

SUPPLEMENTAL DIGITAL CONTENT

Maternal exposure to pyrethroid insecticides during pregnancy and respiratory allergy symptoms among children participating in the Venda Health Examination of Mothers, Babies and their Environment (VHEMBE)

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Section 1. Results table for the associations between pyrethroid metabolites and respiratory allergy symptoms and asthma diagnosis.

Table S1.1. Associations between a 10-fold increase in maternal urinary pyrethroid metabolite concentrations ($\mu\text{g/L}$) and respiratory allergies at 3.5 and 5 years of age among children participating in the VHEMBE study.

Outcome	<i>cis</i> -DBCA RR (95% CI)	<i>cis</i> -DCCA RR (95% CI)	<i>trans</i> -DCCA RR (95% CI)	3-PBA RR (95% CI)
Wheezing or whistling in chest	1.3 (0.8, 2.1)	1.8 (1.1, 3.0) *	1.7 (1.1, 2.6) *	1.8 (1.0, 3.3) *
Chest sounds wheezy during or after exercise	1.0 (0.5, 2.2)	1.0 (0.5, 1.8)	1.2 (0.6, 2.2)	1.2 (0.5, 2.8)
Dry cough at night	3.5 (1.3, 9.5) *	1.4 (0.9, 2.5)	1.6 (0.8, 3.2)	1.8 (0.8, 4.1)
Doctor-diagnosed asthma	0.7 (0.3, 1.4)	2.1 (1.3, 3.3) *	2.1 (1.1, 3.9) *	2.4 (1.0, 5.8) *
Doctor prescribed medicine for asthma	0.9 (0.4, 2.1)	1.4 (1.0, 1.9)	1.0 (0.6, 1.6)	1.0 (0.5, 2.0)
Suspected asthma ^a	1.3 (0.7, 2.3)	1.8 (1.1, 3.1) *	1.8 (1.1, 2.8) *	1.7 (1.0, 3.2)
Sneezing, runny or blocked nose	0.9 (0.6, 1.2)	1.1 (0.7, 1.5)	1.0 (0.8, 1.4)	1.2 (0.8, 1.7)
Itchy-watery eyes accompanied by nose problems	1.2 (0.7, 2.1)	1.3 (0.7, 2.3)	1.4 (0.8, 2.3)	1.5 (0.8, 2.7)
Hay fever	0.7 (0.3, 1.9)	1.4 (0.4, 5.8)	1.2 (0.4, 3.5)	2.2 (0.6, 8.5)
Seasonal rhinitis ^b	1.0 (0.6, 1.5)	1.0 (0.6, 1.7)	0.9 (0.6, 1.4)	1.2 (0.7, 2.0)
Seasonal rhinoconjunctivitis ^c	1.9 (1.0, 3.6)	1.7 (0.8, 3.3)	1.5 (0.8, 2.8)	2.0 (1.1, 3.9) *
Any respiratory allergy symptom ^d	1.0 (0.8, 1.4)	1.2 (0.9, 1.6)	1.2 (0.9, 1.5)	1.3 (1.0, 1.8)

Any asthma symptom ^e	1.4 (0.9, 2.2)	1.5 (0.9, 2.4)	1.4 (0.9, 2.1)	1.6 (0.9, 2.7)
Any rhinitis symptom ^f	0.9 (0.6, 1.2)	1.1 (0.7, 1.5)	1.0 (0.8, 1.4)	1.2 (0.8, 1.7)

^a Variable combining wheezing and at least one other symptom. Other symptoms: Chest sounds wheezy during or after exercise or dry cough at night or sleep disturbed due to wheezing or wheezing severe enough to limit speech.

^b Sneezing, runny or blocked nose had they occurred during spring or summer seasons.

^c Itchy-watery eyes accompanied by nose problems had they occurred during spring or summer seasons.

^d Respiratory allergy symptoms: Wheezing or whistling in chest, chest sounds wheezy during or after exercise, sneezing, runny or blocked nose, dry cough at night or itchy-watery eyes accompanied by nose problems.

^e Asthma symptoms: Wheezing or whistling in chest, chest sounds wheezy during or after exercise or dry cough at night.

^f Rhinitis symptoms: Sneezing, runny or blocked nose or itchy-watery eyes accompanied by nose problems.

* 95% CI excludes the null (p-value < 0.05).

Abbreviations: RR: Risk Ratio; CI, confidence interval; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Section 2. Results table for the associations between pyrethroid metabolites and respiratory allergy symptoms and asthma diagnosis by child age and child sex.

Table S2.1. Associations between a 10-fold increase in maternal urinary pyrethroid metabolite concentrations ($\mu\text{g/L}$) and respiratory allergies by child age

	Wheezing or whistling in chest			Chest sounds wheezy during or after exercise		
	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	1.3 (0.7, 2.6)	1.1 (0.5, 2.4)	0.75	1.7 (0.7, 4.4)	0.4 (0.1, 1.1)	0.04 ⁺
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.4 (0.8, 2.7)	2.3 (1.0, 5.5)	0.37	1.0 (0.5, 1.8)	1.0 (0.3, 2.9)	0.99
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.4 (0.8, 2.6)	2.1 (0.9, 4.8)	0.47	1.3 (0.7, 2.5)	1.0 (0.3, 3.5)	0.69
3-PBA ($\mu\text{g/L}$)	1.3 (0.6, 2.8)	2.7 (1.1, 6.5) [*]	0.21	1.5 (0.7, 3.4)	0.9 (0.2, 4.8)	0.54
	Dry cough at night			Doctor-diagnosed asthma		
	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	4.7 (1.4, 16.1) [*]	2.6 (0.6, 11.3)	0.55	0.6 (0.2, 1.6)	0.8 (0.2, 2.5)	0.75
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.2 (0.6, 2.5)	1.7 (0.8, 3.6)	0.49	1.8 (1.0, 3.5)	2.4 (1.1, 5.3) [*]	0.59
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.1 (0.5, 2.4)	2.0 (0.7, 6.1)	0.41	1.9 (0.9, 4.1)	2.3 (0.6, 8.5)	0.81
3-PBA ($\mu\text{g/L}$)	1.4 (0.4, 5.1)	2.4 (0.8, 7.0)	0.52	2.5 (1.0, 6.4)	2.2 (0.3, 14.8)	0.90
	Doctor prescribed medicine for asthma			Suspected asthma		
	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	0.7 (0.2, 2.2)	1.2 (0.3, 4.0)	0.54	1.5 (0.7, 3.2)	1.0 (0.4, 2.5)	0.47
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.1 (0.7, 1.8)	1.7 (1.0, 2.7)	0.26	1.6 (0.9, 3.1)	2.1 (0.8, 5.3)	0.65
<i>trans</i> -DCCA ($\mu\text{g/L}$)	0.9 (0.5, 1.7)	1.1 (0.5, 2.1)	0.77	1.7 (0.9, 3.1)	1.9 (0.8, 4.2)	0.86
3-PBA ($\mu\text{g/L}$)	1.1 (0.4, 3.1)	0.9 (0.4, 2.2)	0.85	1.7 (0.8, 3.5)	1.9 (0.7, 5.0)	0.86
	Sneezing, runny or blocked nose			Itchy-watery eyes accompanied by nose problems		
	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}	3.5 years RR (95% CI)	5 years RR (95% CI)	<i>p</i> _{inter}

<i>cis</i> -DBCA (µg/L)	0.8 (0.5, 1.2)	1.0 (0.5, 1.8)	0.56	1.0 (0.5, 1.9)	1.7 (0.6, 4.4)	0.39
<i>cis</i> -DCCA (µg/L)	1.0 (0.6, 1.6)	1.1 (0.6, 1.8)	0.89	1.7 (0.8, 3.4)	0.7 (0.3, 1.8)	0.15
<i>trans</i> -DCCA (µg/L)	1.0 (0.7, 1.5)	1.1 (0.7, 1.7)	0.88	1.5 (0.8, 2.9)	1.0 (0.4, 2.3)	0.40
3-PBA (µg/L)	1.1 (0.7, 1.7)	1.4 (0.7, 2.6)	0.49	1.7 (0.9, 3.5)	1.2 (0.5, 3.1)	0.55
Hay fever			Seasonal rhinitis			
	3.5 years	5 years	p_{inter}	3.5 years	5 years	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.5 (0.7, 3.3)	0.1 (0.01, 1.5)	0.06 ⁺	0.8 (0.5, 1.4)	1.3 (0.6, 2.8)	0.34
<i>cis</i> -DCCA (µg/L)	2.0 (0.4, 8.9)	0.6 (0.1, 3.9)	0.32	1.0 (0.5, 2.1)	1.1 (0.6, 2.1)	0.83
<i>trans</i> -DCCA (µg/L)	1.8 (0.6, 5.4)	0.5 (0.1, 1.9)	0.14	0.9 (0.5, 1.6)	1.0 (0.6, 1.7)	0.78
3-PBA (µg/L)	3.8 (1.0, 14.1)	0.4 (0.06, 3.2)	0.08 ⁺	1.0 (0.5, 1.9)	1.6 (0.7, 3.5)	0.37
Seasonal rhinoconjunctivitis			Any respiratory allergy symptom			
	3.5 years	5 years	p_{inter}	3.5 years	5 years	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.6 (0.8, 3.3)	2.5 (0.8, 7.9)	0.53	1.0 (0.7, 1.5)	1.0 (0.6, 1.7)	0.96
<i>cis</i> -DCCA (µg/L)	1.9 (0.8, 4.6)	1.3 (0.5, 3.4)	0.59	1.1 (0.8, 1.6)	1.3 (0.8, 2.2)	0.58
<i>trans</i> -DCCA (µg/L)	1.5 (0.7, 3.6)	1.3 (0.6, 2.9)	0.81	1.1 (0.8, 1.5)	1.3 (0.8, 2.0)	0.52
3-PBA (µg/L)	1.9 (0.8, 4.6)	2.2 (0.8, 6.0)	0.82	1.2 (0.8, 1.8)	1.5 (0.9, 2.6)	0.50
Any asthma symptom			Any rhinitis symptom			
	3.5 years	5 years	p_{inter}	3.5 years	5 years	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.6 (0.9, 2.8)	1.1 (0.5, 2.4)	0.49	0.8 (0.5, 1.2)	1.0 (0.5, 1.8)	0.56
<i>cis</i> -DCCA (µg/L)	1.3 (0.8, 2.3)	1.7 (0.8, 3.6)	0.61	1.0 (0.6, 1.6)	1.1 (0.6, 1.8)	0.89
<i>trans</i> -DCCA (µg/L)	1.3 (0.8, 2.2)	1.6 (0.8, 3.0)	0.66	1.0 (0.7, 1.5)	1.1 (0.7, 1.7)	0.88
3-PBA (µg/L)	1.5 (0.8, 2.7)	1.7 (0.7, 4.1)	0.77	1.1 (0.7, 1.7)	1.4 (0.7, 2.6)	0.49

*95% CI excludes the null. ⁺ p-value for interaction < 0.1. Abbreviations: RR: Risk Ratio; CI, confidence interval; p_{inter}, p-value for interaction; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Table S2.2. Associations between a 10-fold increase in maternal urinary pyrethroid metabolite concentrations ($\mu\text{g/L}$) and respiratory allergies by child sex

	Wheezing or whistling in chest			Chest sounds wheezy during or after exercise		
	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	1.4 (0.7, 2.8)	1.2 (0.6, 2.4)	0.77	1.0 (0.3, 3.2)	1.0 (0.4, 2.7)	0.95
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.8 (1.0, 3.4)	1.6 (0.6, 4.4)	0.81	1.0 (0.5, 1.8)	0.9 (0.3, 3.2)	0.97
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.6 (1.0, 2.5)	2.1 (0.8, 5.3)	0.61	1.1 (0.6, 1.8)	1.5 (0.4, 6.8)	0.64
3-PBA ($\mu\text{g/L}$)	1.5 (0.8, 2.8)	2.6 (0.8, 8.5)	0.46	1.0 (0.4, 2.4)	1.8 (0.3, 8.9)	0.55
	Dry cough at night			Doctor-diagnosed asthma		
	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	7.8 (1.0, 59.6)	2.2 (0.8, 5.8)	0.27	1.7 (0.5, 6.0)	0.5 (0.2, 1.0)	0.09 ⁺
<i>cis</i> -DCCA ($\mu\text{g/L}$)	0.9 (0.4, 2.0)	2.0 (1.0, 4.1)	0.12	1.6 (1.0, 2.6)	2.6 (1.3, 5.1) [*]	0.26
<i>trans</i> -DCCA ($\mu\text{g/L}$)	0.5 (0.4, 0.7)	2.9 (1.1, 7.7) [*]	< 0.01 ⁺	1.0 (0.5, 2.2)	3.7 (1.4, 9.3) [*]	0.04 ⁺
3-PBA ($\mu\text{g/L}$)	0.7 (0.4, 1.4)	2.9 (0.9, 9.2)	0.04 ⁺	1.6 (0.8, 3.2)	3.1 (0.8, 11.8)	0.37
	Doctor prescribed medicine for asthma			Suspected asthma		
	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	1.3 (0.3, 5.2)	0.6 (0.2, 1.6)	0.40	1.4 (0.6, 3.1)	1.2 (0.5, 2.8)	0.82
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.5 (0.9, 2.3)	1.2 (0.7, 1.9)	0.51	2.0 (1.1, 3.8) [*]	1.2 (0.5, 3.1)	0.36
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.3 (0.7, 2.1)	0.7 (0.4, 1.3)	0.16	1.7 (1.1, 2.8) [*]	1.9 (0.7, 5.2)	0.87
3-PBA ($\mu\text{g/L}$)	1.5 (0.9, 2.6)	0.5 (0.2, 1.5)	0.08 ⁺	1.8 (0.9, 3.4)	1.7 (0.5, 5.7)	0.94
	Sneezing, runny or blocked nose			Itchy-watery eyes accompanied by nose problems		
	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}	Boy RR (95% CI)	Girl RR (95% CI)	<i>p</i> _{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	0.8 (0.5, 1.3)	1.0 (0.6, 1.5)	0.63	1.6 (0.8, 3.4)	0.9 (0.4, 1.8)	0.27
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.0 (0.6, 1.7)	1.1 (0.7, 1.9)	0.71	1.2 (0.5, 2.8)	1.4 (0.6, 3.4)	0.78

<i>trans</i> -DCCA (µg/L)	1.1 (0.7, 1.6)	1.0 (0.6, 1.5)	0.73	1.5 (0.8, 2.7)	1.1 (0.5, 2.6)	0.57
3-PBA (µg/L)	1.2 (0.7, 1.9)	1.2 (0.7, 2.1)	0.87	1.6 (0.8, 3.1)	1.3 (0.5, 3.6)	0.75
Hay fever				Seasonal rhinitis		
	Boy	Girl	p_{inter}	Boy	Girl	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.5 (0.2, 11.0)	0.5 (0.2, 1.5)	0.33	0.9 (0.5, 1.7)	1.0 (0.5, 2.0)	0.90
<i>cis</i> -DCCA (µg/L)	2.0 (1.1, 3.7) *	1.1 (0.1, 17.5)	0.69	0.7 (0.3, 1.7)	1.6 (0.9, 2.9)	0.14
<i>trans</i> -DCCA (µg/L)	1.8 (1.0, 3.1)	1.1 (0.2, 8.1)	0.66	0.9 (0.5, 1.6)	1.0 (0.6, 1.9)	0.73
3-PBA (µg/L)	2.6 (1.4, 4.7) *	1.8 (0.1, 25.7)	0.80	0.9 (0.4, 1.9)	1.6 (0.8, 3.4)	0.29
Seasonal rhinoconjunctivitis				Any respiratory allergy symptom		
	Boy	Girl	p_{inter}	Boy	Girl	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	2.7 (1.2, 5.9) *	1.2 (0.4, 3.4)	0.24	0.9 (0.6, 1.4)	1.1 (0.8, 1.7)	0.47
<i>cis</i> -DCCA (µg/L)	1.4 (0.5, 3.9)	2.1 (0.8, 5.5)	0.56	1.2 (0.8, 1.8)	1.2 (0.8, 1.9)	0.92
<i>trans</i> -DCCA (µg/L)	1.8 (0.9, 3.3)	0.8 (0.3, 2.6)	0.26	1.2 (0.8, 1.6)	1.2 (0.8, 1.8)	0.90
3-PBA (µg/L)	2.1 (1.0, 4.5)	1.7 (0.5, 6.1)	0.77	1.1 (0.7, 1.7)	1.7 (1.1, 2.7) *	0.22
Any asthma symptom				Any rhinitis symptom		
	Boy	Girl	p_{inter}	Boy	Girl	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.2 (0.6, 2.4)	1.6 (0.9, 2.9)	0.52	0.8 (0.5, 1.3)	1.0 (0.6, 1.5)	0.63
<i>cis</i> -DCCA (µg/L)	1.5 (0.9, 2.8)	1.4 (0.7, 2.8)	0.81	1.0 (0.6, 1.7)	1.1 (0.7, 1.9)	0.71
<i>trans</i> -DCCA (µg/L)	1.3 (0.9, 2.1)	1.6 (0.7, 3.5)	0.70	1.1 (0.7, 1.7)	1.0 (0.6, 1.5)	0.73
3-PBA (µg/L)	1.2 (0.6, 2.2)	2.4 (1.0, 5.7)	0.20	1.2 (0.7, 1.9)	1.2 (0.7, 2.1)	0.87

*95% CI excludes the null. † p-value for interaction < 0.1. Abbreviations: RR: Risk Ratio; CI, confidence interval; p_{inter}, p-value for interaction; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Table S2.3. Associations between a 10-fold increase in maternal urinary pyrethroid metabolite concentrations ($\mu\text{g/L}$) and respiratory allergies by mode of delivery

	Wheezing or whistling in chest			Chest sounds wheezy during or after exercise		
	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	1.1 (0.6, 2.1)	2.0 (0.8, 4.6)	0.29	0.8 (0.3, 2.1)	2.4 (0.7, 7.9)	0.14
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.9 (1.1, 3.3) *	1.2 (0.5, 3.2)	0.47	1.0 (0.5, 1.9)	1.0 (0.2, 4.1)	0.99
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.8 (1.1, 2.9) *	1.3 (0.6, 2.8)	0.49	1.2 (0.6, 2.4)	0.9 (0.3, 3.0)	0.71
3-PBA ($\mu\text{g/L}$)	2.3 (1.2, 4.2) *	0.6 (0.1, 2.9)	0.12	1.4 (0.5, 3.7)	0.7 (0.2, 3.1)	0.48
	Dry cough at night			Doctor-diagnosed asthma		
	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	4.0 (1.3, 12.6) *	2.5 (0.5, 12.4)	0.65	0.4 (0.2, 1.1)	1.5 (0.6, 4.3)	0.08 ⁺
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.4 (0.8, 2.6)	1.6 (0.8, 3.2)	0.81	2.2 (1.3, 3.8) *	1.3 (0.9, 1.9)	0.13
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.6 (0.7, 3.7)	1.2 (0.6, 2.7)	0.63	2.4 (1.2, 4.8) *	1.0 (0.4, 2.7)	0.16
3-PBA ($\mu\text{g/L}$)	2.1 (0.8, 5.3)	0.6 (0.3, 1.1)	0.02 ⁺	3.4 (1.5, 7.9) *	0.5 (0.1, 5.7)	0.14
	Doctor prescribed medicine for asthma			Suspected asthma		
	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	0.6 (0.2, 2.3)	1.5 (0.6, 4.3)	0.30	1.2 (0.6, 2.4)	1.9 (0.7, 4.7)	0.44
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.4 (0.9, 2.2)	1.3 (0.9, 1.9)	0.91	1.9 (1.1, 3.4) *	1.2 (0.4, 3.5)	0.47
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.0 (0.6, 1.7)	1.0 (0.4, 2.7)	0.94	1.9 (1.2, 3.2) *	1.0 (0.4, 2.6)	0.24
3-PBA ($\mu\text{g/L}$)	1.3 (0.9, 2.0)	0.5 (0.1, 5.7)	0.44	2.3 (1.3, 4.2) *	0.4 (0.1, 2.3)	0.07 ⁺
	Sneezing, runny or blocked nose			Itchy-watery eyes accompanied by nose problems		
	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}	Vaginal delivery RR (95% CI)	C-section RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	0.9 (0.6, 1.4)	0.8 (0.5, 1.5)	0.76	1.3 (0.7, 2.5)	1.0 (0.4, 2.9)	0.68
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.2 (0.8, 1.7)	0.8 (0.4, 1.6)	0.36	1.4 (0.7, 2.8)	0.8 (0.2, 3.1)	0.46

<i>trans</i> -DCCA (µg/L)	1.1 (0.7, 1.5)	1.1 (0.6, 1.8)	0.97	1.4 (0.7, 2.5)	1.4 (0.6, 3.3)	0.98
3-PBA (µg/L)	1.3 (0.8, 2.0)	1.0 (0.5, 2.0)	0.61	1.6 (0.8, 3.2)	1.4 (0.6, 3.5)	0.85
Hay fever				Seasonal rhinitis		
	Vaginal delivery	C-section	p_{inter}	Vaginal delivery	C-section	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	0.7 (0.3, 1.9)	0.6 (0.0, 10.0)	0.85	1.0 (0.5, 1.7)	1.1 (0.5, 2.2)	0.79
<i>cis</i> -DCCA (µg/L)	1.6 (0.4, 6.9)	0.6 (0.0, 19.5)	0.61	1.1 (0.7, 2.0)	0.7 (0.3, 1.9)	0.40
<i>trans</i> -DCCA (µg/L)	1.5 (0.5, 4.6)	0.8 (0.2, 4.7)	0.61	0.9 (0.6, 1.6)	1.0 (0.5, 1.9)	0.80
3-PBA (µg/L)	2.6 (0.5, 12.5)	0.9 (0.1, 19.1)	0.55	1.2 (0.7, 2.2)	1.4 (0.5, 3.5)	0.81
Seasonal rhinoconjunctivitis				Any respiratory allergy symptom		
	Vaginal delivery	C-section	p_{inter}	Vaginal delivery	C-section	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.9 (0.9, 3.9)	2.0 (0.5, 7.4)	0.94	1.1 (0.8, 1.5)	0.9 (0.6, 1.6)	0.72
<i>cis</i> -DCCA (µg/L)	1.8 (0.9, 3.5)	0.8 (0.1, 10.6)	0.57	1.3 (0.9, 1.8)	0.9 (0.5, 1.6)	0.29
<i>trans</i> -DCCA (µg/L)	1.6 (0.8, 3.1)	1.1 (0.3, 4.4)	0.66	1.2 (0.9, 1.6)	1.1 (0.7, 1.7)	0.67
3-PBA (µg/L)	2.0 (0.9, 4.2)	2.3 (0.6, 8.6)	0.86	1.5 (1.0, 2.2)	1.0 (0.5, 1.8)	0.24
Any asthma symptom				Any rhinitis symptom		
	Vaginal delivery	C-section	p_{inter}	Vaginal delivery	C-section	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.3 (0.7, 2.2)	2.0 (1.0, 4.0)	0.32	0.9 (0.6, 1.4)	0.8 (0.5, 1.5)	0.75
<i>cis</i> -DCCA (µg/L)	1.5 (0.9, 2.6)	1.0 (0.4, 2.5)	0.44	1.2 (0.8, 1.7)	0.8 (0.4, 1.6)	0.36
<i>trans</i> -DCCA (µg/L)	1.5 (0.9, 2.3)	1.1 (0.6, 2.2)	0.53	1.1 (0.7, 1.5)	1.1 (0.6, 1.8)	0.97
3-PBA (µg/L)	1.8 (1.0, 3.3)	0.7 (0.2, 2.3)	0.16	1.3 (0.8, 2.0)	1.0 (0.5, 2.0)	0.61

* 95% CI excludes the null. ⁺ p-value for interaction < 0.1. Abbreviations: RR: Risk Ratio; CI, confidence interval; C-section, caesarian section; p_{inter}, p-value for interaction; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Table S2.4. Associations between a 10-fold increase in maternal urinary pyrethroid metabolite concentrations ($\mu\text{g/L}$) and respiratory allergies by duration of breastfeeding

	Wheezing or whistling in chest			Chest sounds wheezy during or after exercise		
	≤ 18 months RR (95% CI)	> 18 months RR (95% CI)	p_{inter}	≤ 18 months RR (95% CI)	> 18 months RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	1.3 (0.6, 2.9)	1.2 (0.7, 2.1)	0.84	0.6 (0.2, 2.1)	2.2 (1.0, 4.9)	0.08 ⁺
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.8 (0.9, 3.4)	1.8 (0.7, 4.5)	0.96	1.2 (0.6, 2.5)	0.5 (0.2, 1.3)	0.17
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.6 (1.0, 2.7)	1.7 (0.8, 3.6)	0.90	1.5 (0.8, 2.7)	0.5 (0.2, 1.2)	0.05 ⁺
3-PBA ($\mu\text{g/L}$)	1.7 (0.8, 3.4)	2.0 (0.7, 5.6)	0.78	1.7 (0.7, 4.1)	0.5 (0.1, 1.9)	0.13
	Dry cough at night			Doctor-diagnosed asthma		
	≤ 18 months RR (95% CI)	> 18 months RR (95% CI)	p_{inter}	≤ 18 months RR (95% CI)	> 18 months RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	6.1 (1.8, 20.9) [*]	1.6 (0.5, 5.6)	0.13	0.3 (0.1, 1.4)	1.0 (0.5, 2.2)	0.18
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.4 (0.7, 2.8)	1.5 (0.7, 3.2)	0.84	2.4 (1.2, 4.8) [*]	1.8 (1.1, 2.9) [*]	0.50
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.7 (0.8, 3.6)	1.1 (0.4, 3.1)	0.51	2.5 (1.2, 5.5) [*]	1.2 (0.6, 2.5)	0.17
3-PBA ($\mu\text{g/L}$)	1.5 (0.5, 4.5)	1.9 (0.5, 7.1)	0.79	3.9 (1.3, 11.4) [*]	1.1 (0.4, 2.9)	0.10
	Doctor prescribed medicine for asthma			Suspected asthma		
	≤ 18 months RR (95% CI)	> 18 months RR (95% CI)	p_{inter}	≤ 18 months RR (95% CI)	> 18 months RR (95% CI)	p_{inter}
<i>cis</i> -DBCA ($\mu\text{g/L}$)	0.4 (0.0, 2.7)	1.3 (0.5, 3.1)	0.26	1.5 (0.6, 3.5)	1.1 (0.6, 2.2)	0.65
<i>cis</i> -DCCA ($\mu\text{g/L}$)	1.6 (1.0, 2.5)	1.2 (0.8, 2.1)	0.51	1.8 (0.9, 3.7)	1.6 (0.8, 3.1)	0.78
<i>trans</i> -DCCA ($\mu\text{g/L}$)	1.4 (0.6, 3.0)	0.7 (0.5, 1.2)	0.18	1.7 (1.0, 3.0)	1.6 (0.9, 3.1)	0.94
3-PBA ($\mu\text{g/L}$)	1.3 (0.5, 3.4)	0.8 (0.3, 2.1)	0.42	1.8 (0.8, 4.0)	1.3 (0.6, 3.1)	0.59
	Sneezing, runny or blocked nose			Itchy-watery eyes accompanied by nose problems		

	≤ 18 months	> 18 months	p_{inter}	≤ 18 months	> 18 months	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	0.8 (0.5, 1.3)	0.9 (0.6, 1.5)	0.62	1.2 (0.6, 2.5)	1.2 (0.6, 2.6)	0.97
<i>cis</i> -DCCA (µg/L)	1.1 (0.7, 1.7)	1.0 (0.6, 1.6)	0.72	1.3 (0.7, 2.5)	1.1 (0.3, 4.3)	0.77
<i>trans</i> -DCCA (µg/L)	1.1 (0.7, 1.5)	1.0 (0.6, 1.5)	0.73	1.4 (0.9, 2.4)	1.1 (0.3, 4.0)	0.72
3-PBA (µg/L)	1.2 (0.8, 1.9)	1.1 (0.6, 1.9)	0.79	1.6 (0.8, 2.9)	1.4 (0.4, 4.7)	0.85
Hay fever				Seasonal rhinitis		
	≤ 18 months	> 18 months	p_{inter}	≤ 18 months	> 18 months	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	0.4 (1.0, 1.7)	1.0 (0.3, 3.3)	0.37	0.9 (0.5, 1.8)	1.0 (0.5, 1.9)	0.81
<i>cis</i> -DCCA (µg/L)	0.7 (0.3, 1.4)	2.3 (0.3, 18.1)	0.26	1.0 (0.5, 2.1)	1.0 (0.5, 1.8)	0.88
<i>trans</i> -DCCA (µg/L)	1.1 (0.6, 2.1)	1.8 (0.3, 11.8)	0.65	0.9 (0.5, 1.6)	0.9 (0.6, 1.5)	0.95
3-PBA (µg/L)	1.0 (0.3, 3.1)	3.2 (0.4, 23.5)	0.33	1.1 (0.5, 2.3)	1.3 (0.6, 2.6)	0.78
Seasonal rhinoconjunctivitis				Any respiratory allergy symptom		
	≤ 18 months	> 18 months	p_{inter}	≤ 18 months	> 18 months	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	2.1 (0.9, 4.5)	1.7 (0.6, 4.8)	0.77	0.9 (0.6, 1.3)	1.3 (0.9, 1.8)	0.21
<i>cis</i> -DCCA (µg/L)	1.7 (0.8, 3.6)	1.3 (0.3, 5.8)	0.79	1.2 (0.8, 1.8)	1.2 (0.8, 1.9)	0.94
<i>trans</i> -DCCA (µg/L)	1.3 (0.6, 2.8)	1.6 (0.6, 4.6)	0.79	1.2 (0.8, 1.6)	1.1 (0.8, 1.7)	0.99
3-PBA (µg/L)	2.0 (0.9, 4.4)	2.0 (0.6, 6.8)	0.99	1.2 (0.8, 1.9)	1.4 (0.9, 2.3)	0.70
Any asthma symptom				Any rhinitis symptom		
	≤ 18 months	> 18 months	p_{inter}	≤ 18 months	> 18 months	p_{inter}
	RR (95% CI)	RR (95% CI)		RR (95% CI)	RR (95% CI)	
<i>cis</i> -DBCA (µg/L)	1.3 (0.6, 2.7)	1.6 (0.9, 2.6)	0.67	0.8 (0.5, 1.3)	0.9 (0.6, 1.5)	0.63
<i>cis</i> -DCCA (µg/L)	1.5 (0.8, 2.8)	1.4 (0.7, 2.9)	0.87	1.1 (0.7, 1.7)	1.0 (0.6, 1.6)	0.72
<i>trans</i> -DCCA (µg/L)	1.4 (0.9, 2.3)	1.2 (0.6, 2.4)	0.71	1.1 (0.7, 1.6)	1.0 (0.6, 1.5)	0.73
3-PBA (µg/L)	1.5 (0.8, 2.8)	1.6 (0.6, 3.9)	0.93	1.2 (0.8, 1.9)	1.1 (0.6, 1.9)	0.79

*95% CI excludes the null. † p-value for interaction < 0.1. Abbreviations: RR: Risk Ratio; CI, confidence interval; p_{inter}, p-value for interaction; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Section 3. Sensitivity analyses results for doctor-diagnosed asthma and asthma suspicion

Sensitivity analysis was conducted to evaluate the robustness of the results. Because a child diagnosed with asthma at the age of 3.5 years is not likely to outgrow the disease at the age of 5 years [1], we performed additional analyses where doctor-diagnosed and suspected asthma at 3.5 years was also carried forward to the 5-year visit. Consistent with the results of the main analyses, *cis*-DCCA, *trans*-DCCA and 3-PBA were associated with almost twice the risk of the new defined doctor-diagnosed asthma and both *cis*- and *trans*-DCCA increased the risk of suspected asthma by about 60% (Table S3.1)

Table S3.1. Association between a 10-fold increase in maternal urinary pyrethroid metabolite concentrations ($\mu\text{g/L}$) and new variables for doctor-diagnosed asthma and asthma suspicion

Outcome	<i>cis</i> -DBCA RR (95% CI)	<i>cis</i> -DCCA RR (95% CI)	<i>trans</i> -DCCA RR (95% CI)	3-PBA RR (95% CI)
Doctor-diagnosed asthma	0.6 (0.3, 1.1)	2.0 (1.3, 3.0) *	2.0 (1.2, 3.4) *	2.5 (1.3, 4.9) *
Suspected asthma	1.4 (0.9, 2.2)	1.6 (1.0, 2.6) *	1.6 (1.1, 2.3) *	1.5 (0.9, 2.5)

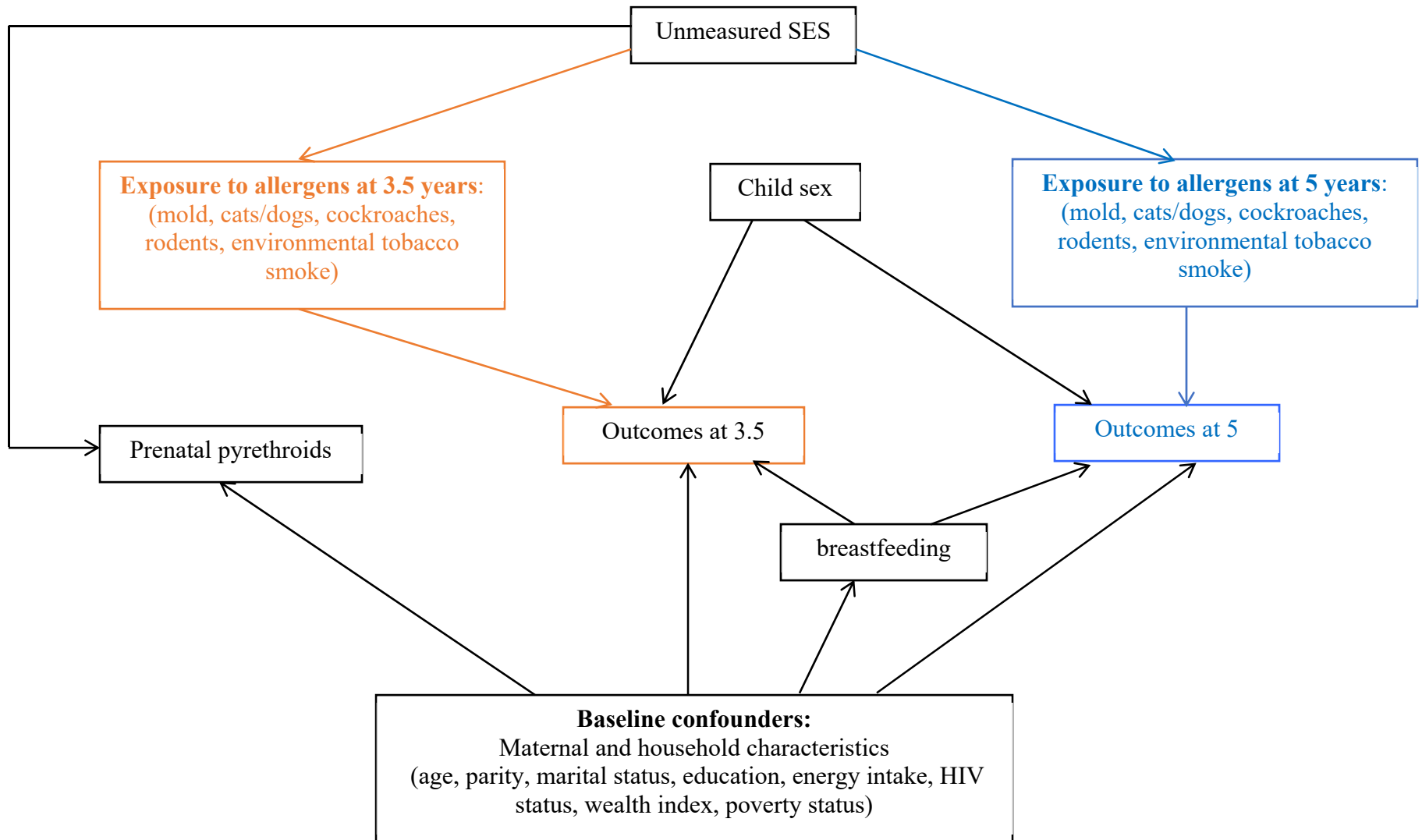
* 95% CI excludes the null (p-value < 0.05).

Abbreviations: RR: Risk Ratio; CI, confidence interval; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)- 2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Section 4. Directed acyclic graph of the relationship between pyrethroid metabolite concentrations and respiratory allergy symptoms and asthma diagnoses.

We used a directed acyclic graph (Figure S4.1) to identify the following potential confounders of the exposure-outcome relationship and predictors of censoring and outcomes to be included in both the censoring and propensity score models: child sex (boy/girl); duration of non-exclusive breastfeeding (months, continuous); maternal age (years, continuous); education (high school/no high school); marital status (married or living-as-married/not married); parity (continuous); energy intake (sufficient/insufficient); HIV status (positive/negative); as well as household wealth index (continuous) and poverty status (yes/no) during pregnancy. In the propensity score models, we included the following time-varying covariates related to exposure to allergens at 3.5 and 5 years: presence of mold or mildew (yes/no); dogs or cats (yes/no); cockroaches (yes/no); rats, mice or other rodents in the home (yes/no); and child exposure to environmental tobacco smoke (yes/no). In the censoring models, we also included pyrethroid metabolite concentrations.

Figure S4.1. Directed acyclic graph of the relationship between pyrethroid metabolite concentrations and respiratory allergy symptoms and asthma diagnoses



Section 5. Balance diagnostics

We assessed covariate balance for the final inverse probability weights (IPCW \times IPTW) (Table S5.1) [2, 3].

For the final sets of inverse probability weights, we assessed balance using three metrics:

- i) Standardized differences comparing all covariates across each quintile of exposure versus all other quintiles. Their absolute values were then averaged across the five comparisons (Figure S5.1). Quintiles of exposure were used to avoid small cell sizes and finite sample bias when assessing standardized differences.
- ii) Variance ratios comparing the variance of all covariates across each quintile of exposure versus all other quintiles, which were then averaged across the five comparisons (Figure S5.2).
- iii) Pearson correlation coefficients between the exposure and each continuous covariate (Figure S5.3)

As per published guidelines, variables with mean absolute standardized differences below 0.2 and correlations below 0.1 [2, 3] were considered to be balanced. Variance ratios of 1.0 describes a covariate which has equal variance across exposure categories, and a threshold of <2.0 has been suggested to indicate balance [4].

Table S5.1 Distribution of the final inverse probability weights for the overall model

Exposure	n	Mean	SD	Min	Max
<i>cis</i> -DBCA	1267	1.00	0.39	0.34	4.17
<i>cis</i> -DCCA	1267	1.01	0.44	0.28	5.23
<i>trans</i> -DCCA	1267	1.00	0.44	0.33	5.20
3-PBA	1286	1.00	0.38	0.34	3.72

Abbreviations: SD, standard deviation; Min, minimum; Max, Maximum; *cis*-DBCA, *cis*-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *cis*-DCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; *trans*-DCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid; 3-PBA, 3-phenoxybenzoic acid

Figure S5.1. Absolute standardized differences of all potential confounders, averaged across exposure quintiles, before (×) and after (●) inverse probability weighting

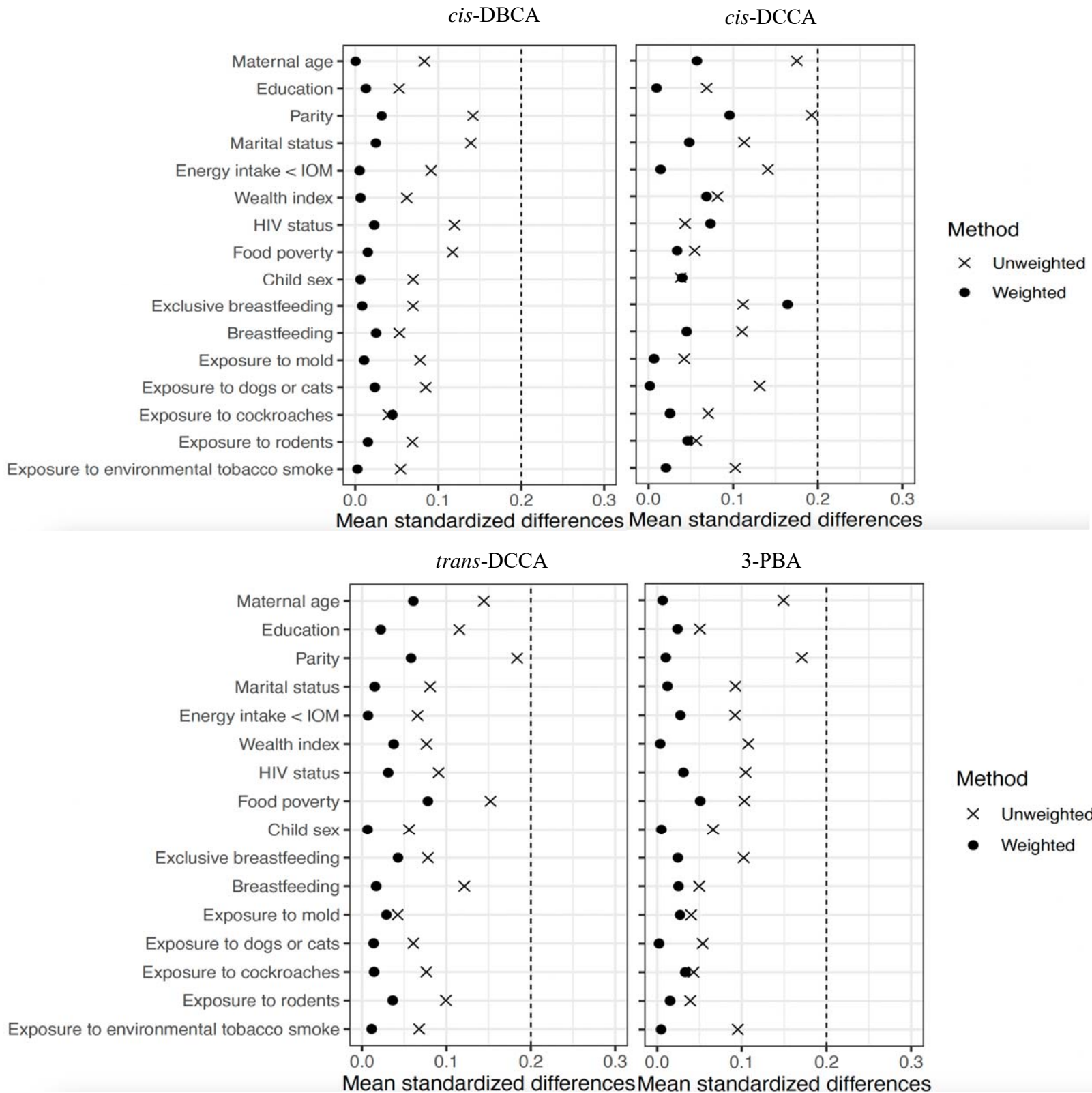


Figure S5.2. Variance ratios for all potential confounders, averaged across exposure quintiles, after inverse probability weighting

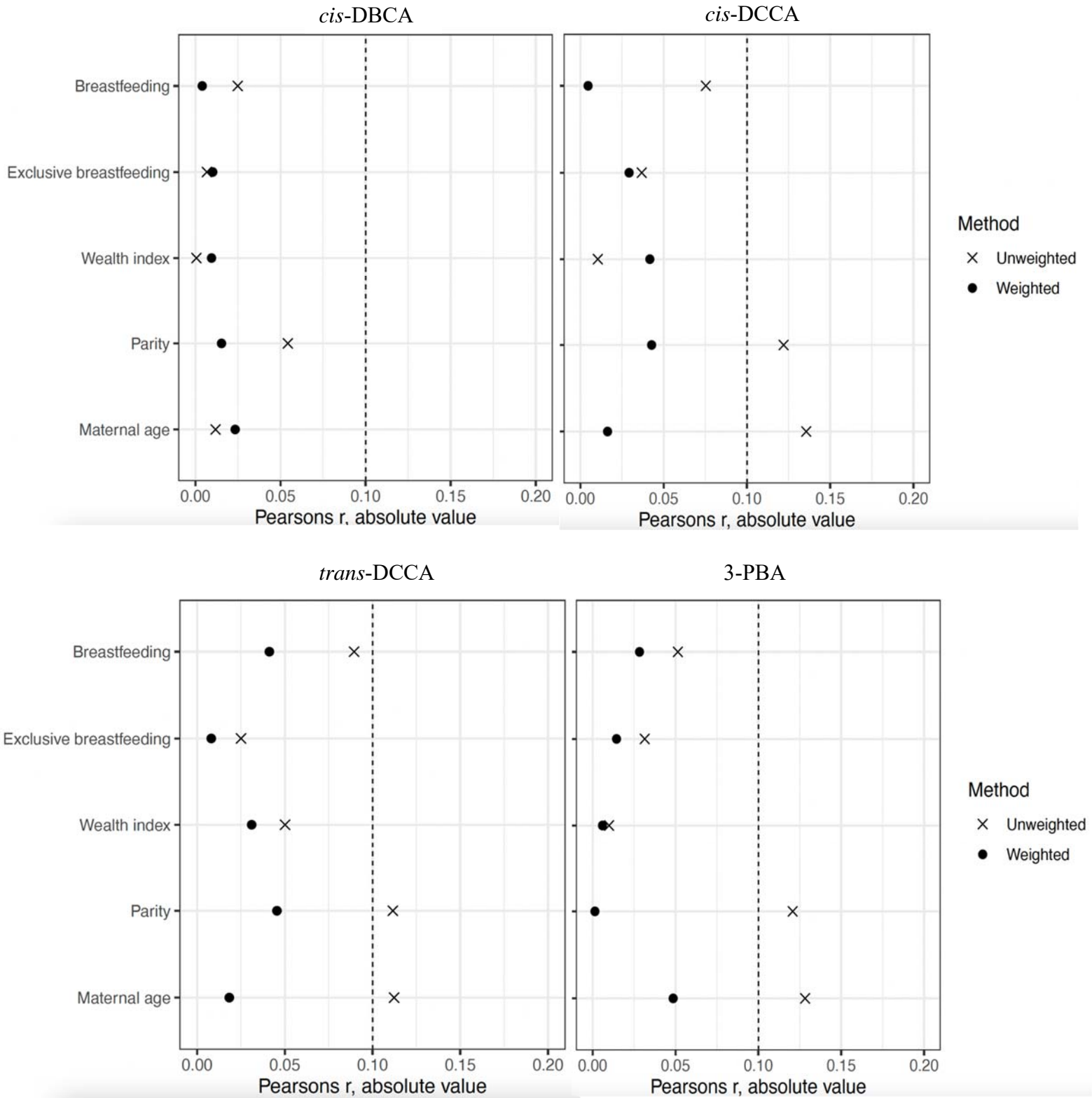
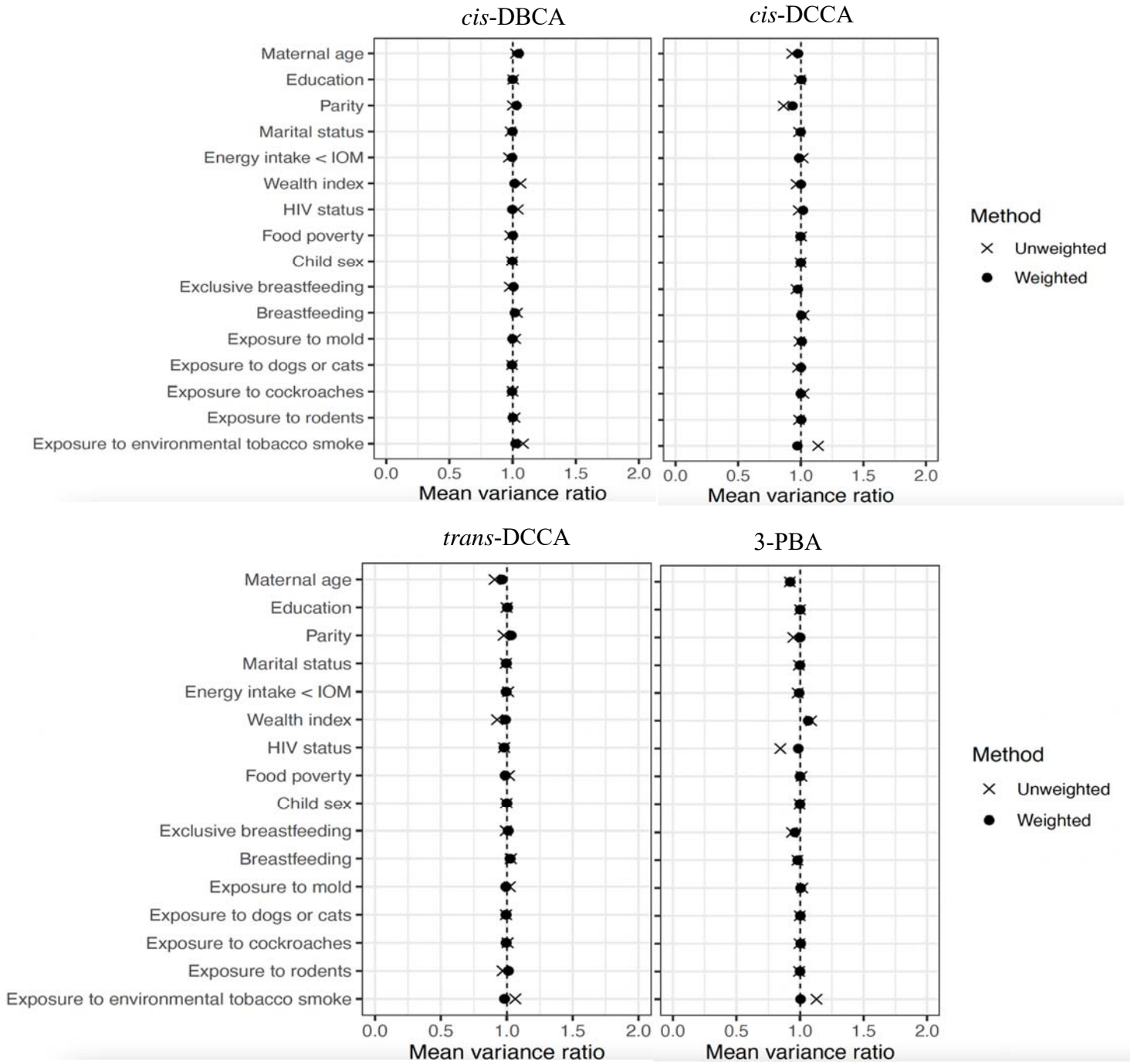


Figure S5.3. Correlations between each exposure and continuous potential confounders, before (×) and after (●) inverse probability weighting



References

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- [2] P. C. Austin, "Assessing covariate balance when using the generalized propensity score with quantitative or continuous exposures," *Statistical methods in medical research*, vol. 28, no. 5, pp. 1365-1377, 2019.
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- [4] Z. Zhang, H. J. Kim, G. Lonjon, and Y. Zhu, "Balance diagnostics after propensity score matching," *Annals of translational medicine*, vol. 7, no. 1, 2019.