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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 ^a	% Quantifiable ^b	Geo. Mean	± GSD	Min	Percentile					Max
							10	25	50	75	90	
Wet Weight Concentrations												
<i>cis</i> -DBCA	695	100	99.6	0.227	± 3.42	0.005	0.050	0.099	0.226	0.483	1.141	18.416
<i>cis</i> -DCCA	695	100	99.9	0.312	± 2.96	0.015	0.085	0.154	0.305	0.611	1.058	104.744
<i>trans</i> -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	0.431
Creatinine-Adjusted Concentrations												
<i>cis</i> -DBCA	695	100	99.6	0.181	± 3.08	0.008	0.044	0.075	0.167	0.377	0.834	8.213
<i>cis</i> -DCCA	695	100	99.9	0.248	± 2.51	0.034	0.086	0.137	0.234	0.400	0.726	171.788
<i>trans</i> -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'*-DDT and *p,p'*-DDE (log₁₀ transformed; lipid-adjusted), and urinary concentrations of pyrethroid metabolites (log₁₀ transformed; specific-gravity adjusted), VHEMBE study (n=705), Limpopo South Africa.

Compound	<i>p,p'</i> -DDT	<i>p,p'</i> -DDE	<i>cis</i> -DBCA	<i>cis</i> -DCCA	<i>trans</i> -DCCA	3PBA
<i>p,p'</i> -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)
<i>p,p'</i> -DDE	-	-	-0.03 (p=0.48)	0.03 (p=0.49)	0.02 p=(0.65)	0.03 (p=0.48)
<i>cis</i> -DBCA	-	-	-	0.46 (p<0.001)	0.47 (p<0.001)	0.62 (p<0.001)
<i>cis</i> -DCCA	-	-	-	-	0.90 (p<0.001)	0.88 (p<0.001)
<i>trans</i> -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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -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 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) (3rd 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 β (95% CI)	p,p' -DDE β (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.

^aModels 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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -DCCA β (95% CI)	3PBA ^a 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-Emotional ^b	-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 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) (3rd edition) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

Sensitivity analysis: Maternal HIV status included in models.

BSID Measure	<i>p,p'</i> -DDT β (95% CI)	<i>p,p'</i> -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.

^aModels 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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -DCCA β (95% CI)	3PBA ^a 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 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	<i>p,p'</i> -DDT β (95% CI)	<i>p,p'</i> -DDE β (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.

^aModels 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) (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 levels are not controlled for in models.(for comparison with Table S8).

BSID Measure	<i>p,p'</i> -DDT β (95% CI)	<i>p,p'</i> -DDE 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.

^aModels 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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -DCCA β (95% CI)	3PBA ^a 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-Emotional ^b	-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 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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -DCCA β (95% CI)	3PBA ^a 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)*	0.61 (0.13, 1.08)*	0.65 (0.07, 1.23)*
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 ^b	-0.24 (-0.78, 0.29)	-0.82 (-1.39, -0.24)*	-0.62 (-1.13, -0.12)*	-0.64 (-1.27, -0.02)*
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 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 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 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 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	0.17 (-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 ^a	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.

^aModels 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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -DCCA β (95% CI)	3PBA ^a 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-Emotional ^b	-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 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	<i>cis</i> -DBCA β (95% CI)	<i>cis</i> -DCCA β (95% CI)	<i>trans</i> -DCCA β (95% CI)	3PBA ^a β (95% CI)
At 1 year (n=567)				
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-Emotional ^b	-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)				
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 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).

^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.

* $p < 0.05$

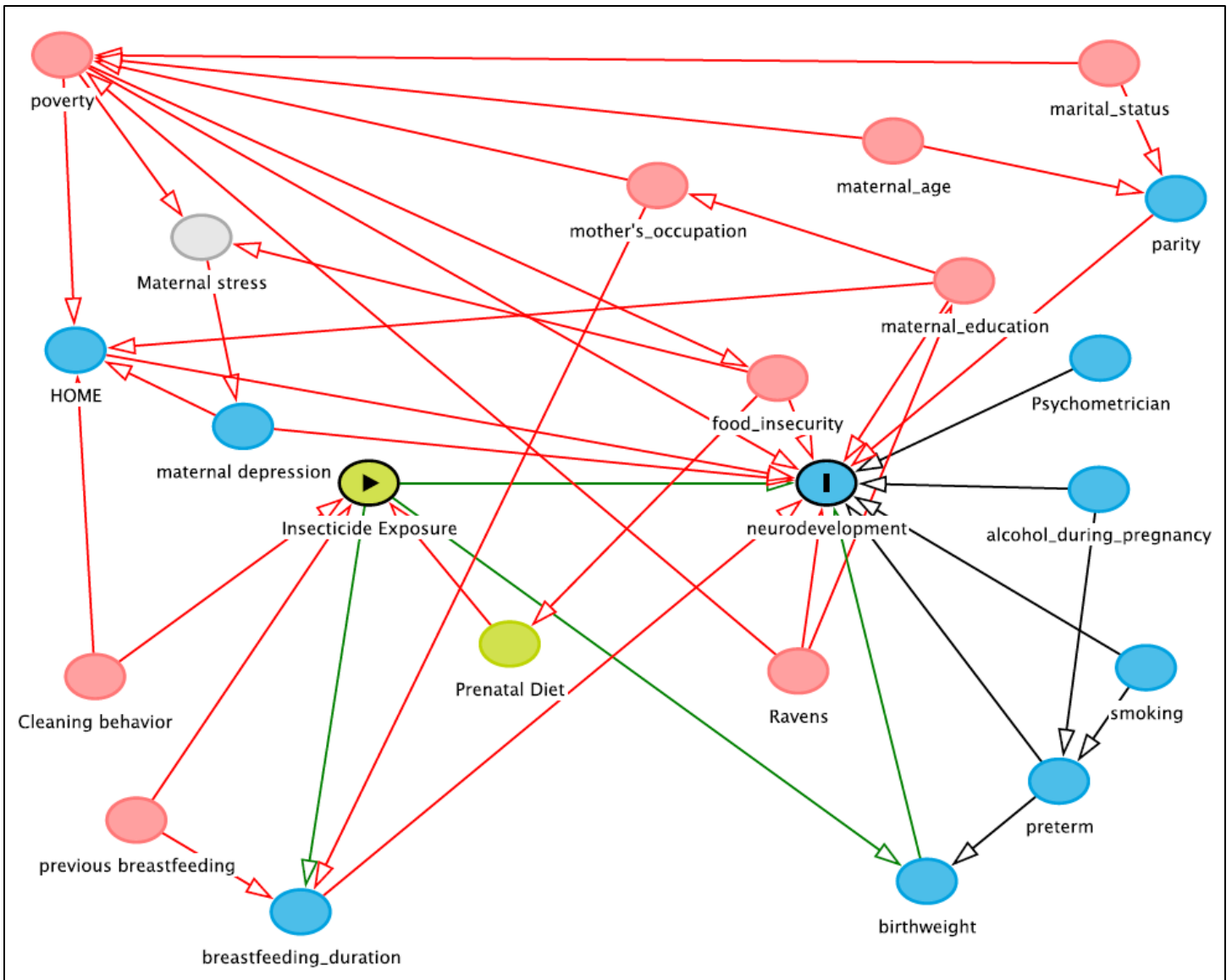


Figure S1. Directed Acyclic Graph (DAG) of possible confounding in the relationship between DDT/pyrethroid insecticides and children's performance on the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 and 2 years, VHEMBE study, Limpopo, South Africa.

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.dagitty.net>

Cognitive Scores at 1 year: Bivariate relationships of Chemical Exposures

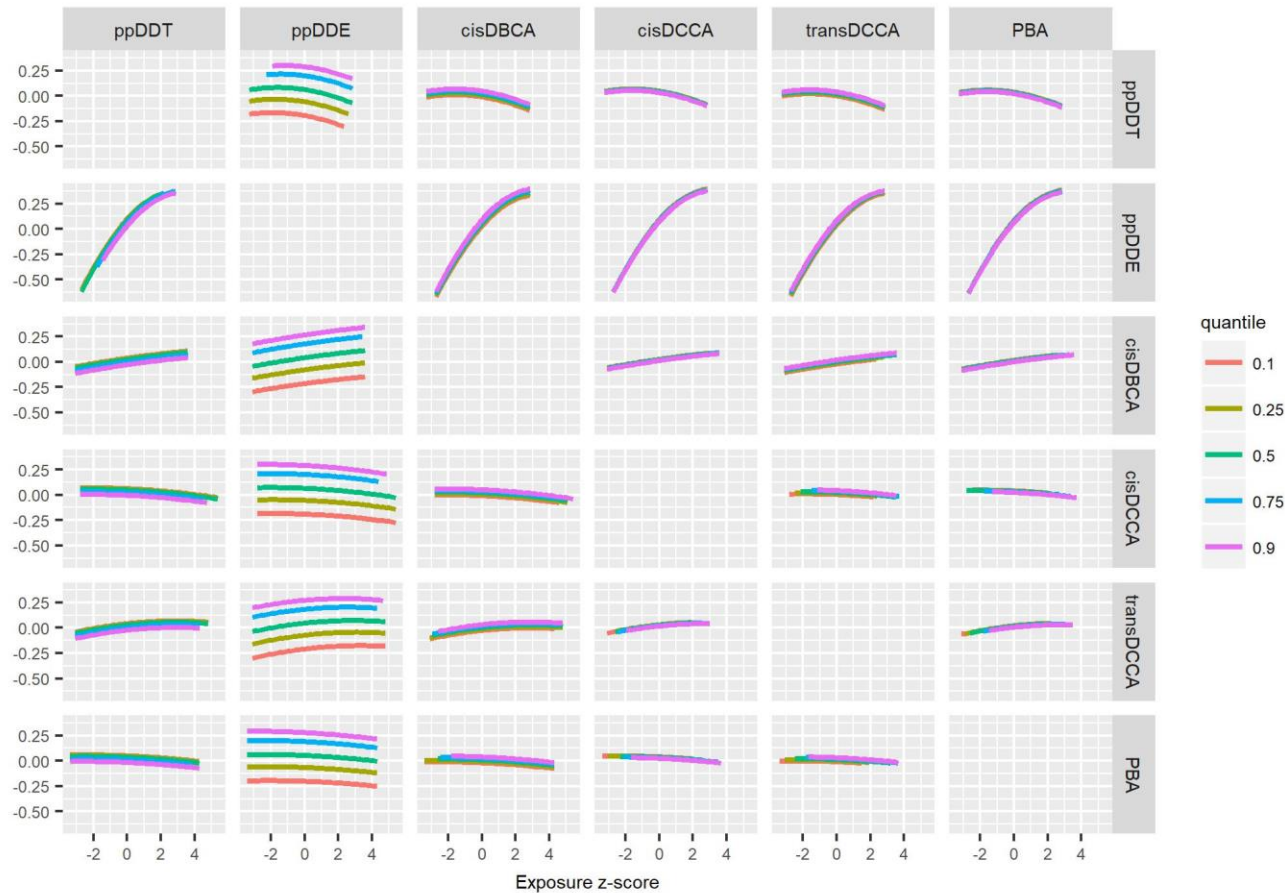


Figure S2. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Cognitive subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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.

Expressive Communication Scores at 1 year: Bivariate relationships of Chemical Exposures

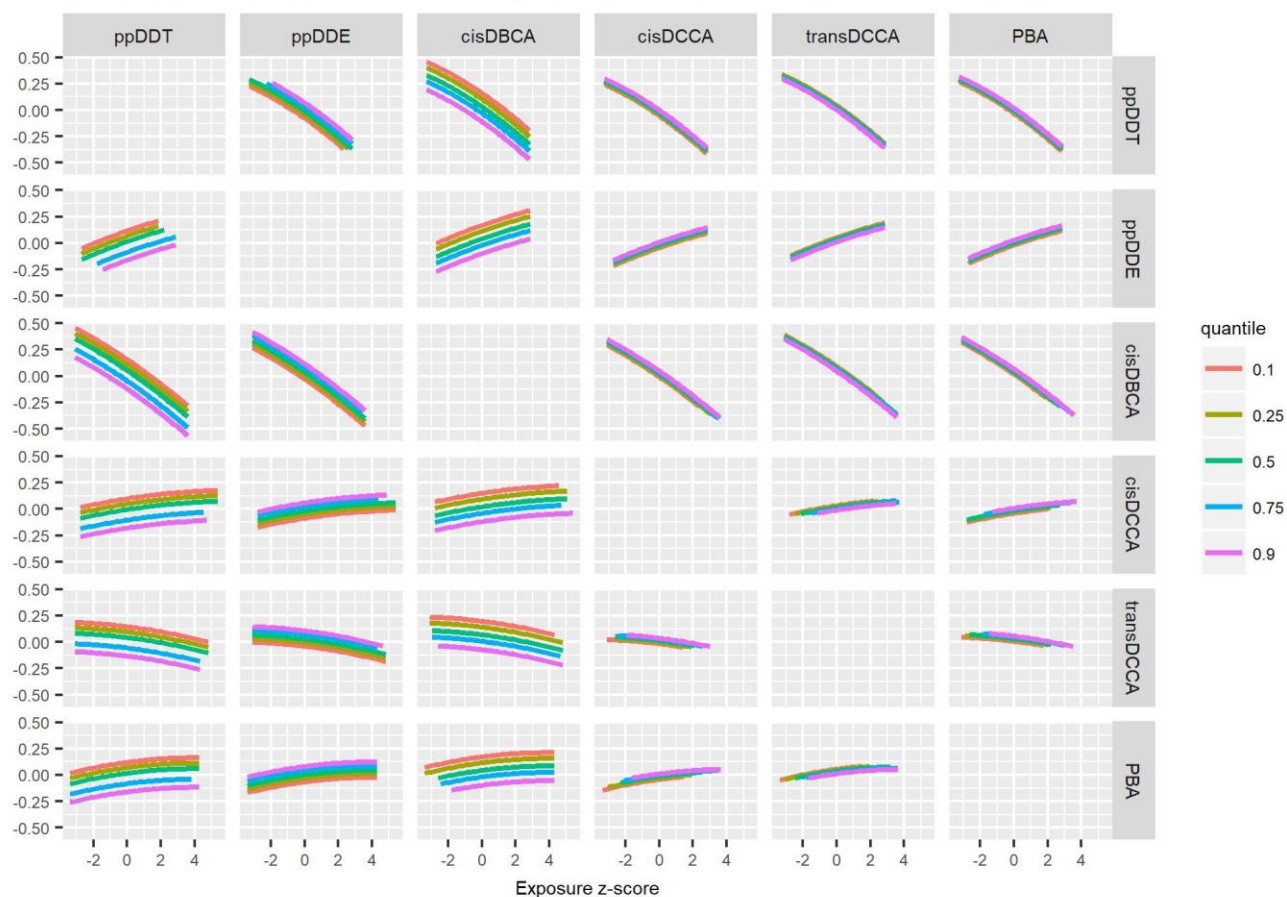


Figure S3. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Expressive Communication scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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.

Receptive Communication Scores at 1 year: Bivariate relationships of Chemical Exposures

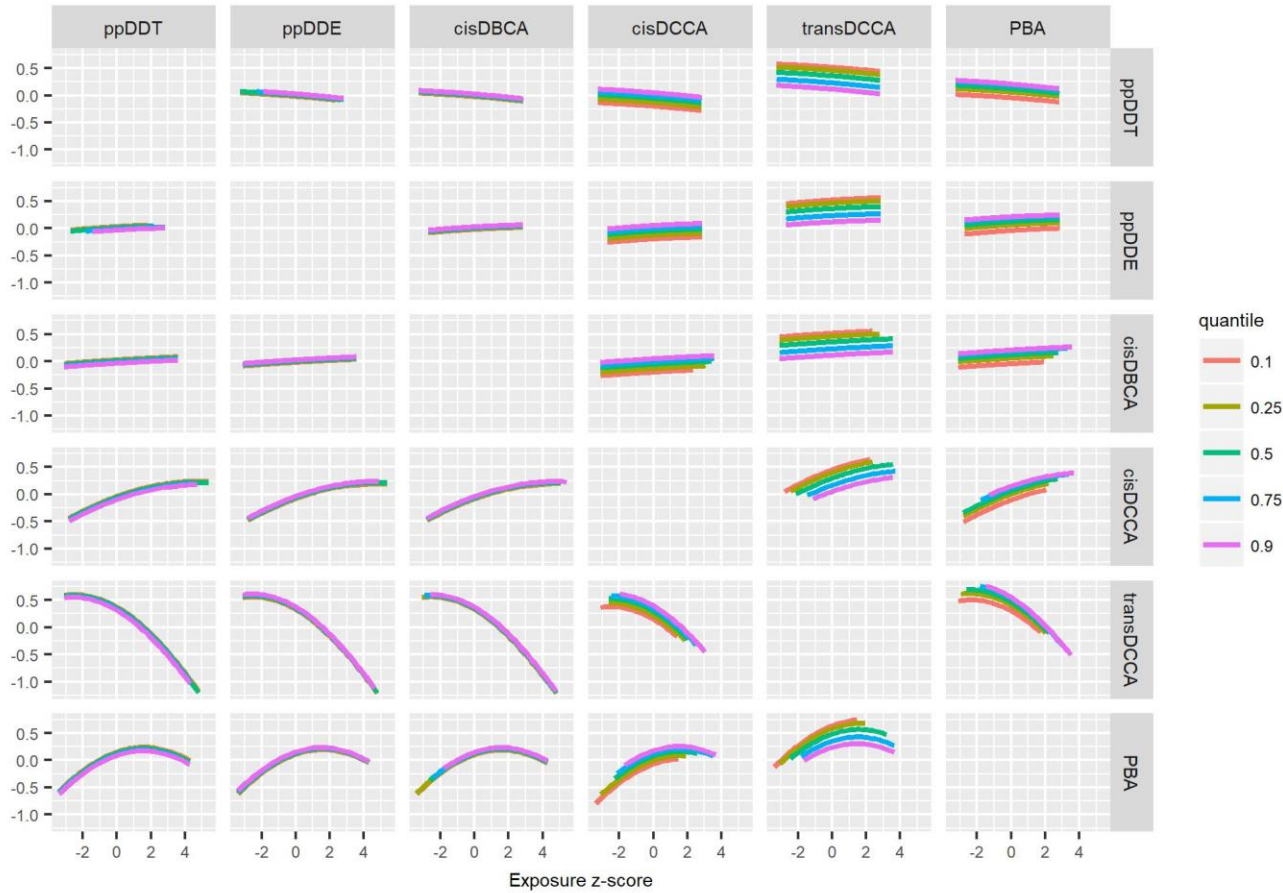


Figure S4. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Receptive Communication subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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 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.

Fine Motor Scores at 1 year: Bivariate relationships of Chemical Exposures

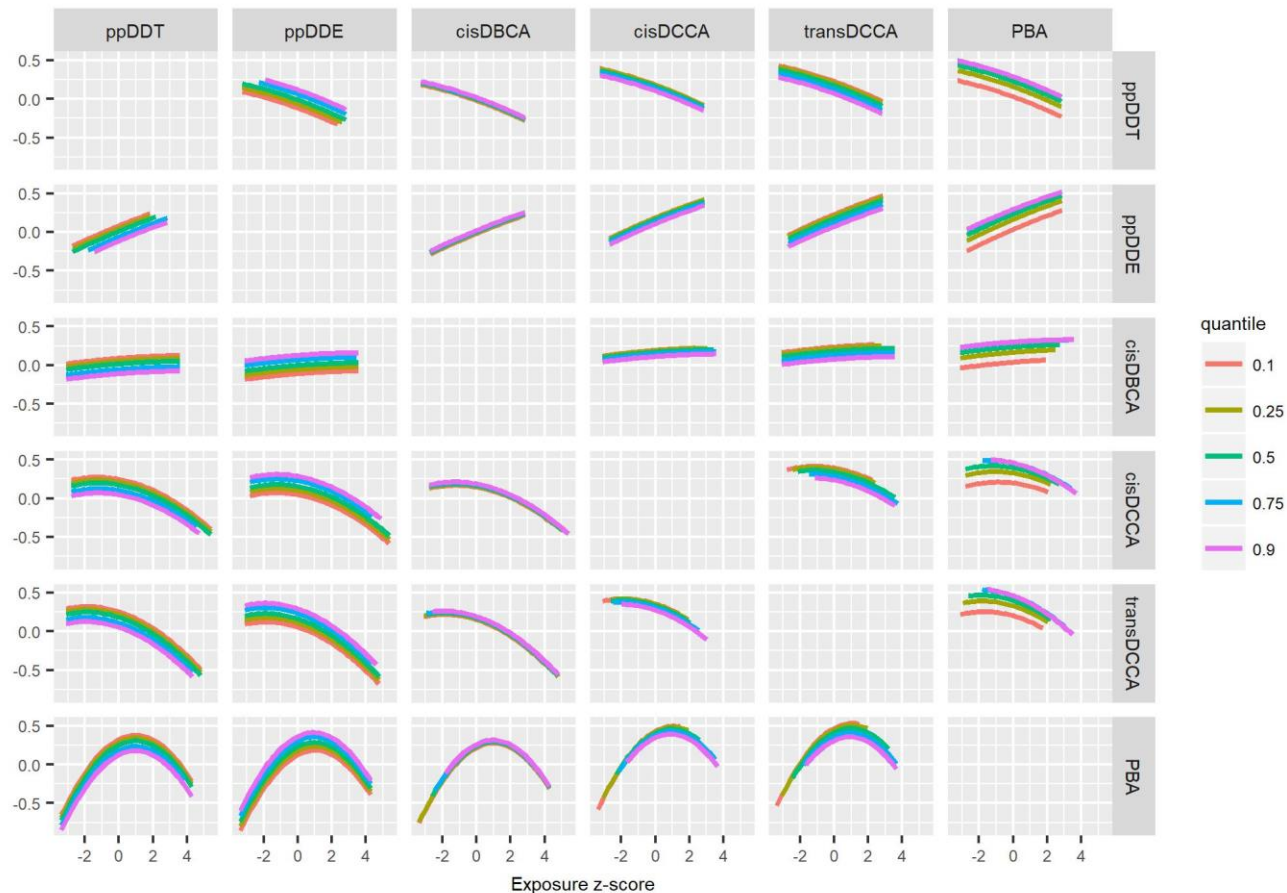


Figure S5. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Fine Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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.

Gross Motor Scores at 1 year: Bivariate relationships of Chemical Exposures

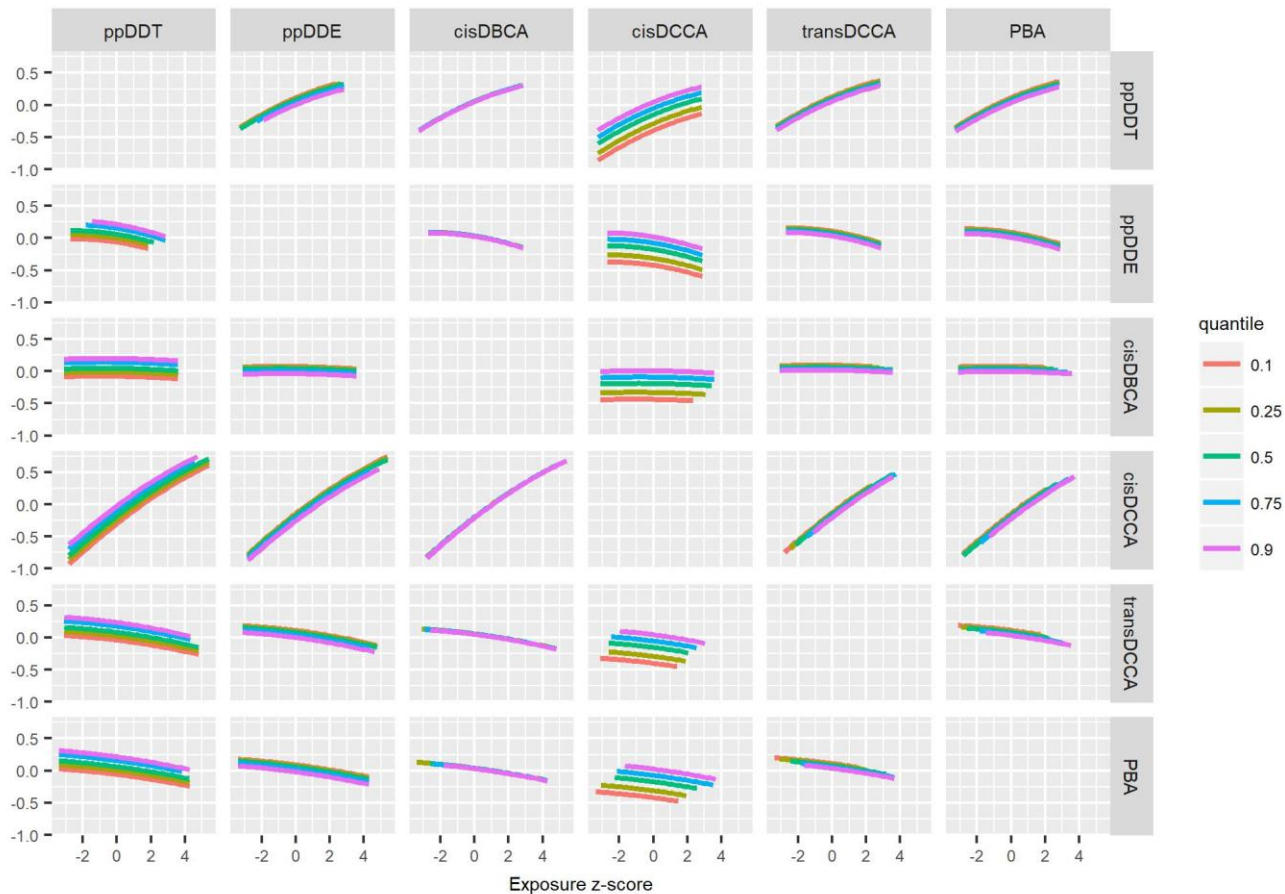


Figure S6. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Gross Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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 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.

Language Composite Scores at 1 year: Bivariate relationships of Chemical Exposures

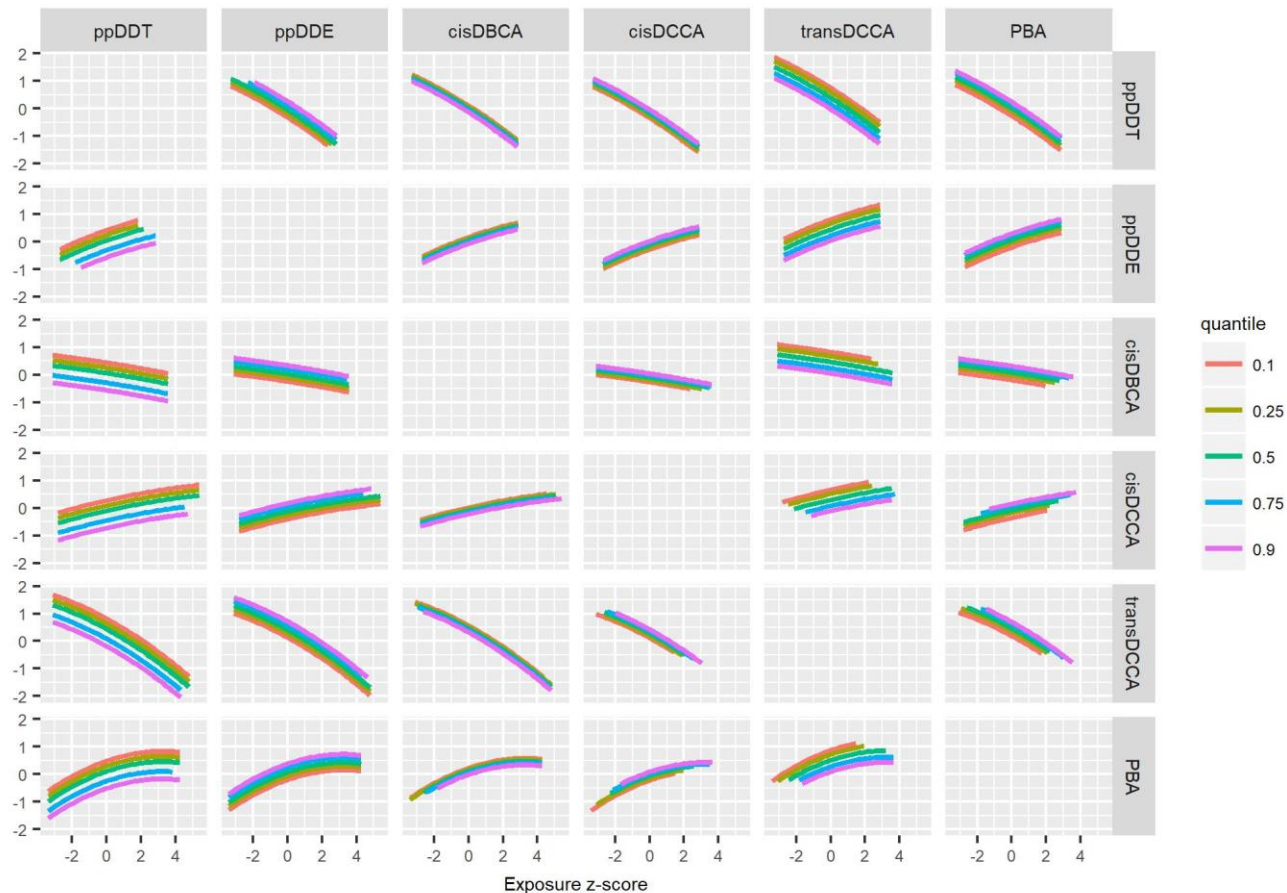


Figure S7. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Language Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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.

Motor Composite Scores at 1 year: Bivariate relationships of Chemical Exposures

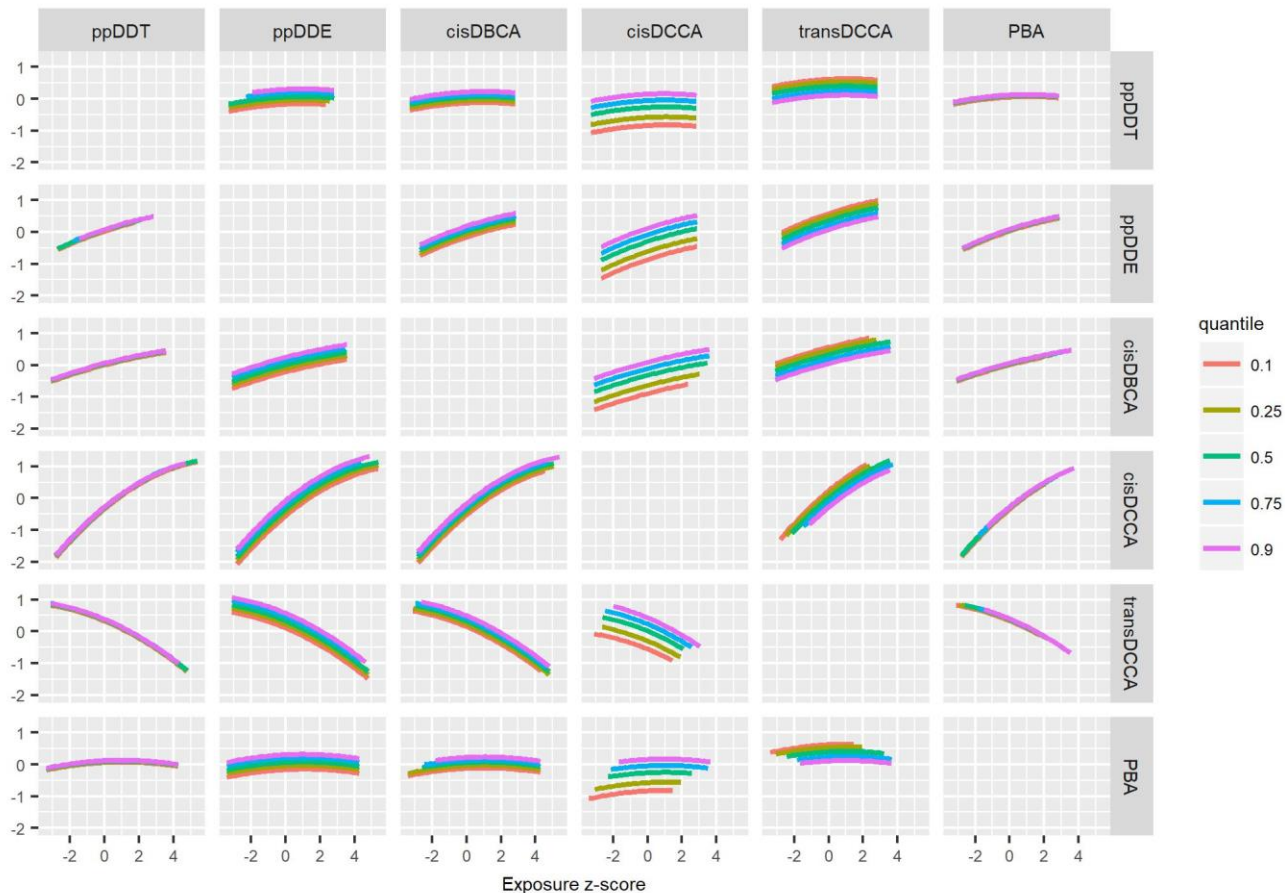


Figure S8. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Motor Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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.

Social-Emotional Scores at 1 year: Bivariate relationships of Chemical Exposures

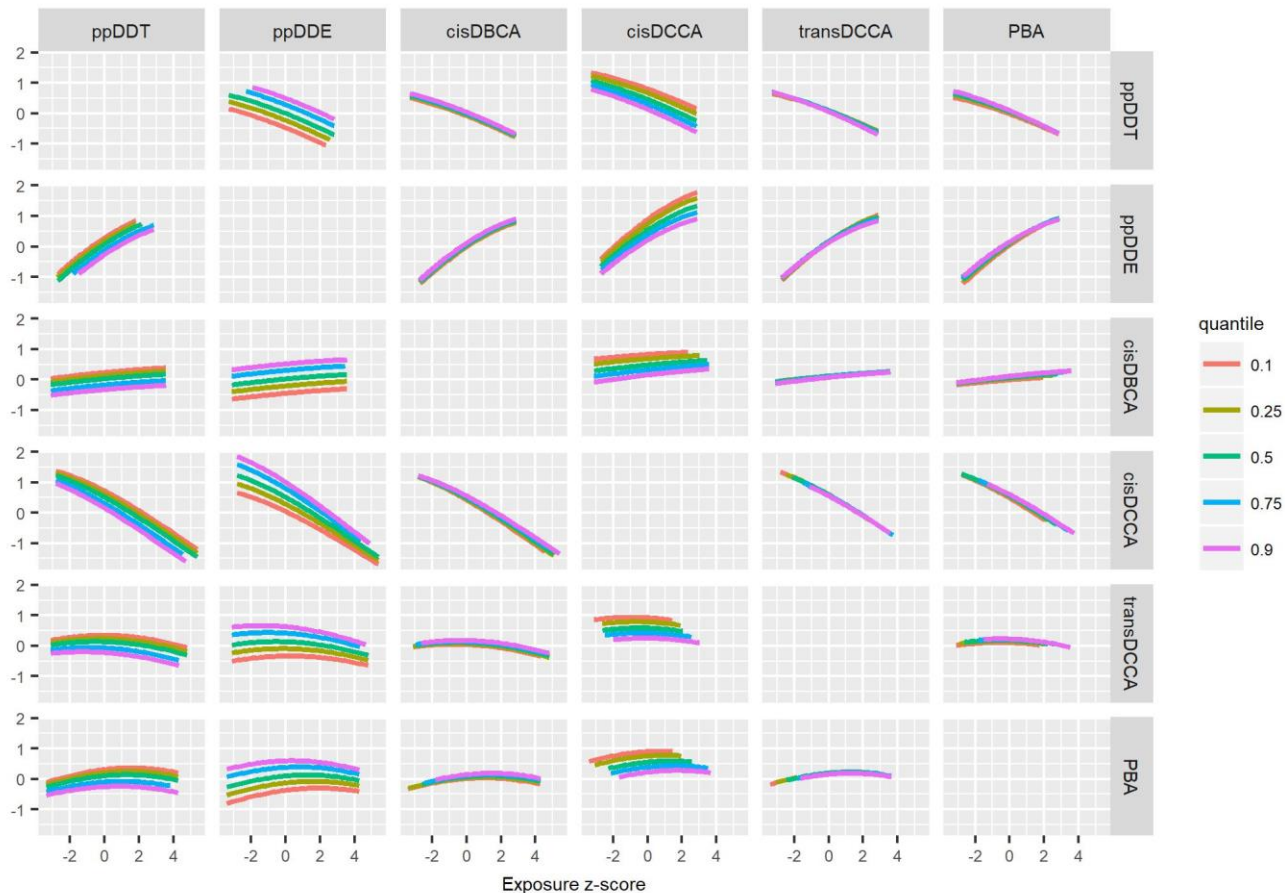


Figure S9. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Bayley Social-Emotional subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 1 year, VHEMBE study, Limpopo, South Africa.

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 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.

Cognitive Scores at 2 years: Bivariate relationships of Chemical Exposures

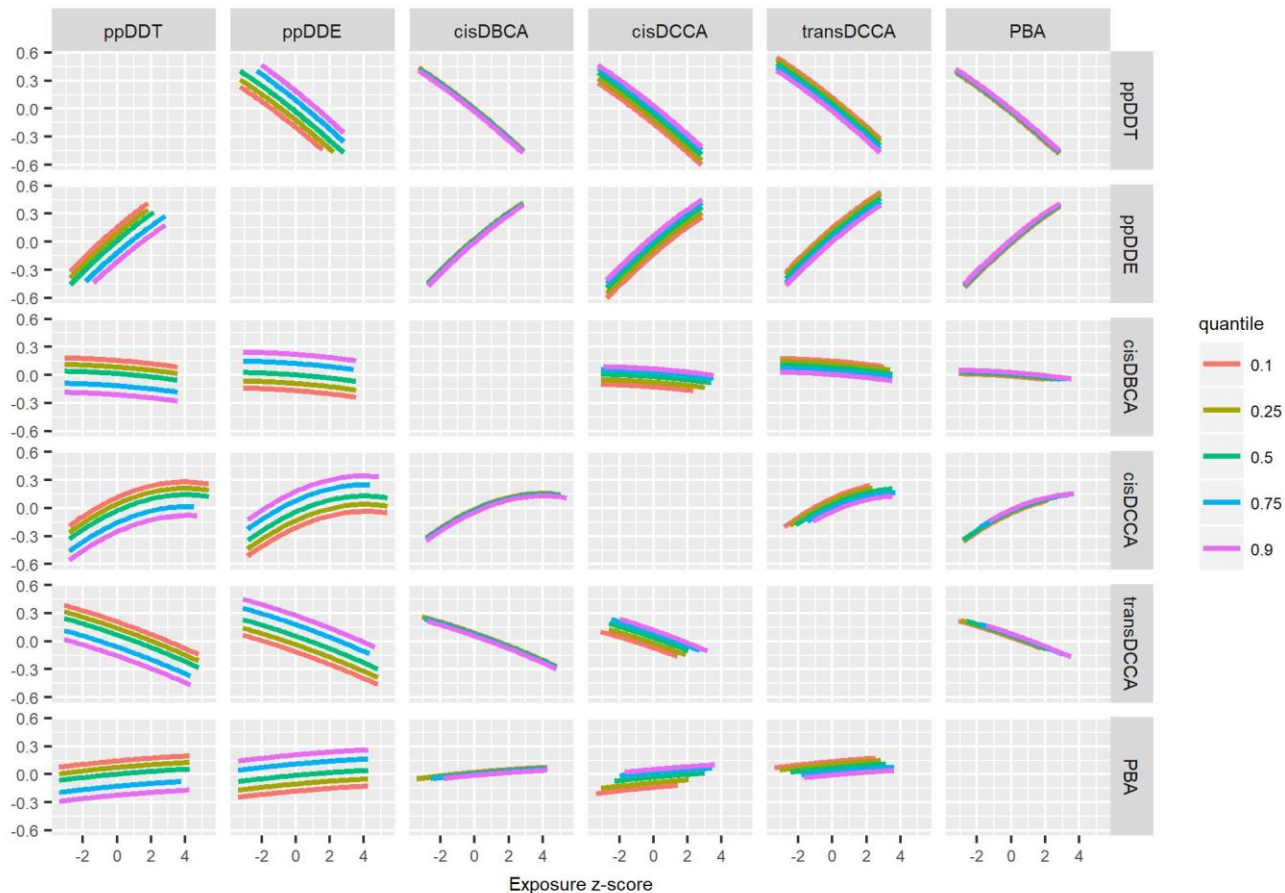


Figure S10. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Cognitive subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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 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.

Expressive Communication Scores at 2 years: Bivariate relationships of Chemical Exposures

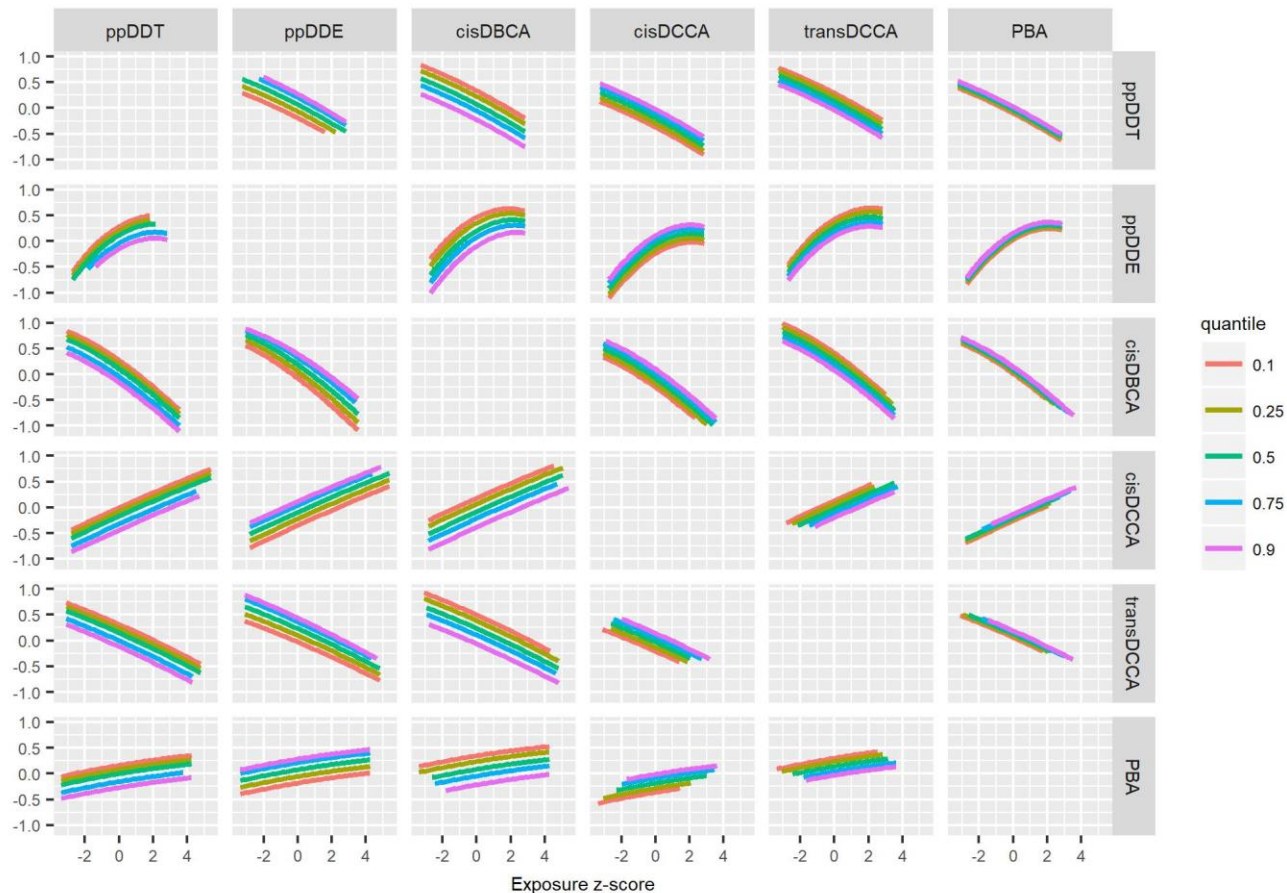


Figure S11. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Expressive Communication subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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.

Receptive Communication Scores at 2 years: Bivariate relationships of Chemical Exposures

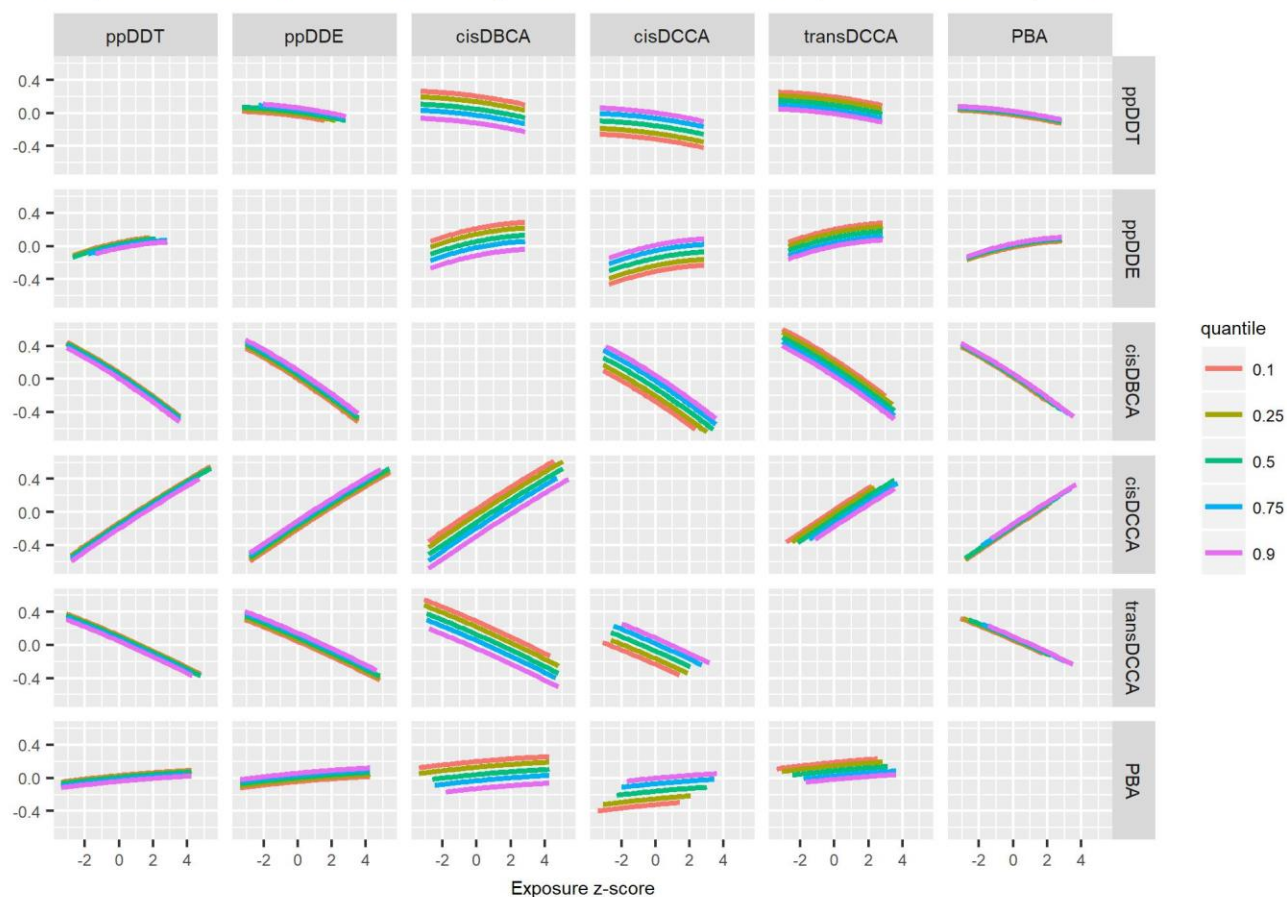


Figure S12. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Receptive Communication subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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.

Fine Motor Scores at 2 years: Bivariate relationships of Chemical Exposures

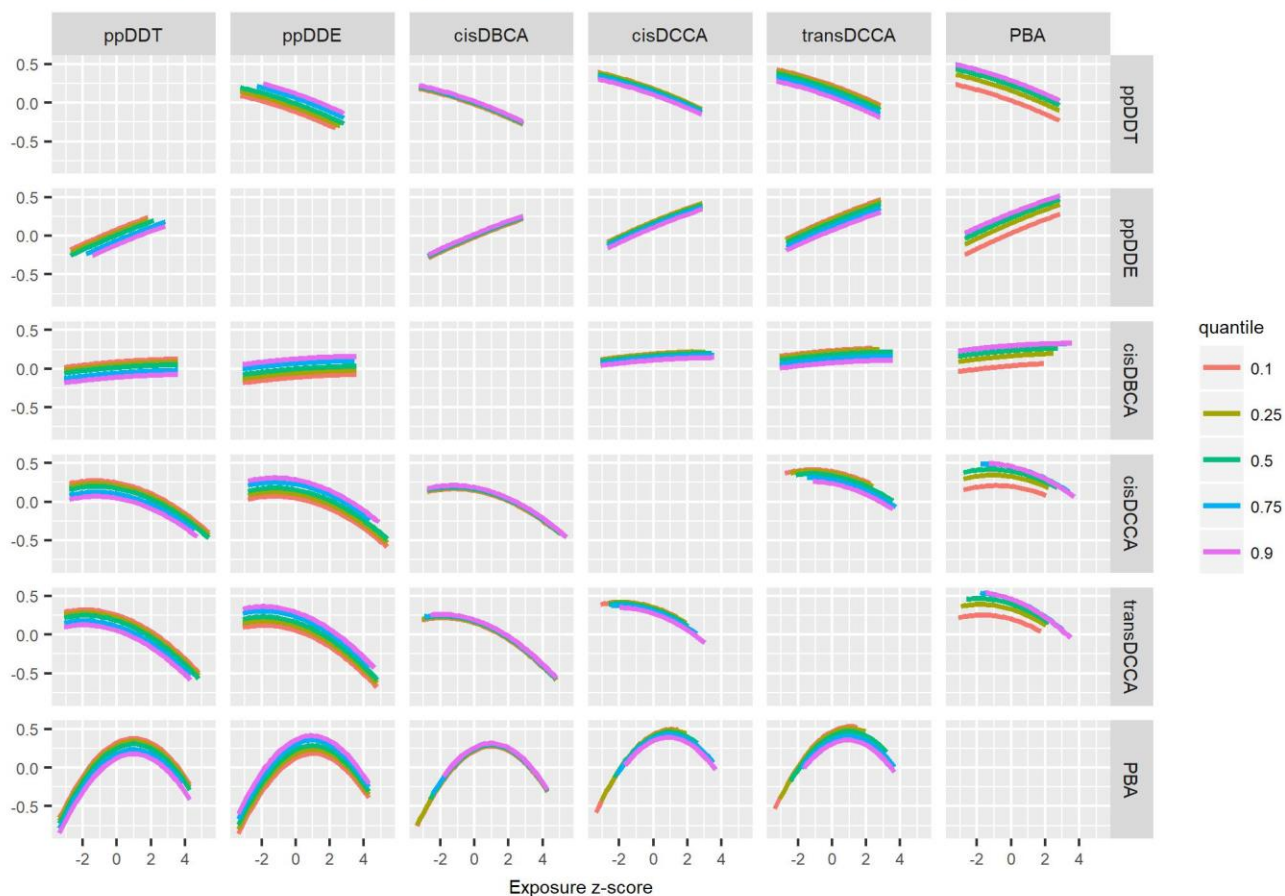


Figure S13. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Fine Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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.

Gross Motor Scores at 2 years: Bivariate relationships of Chemical Exposures

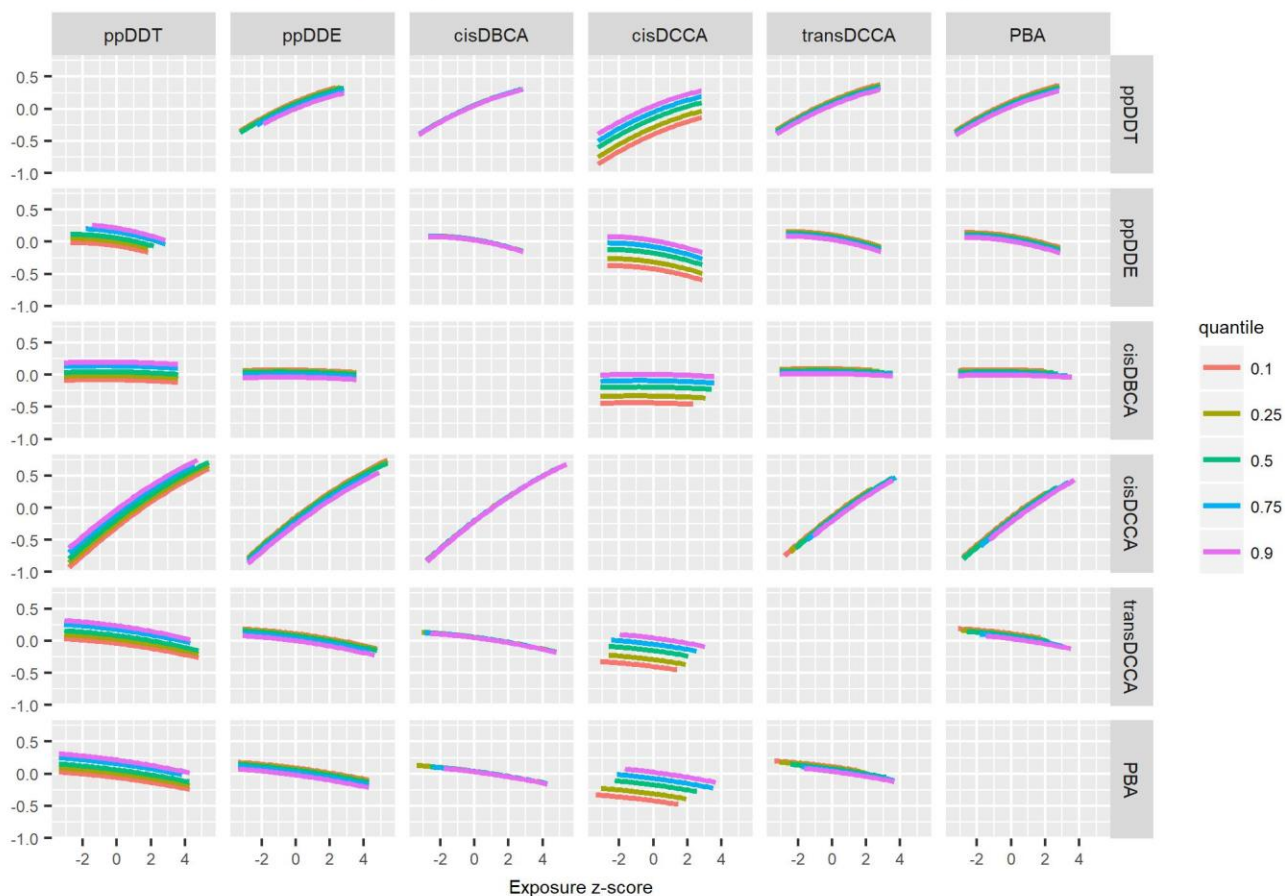


Figure S14. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Gross Motor subscale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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.

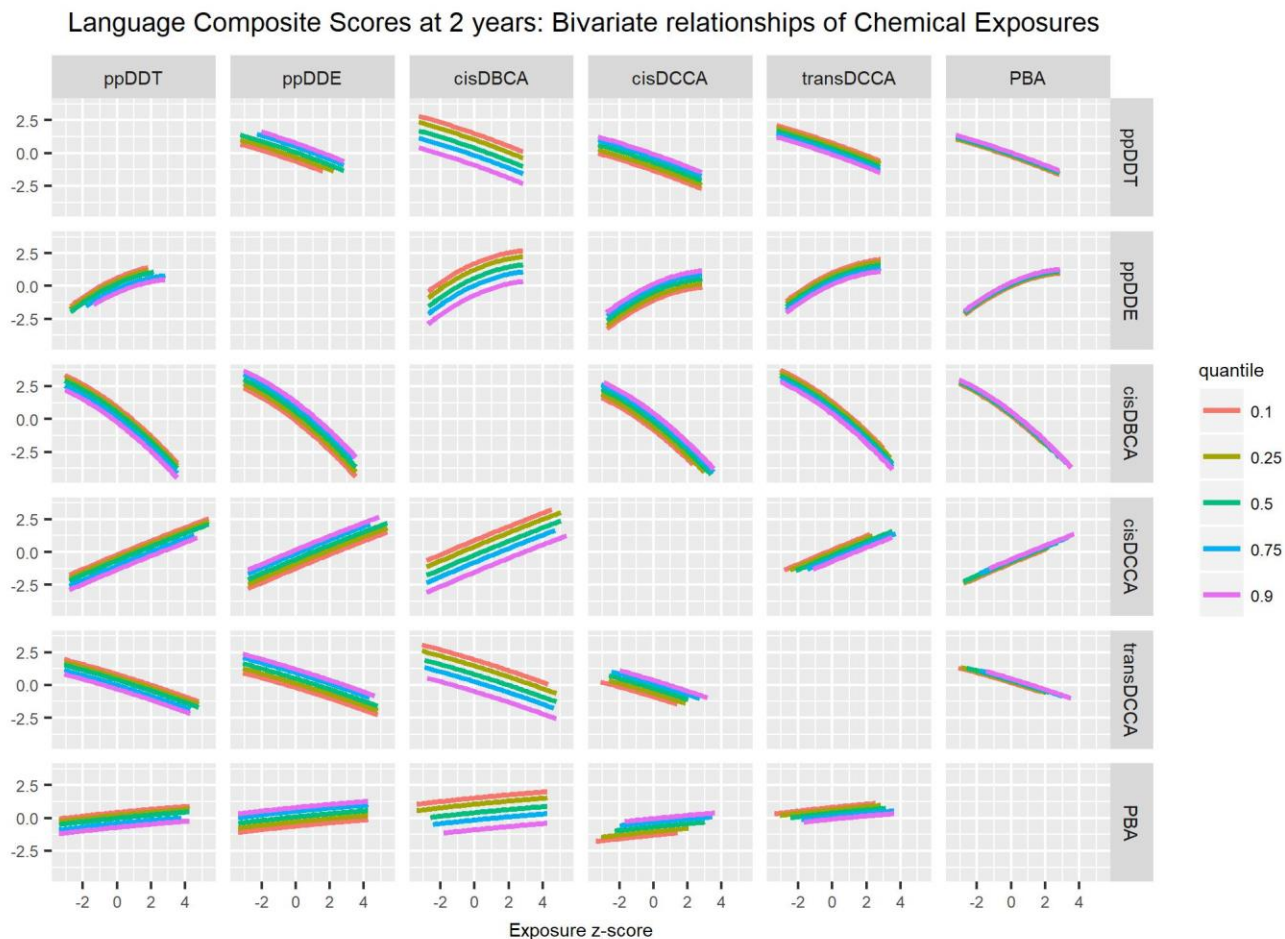


Figure S15. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Language Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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.

Motor Composite Scores at 2 years: Bivariate relationships of Chemical Exposures

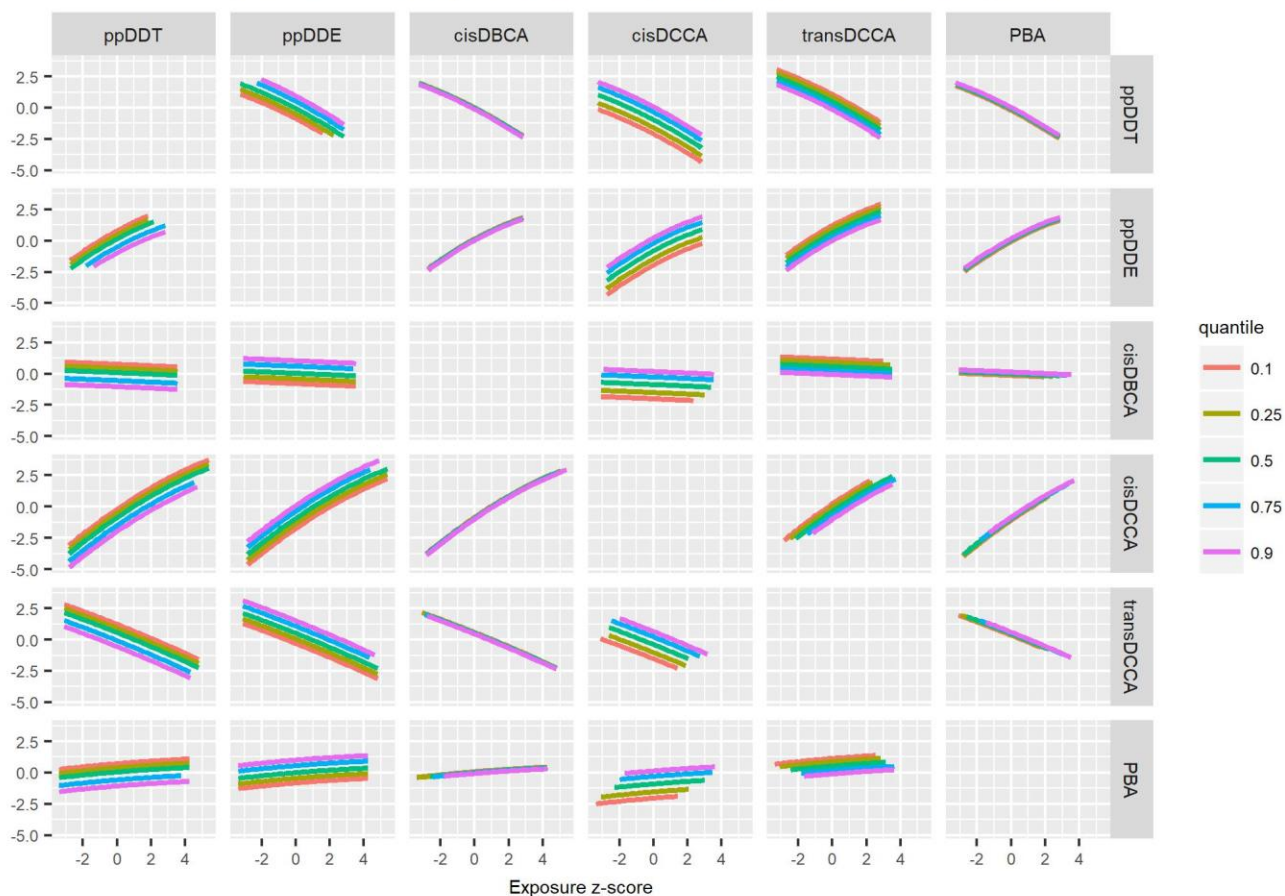


Figure S16. Bivariate relationships of chemical exposures in the relationship between DDT/pyrethroid insecticides and children’s performance on the Motor Composite scale of the Bayley Scales of Infant Assessment (3rd edition) (BSID) at 2 years, VHEMBE study, Limpopo, South Africa.

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.