Figure S12 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for $p,p'$-DDE with the Bayley score when $p,p'$-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S13. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Fine Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

Figure S13 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for \( p,p' \)-DDE with the Bayley score when \( p,p' \)-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S14. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Gross Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

Figure S14 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for p,p’-DDE with the Bayley score when p,p’-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S15 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for $p,p'$-DDE with the Bayley score when $p,p'$-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.
Figure S16. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Motor Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

Figure S16 displays graphical output from Bayesian Kernel Machine Regression (BKMR) to indicate whether there is evidence for pair-wise interactions between chemical exposures. Plots show the exposure-response relationships of a specific chemical exposure, when the other member of the paired exposure is held at specified quantiles. For example, the second plot in the first row shows the exposure-response relationships for p,p’-DDE with the Bayley score when p,p’-DDT is held a quantiles of 10%, 25%, 50%, 75%, and 90%. The presence of non-parallel lines in these plots would provide evidence of a bivariate interaction between the paired exposures; however, each pair-wise exposure resulted in parallel lines and therefore suggests no between-chemical interactions in our study.