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Intercomparison programme 57, 2016 for toxicological analyses in biological materials

Inst. für Arbeits-, Sozial- und Umweltmedizin, Schillerstr. 25, 91054 Erlangen

Environmental Analysis Unit
Occupational and Environmental Medicine
Att: Thomas Lundh, Dr Med Sci , Skånes
University Hospital
22185 Lund
Sweden

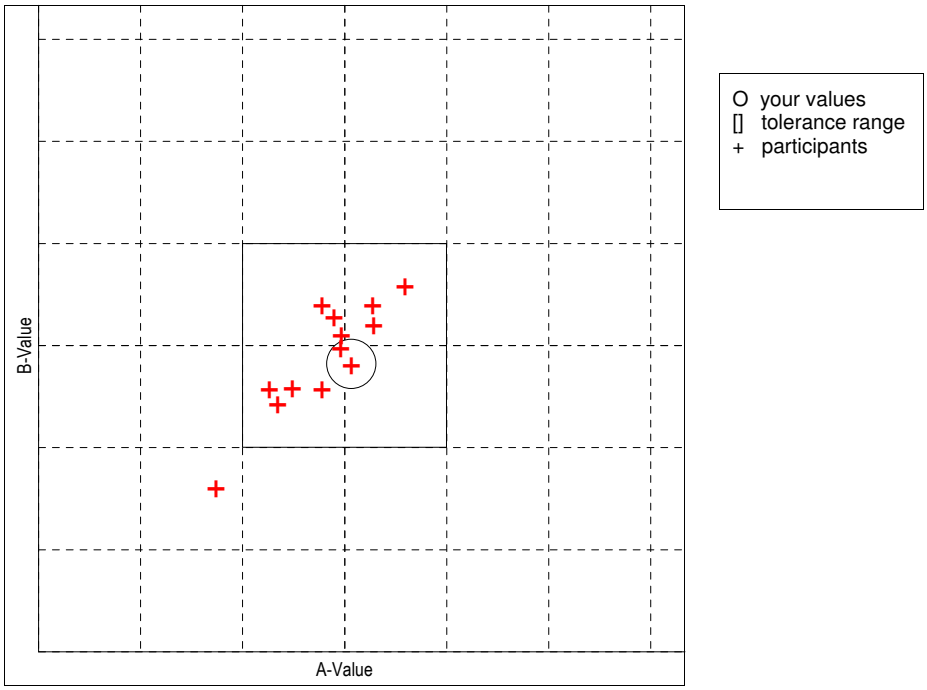
Labor: 336

Erlangen, 2016/06/24

Youden Plot

No.	parameter	evaluation	your results	ref. value	tolerance range	unit
83	3-PBA in urine	A: +	2.100	2.072	1.655 - 2.489	µg/l
		B: +	5.840	6.063	4.833 - 7.293	µg/l

3-PBA in urine (Environmental medical field)



	A	B
number of participants	15	15
within 3-fold tolerance range	13	14
mean of 3-fold tolerance range	1.991	5.717
standard deviation 3-fold tolerance range	0.198	0.636
both values within tolerance range		12 Labs; (80.0%)

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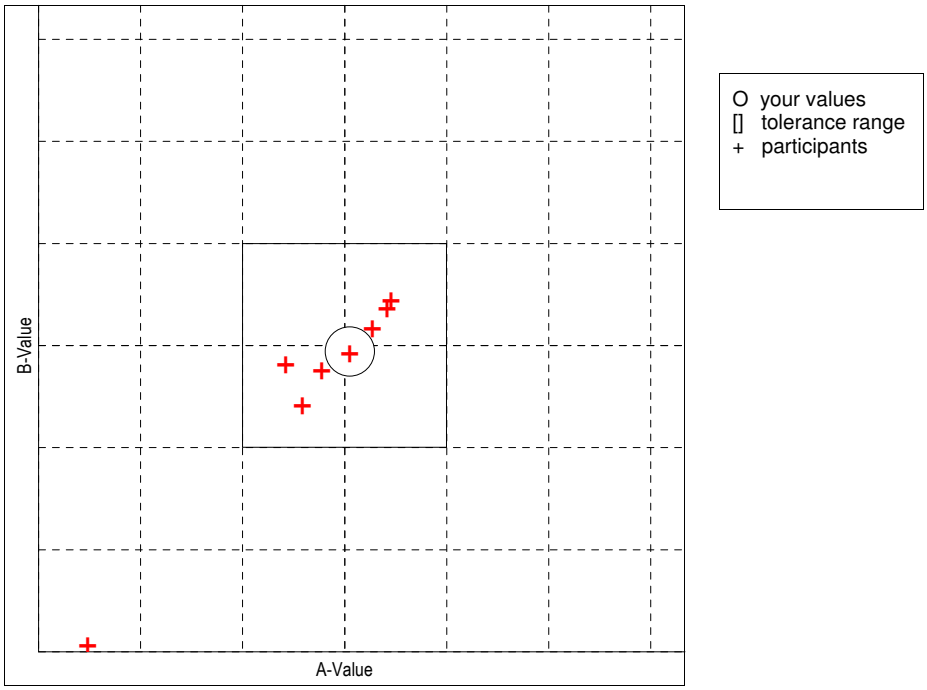
Erlangen, 2016/06/24

Youden Plot

No.	parameter	evaluation	your results	ref. value(**)	tolerance range	unit
166	Trichloropyridinol in urine	A: +	6.41	6.33	4.80 - 7.86	µg/l
		B: +	12.09	12.24	9.72 - 14.76	µg/l

Trichloropyridinol in urine (Environmental medical field)



	A	B
number of participants	9	9
within 3-fold tolerance range	8	8
mean of 3-fold tolerance range	5.85	11.32
standard deviation 3-fold tolerance range	1.38	2.56
both values within tolerance range		7 Labs; (77.8%)

(**) consensus value: reference value based on dataset of participants

German External Quality Assessment Scheme

Intercomparison programme 57, 2016
for toxicological analyses in biological materials

Prof. Dr. med. H. Drexler
on behalf of the German Society for Occupational and Environmental Medicine .e.V

Schillerstr 25, D-91054 Erlangen

External Quality Control acc. to the Guidelines of the German Federal Medical Council

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Certificate

valid until July 31, 2017

This is to certify you participated in the intercomparison programme 57 / 2016 for occupational / environmental medical - toxicological analyses. In accordance with the guidelines issued by the German Federal Medical Council (Bundesärztekammer) of January 16th, 1987 and October 16th, 1987 and August 24th, 2001 on implementation of intercomparison programmes in the medical field you have fullfilled the requirements for the following parameters:

Environmental medical field

Pb in blood	Pt in urine	1-HP in urine
3-PBA in urine	Cotinine in urine	5-OH-MEHP in urine
MEHP in urine	PFOA in serum	PFOS in serum
MBzP in urine	Cu in urine	Sr in urine
Trichloropyridinol in urine	Sb in urine	Mo in urine
Sn in urine		

Erlangen, 2016/06/24

Prof. Dr. med. H. Drexler

Prof. Dr. rer. nat. Th. Göen

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Intercomparison programme 61, 2018 for toxicological analyses in biological materials

Inst. für Arbeits-, Sozial- und Umweltmedizin, Schillerstr. 25, 91054 Erlangen

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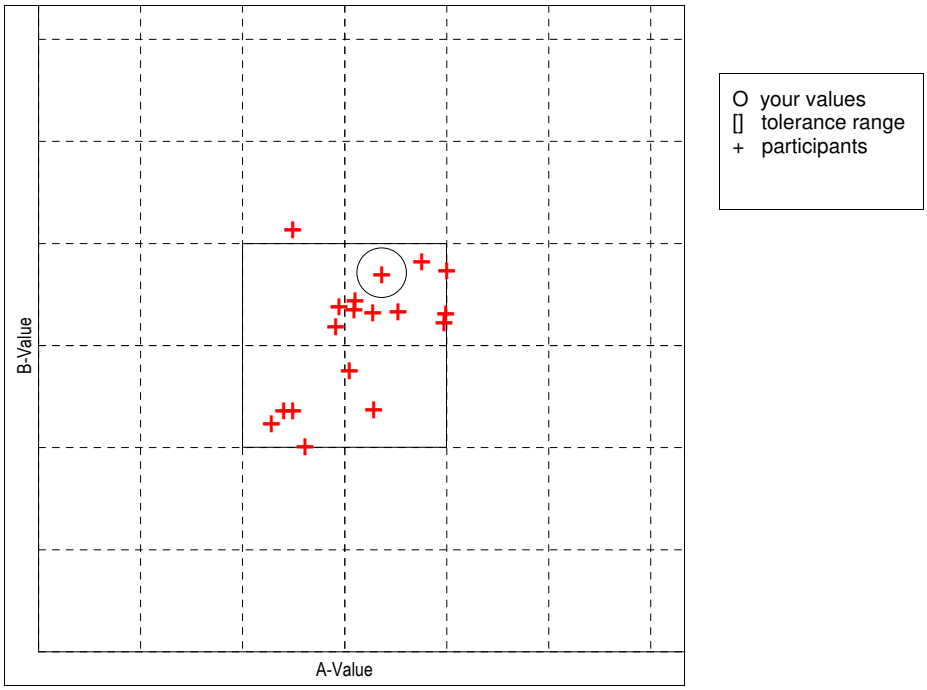
Labor: 336

Erlangen, 2018/07/07

Youden Plot

No.	parameter	evaluation	your results	ref. value	tolerance range	unit
83	3-PBA in urine	A: +	0.660	0.614	0.488 - 0.740	µg/l
		B: +	3.240	2.915	2.459 - 3.371	µg/l

3-PBA in urine (Environmental medical field)



	A	B
number of participants	18	18
within 3-fold tolerance range	18	18
mean of 3-fold tolerance range	0.632	2.976
standard deviation 3-fold tolerance range	0.068	0.273
both values within tolerance range		17 Labs; (94.4%)

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Sweden

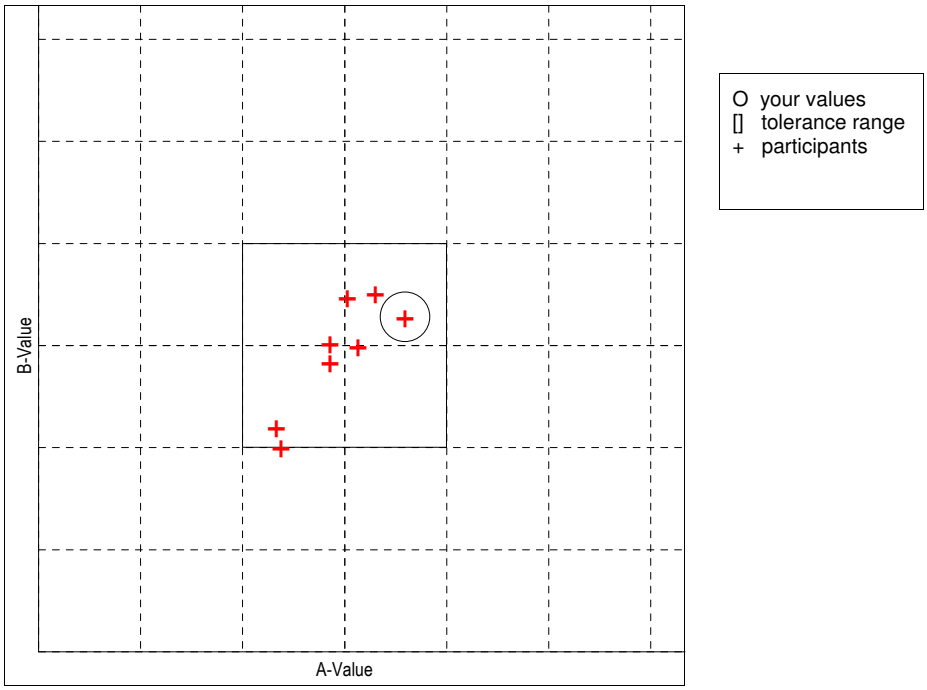
Labor: 336

Erlangen, 2018/07/07

Youden Plot

No.	parameter	evaluation	your results	ref. value	tolerance range	unit
166	Trichloropyridinol in urine	A: +	2.69	2.28	1.59 - 2.97	µg/l
		B: +	50.90	48.38	39.38 - 57.38	µg/l

Trichloropyridinol in urine (Environmental medical field)



	A	B
number of participants	8	8
within 3-fold tolerance range	8	8
mean of 3-fold tolerance range	2.24	47.60
standard deviation 3-fold tolerance range	0.28	4.68
both values within tolerance range		8 Labs; (100.0%)

German External Quality Assessment Scheme

Intercomparison programme 61, 2018
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Environmental medical field

Pb in blood	Pt in urine	1-HP in urine
3-PBA in urine	Cotinine in urine	5-OH-MEHP in urine
5-oxo-MEHP in urine	5-carboxy-MEPP in urine	MEHP in urine
PFOA in serum	PFOS in serum	MBzP in urine
Sr in urine	Zn in urine	Trichloropyridinol in urine
Sb in urine	Mo in urine	Sn in urine
TCS in urine		

Erlangen, 2018/07/07

Prof. Dr. med. H. Drexler Prof. Dr. rer. nat. Th. Göen

Supplementary Material

Islam JY, *et al. Thorax* 2022;0:1–9. doi: 10.1136/thoraxjnl-2021-218068

Table S1: Questions used to evaluate respiratory and allergic outcomes that form part of the ISAAC-III questionnaire1 unless indicated elsewise

Type of outcome	Outcome	Definition: A positive answer to the following questions:
Respiratory, asthma	Ever wheeze	Has your child ever had wheezing or whistling in the chest at any time in the past?
	Current wheeze*	Has your child had wheezing or whistling in the chest in the past 12 months?
	Severity of asthma symptoms	How many attacks of wheezing has your child had in the past 12 months?
	Severity of asthma symptoms	In the past 12 months, how often, on average, has your child's sleep been disturbed due to wheezing?
	Severity of asthma symptoms	In the past 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths?
	Ever doctor-diagnosed asthma*	Has your child ever been diagnosed with asthma by a doctor? **
	Current dry cough at night*	In the past 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?
Respiratory, LRTI	Ever LRTI	Has your child ever been diagnosed with pneumonia or chest infections (bronchitis, bronchiolitis), at any point in their life?**
	Current LRTI*	Has your child presented any episodes of pneumonia or chest infection (bronchitis, bronchiolitis) in the last 12 months?**
Allergic, Rhinitis	Ever nasal allergies (allergic rhinitis)	Has your child ever had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?
	Current nasal allergies	In the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?
	Current allergic rhinoconjunctivitis	In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?
Allergic, Eczema	Ever itchy rash (symptoms of atopic eczema)	Has your child ever had an itchy rash which was coming and going for at least six months?
	Current itchy rash	Has your child had this itchy rash at any time in the past 12 months?
	Ever doctor-diagnosed eczema*	Has your child ever been diagnosed with, or said to have, eczema or skin allergy?**

Abbreviations: LRTI: lower respiratory tract infection
*Selected for epidemiological analysis
** Not part of ISAAC-III questionnaire

[1] Mallol J, Crane J, von Mutius E, *et al.* The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: A global synthesis. *Allergol Immunopathol (Madr)* 2013;**41**:73–85. doi:10.1016/j.aller.2012.03.001

Table S2: Spearman correlation coefficients of respiratory and allergic outcomes.

Outcome	Ever doctor - diagnosed asthma	Current Dry Cough	Current LRTI	Current Nasal Allergies (Rhinitis)	Current Itchy Rash (Atopic Eczema)	Ever doctor-diagnosed Eczema
Current wheeze	0.49	0.31	0.16	0.19	0.15	-0.04
Ever doctor - diagnosed Asthma		0.16	0.16	0.21	0.10	-0.02
Current Cough			0.18	0.35	0.10	0,02
Current LRTI				0.16	0.20	0.06
Current Nasal Allergies (Rhinitis)					0.05	0.02
Current itchy rash (Atopic Eczema)						0.21

Islam JY, *et al. Thorax* 2022;0:1–9. doi: 10.1136/thoraxjnl-2021-218068

Table S3: Spearman correlation coefficients of averaged maternal specific gravity-adjusted urinary pesticide metabolite concentrations during pregnant with current children's concentration.

Averaged prenatal concentration in Mother's	**Current child concentrations**							
	TCP	**ETU**	**OHP**	**OHT**	**2,4-D**	**3PBA**	**DCCA**	**ΣPyrethroid***
TCP	0.07	0.05	0.06	-0.04	0.02	-0.03	-0.00	-0.03
ETU	0.10	0.12	0.06	-0.02	0.02	-0.03	-0.06	-0.04
OHP	0.13	0.01	0.27	-0.05	0.06	-0.03	-0.04	-0.04
OHT	0.07	0.11	-0.00	0.25	0.04	0.07	0.03	0.05
2,4-D	0.03	-0.11	-0.02	-0.17	0.20	-0.01	0.03	0.02
3PBA	0.13	0.00	-0.06	0.00	0.05	0.14	0.12	0.13
DCCA	0.17	-0.07	-0.00	-0.02	-0.01	0.06	0.06	0.06
∑ Pyrethroid*	0.16	-0.04	-0.03	-0.01	0.02	0.09	0.08	0.08

Abbreviations: TCP: 3,5,6 trichloro-2-pyridinol, ETU: Ethylenethiourea, OHP: Hydroxypyrimethanil, OHT: 5-hydroxythiabendazole, 2,4-D: 2,4-Dichlorophenoxyacetic acid 3-PBA: 3-Phenoxybenzoic acid, DCCA: 3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane-1-carboxylic acid

*∑ Pyrethroid: Sum of PBA and DCCA

Table S4: Odds ratios adjusted for child's sex and maternal smoking during pregnancy for each 10-fold increase in specific pesticide metabolite concentrations and childhood respiratory outcomes. ISA study at five years of age, Matina County, Costa Rica 2015-2016

	Current Wheeze (N = 62)			**Ever doctor-diagnosed Asthma (N= 37)**			**Current Dry Cough (N= 118)**			**Current LRTI (N=15)**		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Prenatal metabolites* (n = 303)												
TCP	1.09	0.41	2.76	0.81	0.22	2.58	0.93	0.41	2.05	2.29	0.43	9.47
ETU	0.88	0.26	2.73	0.42	0.08	1.74	1.40	0.53	3.80	0.30	0.02	2.76
OHP	0.99	0.63	1.53	0.97	0.55	1.65	1.04	0.72	1.49	0.97	0.41	2.07
OHT	0.89	0.63	1.22	0.86	0.56	1.28	1.15	0.89	1.50	0.80	0.39	1.44
2,4-D	1.40	0.67	2.78	0.41	0.12	1.19	0.92	0.48	1.70	1.02	0.21	3.35
3PBA	1.91	0.86	4.26	0.46	0.15	1.29	1.25	0.64	2.44	0.85	0.18	3.62
DCCA	1.02	0.47	2.20	0.35	0.12	0.93	0.78	0.41	1.47	1.55	0.38	6.23
∑ Pyrethroid**	1.32	0.58	2.99	0.33	0.11	0.96	0.96	0.49	1.90	1.26	0.27	5.41
Child metabolites* (n = 293)												
TCP	0.60	0.22	1.53	0.83	0.25	2.56	0.48	0.21	1.06	1.79	0.33	8.57
ETU	0.86	0.43	1.74	0.68	0.29	1.62	0.94	0.52	1.69	2.70	0.72	10.64
OHP	1.30	0.85	1.95	1.09	0.64	1.81	0.96	0.67	1.36	1.45	0.68	2.81
OHT	1.08	0.72	1.59	1.18	0.72	1.90	0.98	0.70	1.36	1.48	0.73	2.85
2,4-D	1.15	0.58	2.17	1.21	0.51	2.57	0.75	0.41	1.30	0.82	0.20	2.53
3PBA	1.84	0.96	3.62	2.17	0.96	5.07	1.36	0.79	2.34	3.81	1.13	13.68
DCCA	1.96	0.98	3.94	2.16	0.92	5.09	1.28	0.72	2.28	3.18	0.94	10.77
∑ Pyrethroid**	1.99	0.98	4.07	2.30	0.96	5.57	1.35	0.75	2.43	3.74	1.06	13.46

Abbreviations: OR: Odds ratios, CI: Confidence Intervals, TCP: 3,5,6 trichloro-2-pyridinol, ETU: Ethylene thiourea, OHP: Hydroxypyrimethanil, OHT: 5-hydroxythiabendazole, 2,4-D: 2,4-Dichlorophenoxyacetic acid 3-PBA: 3-Phenoxybenzoic acid, DCCA: 3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane-1-carboxylic acid

*Variables dichotomized at 75th percentile; Reference: Below 75th percentile

** ∑ Pyrethroid: Sum of PBA and DCCA

Table S5: Odds ratios adjusted for maternal smoking during pregnancy, child's sex of high (≥P75) specific pesticide exposures and childhood respiratory outcomes, including both prenatal and current exposures in the same model. ISA study at five years of age. Matina County. Costa Rica 2015-2016

	Current Wheeze (N = 62)			**Ever doctor-diagnosed Asthma (N= 37)**			**Current Dry Cough (N= 118)**			**Current LRTI (N=15)**		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Prenatal metabolites* (n = 303)												
TCP	1.50	0.79	2.78	0.86	0.36	1.91	1.14	0.66	1.95	1.00	0.27	3.07
ETU	1.29	0.66	2.42	0.90	0.36	2.02	0.95	0.55	1.64	1.04	0.28	3.19
OHP	0.52	0.24	1.06	0.69	0.26	1.58	1.03	0.59	1.77	0.72	0.16	2.38
OHT	0.63	0.30	1.25	0.58	0.22	1.37	1.16	0.67	2.01	0.35	0.05	1.37
2.4-D	1.30	0.66	2.49	0.51	0.17	1.28	0.96	0.54	1.69	1.37	0.39	4.24
3PBA	1.12	0.58	2.12	0.50	0.18	1.20	1.13	0.65	1.95	0.65	0.14	2.15
DCCA	0.82	0.40	1.58	0.21	0.05	0.63	0.78	0.44	1.36	1.03	0.27	3.14
∑ Pyrethroid***	1.05	0.53	2.00	0.31	0.09	0.84	0.92	0.52	1.59	1.01	0.27	3.12
Child metabolites* (n = 293)												
TCP	0.92	0.46	1.76	1.15	0.50	2.48	0.78	0.44	1.34	2.05	0.66	5.91
ETU	0.57	0.26	1.14	0.67	0.26	1.54	0.94	0.54	1.62	2.08	0.67	6.03
OHP	1.26	0.65	2.37	1.43	0.64	3.06	1.28	0.74	2.20	2.13	0.69	6.16
OHT	1.27	0.65	2.42	1.98	0.90	4.23	0.88	0.50	1.53	2.40	0.76	7.08
2.4-D	0.78	0.38	1.54	0.63	0.22	1.54	0.77	0.43	1.35	1.35	0.39	4.16
3PBA	1.71	0.91	3.15	1.82	0.83	3.83	1.40	0.81	2.39	2.80	0.94	8.17
DCCA	1.98	1.06	3.64	2.29	1.06	4.86	1.37	0.80	2.36	2.06	0.67	5.94
∑ Pyrethroid***	2.37	1.28	4.34	2.22	1.03	4.69	1.59	0.93	2.73	2.78	0.94	8.06

Abbreviations: OR: Odds ratios. CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
**∑ Pyrethroid: Sum of PBA and DCCA

Islam JY, *et al. Thorax* 2022;0:1–9. doi: 10.1136/thoraxjnl-2021-218068

Table S6: Odds ratios adjusted for child's sex and maternal smoking during pregnancy for each 10-fold increase in specific pesticide metabolite concentrations and childhood respiratory outcomes, including prenatal and current exposures in the same model. ISA study at five years of age, Matina County, Costa Rica 2015-2016

	Current Wheeze (N = 62)			**Ever doctor-diagnosed Asthma (N= 37)**			**Current Dry Cough (N= 118)**			**Current LRTI (N=15)**		
	OR**	95% CI		OR**	95% CI		OR**	95% CI		OR**	95% CI	
Prenatal metabolites* (n = 303)												
TCP	1.09	0.40	2.81	0.80	0.21	2.59	1.01	0.44	2.26	2.12	0.39	8.81
ETU	0.88	0.26	2.78	0.43	0.08	1.84	1.47	0.54	4.02	0.20	0.01	2.02
OHP	0.91	0.56	1.42	0.88	0.48	1.54	1.05	0.72	1.52	0.93	0.38	2.01
OHT	0.85	0.60	1.18	0.80	0.51	1.21	1.18	0.90	1.56	0.73	0.36	1.33
2,4-D	1.35	0.64	2.73	0.37	0.10	1.10	0.99	0.52	1.86	1.04	0.21	3.47
3PBA	1.85	0.79	4.33	0.33	0.10	1.02	1.26	0.62	2.55	0.71	0.14	3.37
DCCA	0.99	0.44	2.22	0.30	0.10	0.84	0.83	0.43	1.63	1.49	0.34	6.42
∑ Pyrethroid**	1.29	0.54	3.05	0.26	0.08	0.81	1.02	0.50	2.08	1.18	0.24	5.51
Child metabolites* (n = 293)												
TCP	0.59	0.22	1.52	0.84	0.25	2.59	0.48	0.21	1.06	1.70	0.31	8.34
ETU	0.87	0.43	1.77	0.72	0.30	1.77	0.91	0.51	1.65	3.36	0.83	14.84
OHP	1.32	0.86	1.99	1.12	0.64	1.85	0.95	0.66	1.36	1.46	0.68	2.83
OHT	1.13	0.75	1.69	1.25	0.75	2.03	0.93	0.65	1.30	1.60	0.79	3.12
2,4-D	1.10	0.54	2.09	1.39	0.58	3.01	0.75	0.41	1.32	0.81	0.19	2.57
3PBA	1.75	0.90	3.46	2.42	1.06	5.68	1.32	0.77	2.30	3.92	1.16	14.08
DCCA	1.96	0.98	3.95	2.37	1.00	5.69	1.30	0.73	2.32	3.09	0.90	10.50
∑ Pyrethroid**	1.95	0.96	4.01	2.53	1.05	6.23	1.34	0.75	2.43	3.70	1.04	13.37

Abbreviations: OR: Odds ratios, CI: Confidence Intervals

** ∑ Pyrethroid: Sum of PBA and DCCA

Table S8: Odds ratios adjusted for maternal smoking during pregnancy, child's sex, parity, and breastfeeding history (at 75th percentile) of specific pesticide metabolites during pregnancy and childhood respiratory outcomes (at 5 years of age) among Mother Child Cohort in Ecuador 2015-2016

	Current Wheeze (N = 62)			Ever doctor-diagnosed Asthma (N= 37)			Current Dry Cough (N= 118)			Current LRTI (N=15)		
	OR**	95% CI		OR**	95% CI		OR**	95% CI		OR**	95% CI	
Prenatal metabolites* (n = 303)												
TCP	1.61	0.84	3.01	0.89	0.36	1.96	1.10	0.66	1.98	1.09	0.29	3.30
ETU	1.20	0.68	2.19	0.82	0.33	1.88	0.95	0.52	1.66	1.15	0.31	3.54
OHP	0.54	0.25	1.08	0.78	0.30	1.68	1.04	0.60	1.76	0.76	0.17	2.47
OHT	0.68	0.30	1.26	0.69	0.23	1.87	1.06	0.64	1.88	0.43	0.07	1.65
2.4-D	1.39	0.76	2.46	0.49	0.17	1.20	0.90	0.52	1.57	1.48	0.44	4.36
3PBA	1.21	0.68	2.19	0.57	0.21	1.38	1.16	0.68	1.98	0.72	0.16	2.39
DCCA	0.82	0.40	1.58	0.20	0.05	0.64	0.78	0.43	1.38	1.06	0.29	3.23
∑ Pyrethroid***	1.21	0.62	2.30	0.39	0.13	0.90	0.96	0.55	1.66	1.05	0.28	3.19
Child metabolites* (n = 293)												
TCP	0.90	0.45	1.72	1.11	0.48	2.40	0.78	0.45	1.36	2.09	0.68	6.04
ETU	0.56	0.26	1.14	0.65	0.25	1.59	0.94	0.54	1.62	2.08	0.68	6.01
OHP	1.48	0.73	2.87	1.60	0.69	3.42	1.37	0.78	2.35	2.04	0.65	6.02
OHT	1.34	0.67	2.59	1.92	0.89	4.14	0.95	0.54	1.64	2.01	0.65	5.81
2.4-D	0.84	0.40	1.67	0.53	0.19	1.27	0.79	0.45	1.37	1.50	0.46	4.44
3PBA	1.66	0.85	3.12	1.80	0.79	3.64	1.36	0.78	2.31	2.63	0.90	8.00
DCCA	1.98	1.04	3.49	2.05	0.96	4.28	1.34	0.76	2.26	2.05	0.67	5.99
∑ Pyrethroid***	2.40	1.28	4.46	2.19	0.98	4.69	1.57	0.90	2.66	2.78	0.94	8.08

Abbreviations: OR: Odds ratio; CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
**∑ Pyrethroid: Sum of PBA and DCCA

Table S9: Odds ratios adjusted for current smoking in house, child's sex, and parity of high (≥P75) specific pesticide exposures and childhood respiratory outcomes. ISA study at five years of age. Matina County. Costa Rica 2015-2016

	Current Wheeze (N = 62)			**Ever Asthma (N= 37)**			**Current Dry Cough (N= 118)**			**Current LRTI (N=15)**		
	OR**	95% CI		OR**	95% CI		OR**	95% CI		OR**	95% CI	
Prenatal metabolites* (n = 303)												
TCP	1.55	0.82	2.86	0.90	0.38	1.96	1.17	0.68	2.00	1.00	0.27	3.09
ETU	1.09	0.56	2.04	0.76	0.31	1.71	0.88	0.51	1.51	1.19	0.32	3.70
OHP	0.57	0.26	1.13	0.81	0.33	1.81	1.01	0.59	1.73	0.82	0.18	2.75
OHT	0.62	0.30	1.22	0.64	0.25	1.47	1.07	0.62	1.82	0.46	0.07	1.76
2.4-D	1.36	0.71	2.54	0.55	0.20	1.30	0.89	0.51	1.52	1.53	0.46	4.51
3PBA	1.18	0.61	2.20	0.61	0.23	1.40	1.18	0.68	2.01	0.74	0.16	2.47
DCCA	0.82	0.41	1.57	0.22	0.05	0.64	0.76	0.43	1.30	1.05	0.28	3.23
∑ Pyrethroid***	1.12	0.58	2.10	0.40	0.13	0.99	0.93	0.54	1.59	1.03	0.27	3.18
Child metabolites* (n = 293)												
TCP	0.96	0.48	1.83	1.24	0.54	2.70	0.75	0.42	1.30	2.59	0.81	7.94
ETU	0.57	0.27	1.14	0.65	0.25	1.50	0.95	0.55	1.64	2.05	0.66	5.99
OHP	1.36	0.70	2.60	1.53	0.68	3.32	1.28	0.74	2.20	2.09	0.66	6.26
OHT	1.23	0.64	2.32	1.93	0.89	4.06	0.91	0.52	1.56	2.09	0.67	6.12
2.4-D	0.76	0.38	1.48	0.47	0.17	1.15	0.79	0.45	1.37	1.42	0.42	4.25
3PBA	1.77	0.94	3.29	1.72	0.79	3.62	1.51	0.88	2.61	2.46	0.82	7.20
DCCA	1.90	1.02	3.51	1.97	0.92	4.10	1.41	0.82	2.43	1.91	0.61	5.57
∑ Pyrethroid***	2.38	1.28	4.38	2.00	0.93	4.17	1.66	0.96	2.86	2.59	0.86	7.58

Abbreviations: OR: Odds ratios. CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
**∑ Pyrethroid: Sum of PBA and DCCA

Table S10. Odds ratios adjusted for child's sex and maternal smoking during pregnancy for each 10-fold increase in specific pesticide metabolite concentrations and childhood allergic outcomes. ISA study at five years of age, Matina County, Costa Rica 2015-2016

	Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**		
	OR	95% CI		OR	95% CI		OR	95% CI	
Prenatal metabolites (n = 303)									
TCP	0.63	0.22	1.66	1.36	0.42	4.00	1.45	0.31	5.54
ETU	1.06	0.32	3.28	0.91	0.22	3.44	0.87	0.11	5.11
OHP	1.40	0.92	2.13	0.99	0.56	1.66	1.19	0.59	2.25
OHT	0.86	0.61	1.18	1.20	0.82	1.71	1.04	0.61	1.67
2,4-D	1.24	0.59	2.46	0.82	0.29	1.99	0.45	0.09	1.63
3PBA	1.50	0.68	3.30	0.54	0.19	1.47	2.19	0.62	7.40
DCCA	1.57	0.73	3.38	0.69	0.26	1.76	1.86	0.55	6.22
∑ Pyrethroid**	1.52	0.68	3.41	0.57	0.20	1.57	2.15	0.59	7.58
Child metabolites (n = 293)									
TCP	0.80	0.31	2.00	0.77	0.24	2.34	1.35	0.31	5.29
ETU	0.65	0.32	1.30	1.60	0.68	3.85	0.44	0.15	1.30
OHP	1.10	0.72	1.66	1.20	0.72	1.95	0.84	0.40	1.64
OHT	1.04	0.69	1.53	1.61	1.01	2.53	0.83	0.41	1.54
2,4-D	1.00	0.50	1.90	1.13	0.48	2.38	0.93	0.28	2.45
3PBA	0.94	0.49	1.80	3.00	1.34	6.99	1.41	0.51	3.96
DCCA	0.95	0.48	1.89	2.37	1.04	5.47	1.83	0.62	5.26
∑ Pyrethroid**	0.91	0.45	1.84	2.90	1.24	6.92	1.71	0.57	5.11

Abbreviations: OR: Odds ratios, CI: Confidence Intervals
** ∑ Pyrethroid: Sum of PBA and DCCA

Table S11: Odds ratios adjusted for maternal smoking during pregnancy, child's sex of high (≥P75) specific pesticide exposures and childhood allergic outcomes, including prenatal and current exposures in the same model. ISA study at five years of age. Matina County. Costa Rica 2015-2016

	Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**		
	OR**	95% CI		OR**	95% CI		OR**	95% CI	
Prenatal metabolites* (n = 303)									
TCP	0.50	0.23	1.01	0.76	0.31	1.69	0.66	0.18	1.86
ETU	0.78	0.38	1.52	0.63	0.24	1.46	0.70	0.20	1.99
OHP	1.20	0.62	2.23	1.07	0.46	2.29	2.51	0.98	6.23
OHT	0.64	0.30	1.26	1.26	0.56	2.66	1.09	0.34	2.97
2.4-D	1.43	0.74	2.72	1.15	0.50	2.51	0.88	0.27	2.44
3PBA	1.10	0.57	2.08	0.51	0.19	1.19	1.55	0.56	3.91
DCCA	0.99	0.50	1.88	1.13	0.50	2.41	1.21	0.42	3.12
∑ Pyrethroid***	0.90	0.45	1.72	0.81	0.33	1.80	1.58	0.57	4.00
Child metabolites* (n = 293)									
TCP	0.99	0.50	1.87	0.59	0.22	1.35	0.93	0.30	2.48
ETU	0.52	0.24	1.05	1.41	0.64	2.97	0.30	0.05	1.07
OHP	1.30	0.68	2.42	1.23	0.55	2.61	0.62	0.17	1.78
OHT	1.28	0.66	2.43	1.50	0.69	3.15	0.29	0.04	1.04
2.4-D	1.08	0.54	2.06	1.12	0.48	2.43	1.28	0.43	3.42
3PBA	0.85	0.42	1.62	2.71	1.30	5.58	1.19	0.41	3.09
DCCA	0.76	0.37	1.46	2.07	0.98	4.25	1.18	0.41	3.03
∑ Pyrethroid***	0.86	0.43	1.64	2.77	1.34	5.68	1.51	0.55	3.80

Abbreviations: OR: Odds ratios. CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
** ∑ Pyrethroid: Sum of PBA and DCCA

Table S12. Odds ratios adjusted for child's sex and maternal smoking during pregnancy for each 10-fold increase in specific pesticide metabolite concentrations and childhood allergic outcomes, including prenatal and current exposures in the same model. ISA study at five years of age, Matina County, Costa Rica 2015-2016

	Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**		
	OR	95% CI		OR	95% CI		OR	95% CI	
Prenatal metabolites * (n = 303)									
TCP	0.65	0.23	1.74	1.29	0.39	3.84	1.35	0.28	5.20
ETU	1.19	0.35	3.71	0.78	0.18	3.08	0.95	0.13	5.50
OHP	1.32	0.85	2.02	0.98	0.55	1.65	1.26	0.62	2.38
OHT	0.84	0.59	1.18	1.09	0.74	1.57	1.09	0.63	1.78
2,4-D	1.29	0.61	2.61	0.76	0.26	1.88	0.43	0.08	1.60
3PBA	1.38	0.60	3.18	0.46	0.15	1.34	2.33	0.63	8.37
DCCA	1.53	0.69	3.42	0.67	0.24	1.78	1.89	0.54	6.66
∑ Pyrethroid**	1.45	0.62	3.38	0.54	0.18	1.55	2.25	0.60	8.46
Child metabolites * (n = 293)									
TCP	0.82	0.32	2.07	0.76	0.24	2.31	1.32	0.30	5.22
ETU	0.64	0.32	1.29	1.64	0.69	4.06	0.44	0.15	1.31
OHP	1.05	0.68	1.60	1.21	0.71	1.97	0.80	0.36	1.59
OHT	1.09	0.72	1.63	1.57	0.97	2.50	0.80	0.39	1.53
2,4-D	0.96	0.47	1.84	1.18	0.50	2.51	1.06	0.32	2.82
3PBA	0.91	0.47	1.75	3.24	1.44	7.60	1.31	0.46	3.77
DCCA	0.92	0.46	1.83	2.44	1.06	5.67	1.76	0.60	5.08
∑ Pyrethroid**	0.89	0.44	1.80	3.03	1.29	7.29	1.63	0.53	4.92

Abbreviations: OR: Odds ratios. CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
** ∑ Pyrethroid: Sum of PBA and DCCA

Table S13: Odds ratios adjusted for maternal smoking during pregnancy, child's sex, parity, and maternal history of asthma (yes/no), of high (≥P75) specific pesticide exposures and childhood allergic outcomes. ISA study at five years of age. Matina County. Costa Rica 2015-2016

	Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**		
	OR	95% CI		OR	95% CI		OR	95% CI	
Prenatal metabolites* (n = 303)									
TCP	0.49	0.22	0.99	0.80	0.33	1.76	0.71	0.20	2.01
ETU	0.73	0.36	1.41	0.70	0.27	1.61	0.74	0.20	2.12
OHP	1.37	0.73	2.52	1.05	0.46	2.25	2.46	0.96	6.15
OHT	0.62	0.30	1.21	1.38	0.63	2.90	0.90	0.28	2.44
2.4-D	1.43	0.75	2.64	1.22	0.54	2.58	1.02	0.32	2.80
3PBA	1.23	0.64	2.29	0.55	0.21	1.29	1.71	0.61	4.38
DCCA	1.04	0.53	1.95	1.16	0.51	2.45	1.33	0.46	3.48
∑ Pyrethroid***	1.03	0.53	1.94	0.84	0.35	1.84	1.78	0.64	4.61
Child metabolites* (n = 293)									
TCP	0.95	0.48	1.79	0.59	0.22	1.35	0.92	0.29	2.46
ETU	0.51	0.23	1.04	1.37	0.63	2.87	0.29	0.05	1.04
OHP	1.40	0.73	2.63	1.22	0.54	2.60	0.71	0.20	2.05
OHT	1.23	0.64	2.30	1.60	0.74	3.34	0.31	0.05	1.12
2.4-D	1.21	0.62	2.27	1.20	0.53	2.55	1.35	0.46	3.55
3PBA	0.83	0.41	1.59	2.53	1.22	5.18	1.13	0.38	2.95
DCCA	0.74	0.36	1.43	2.07	0.99	4.26	1.13	0.39	2.93
∑ Pyrethroid***	0.84	0.42	1.61	2.70	1.31	5.54	1.48	0.54	3.75

Abbreviations: OR: Odds ratios. CI: Confidence Intervals

*Variables dichotomized at 75th percentile; Reference: Below 75th percentile

**∑ Pyrethroid: Sum of PBA and DCCA

Table S14: Odds ratios adjusted for maternal smoking during pregnancy, child's sex, parity, and breastfeeding of high (≥P75) specific pesticide exposures and childhood allergic outcomes. ISA study at five years of age. Matina County. Costa Rica 2015-2016

	Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**		
	OR**	95% CI		OR**	95% CI		OR**	95% CI	
Prenatal metabolites* (n = 303)									
TCP	0.48	0.22	0.97	0.80	0.33	1.75	0.68	0.19	1.93
ETU	0.71	0.35	1.38	0.68	0.26	1.57	0.68	0.19	1.94
OHP	1.36	0.72	2.49	1.07	0.47	2.30	2.44	0.95	6.03
OHT	0.64	0.31	1.25	1.36	0.62	2.86	0.93	0.29	2.49
2.4-D	1.38	0.73	2.55	1.21	0.54	2.54	0.94	0.30	2.53
3PBA	1.21	0.63	2.25	0.54	0.20	1.27	1.59	0.57	4.05
DCCA	1.02	0.52	1.91	1.13	0.50	2.38	1.21	0.42	3.10
∑ Pyrethroid***	1.01	0.52	1.90	0.81	0.34	1.76	1.56	0.57	3.96
Child metabolites* (n = 293)									
TCP	0.95	0.48	1.80	0.59	0.22	1.36	0.93	0.29	2.47
ETU	0.52	0.23	1.04	1.36	0.62	2.85	0.29	0.05	1.04
OHP	1.32	0.69	2.48	1.22	0.54	2.62	0.67	0.18	1.91
OHT	1.20	0.62	2.24	1.54	0.71	3.19	0.29	0.05	1.03
2.4-D	1.21	0.62	2.26	1.15	0.51	2.45	1.25	0.43	3.24
3PBA	0.85	0.42	1.63	2.59	1.25	5.29	1.23	0.42	3.18
DCCA	0.75	0.37	1.44	2.13	1.01	4.39	1.20	0.41	3.10
∑ Pyrethroid***	0.84	0.42	1.61	2.79	1.34	5.73	1.55	0.57	3.91

Abbreviations: OR: Odds ratios. CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
** ∑ Pyrethroid: Sum of PBA and DCCA

Table S15: Odds ratios adjusted for current smoking in house, child's sex. and parity of high (≥P75) specific pesticide exposures and childhood allergic outcomes. ISA study at five years of age. Matina County. Costa Rica 2015-2016

	Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**		
	OR**	95% CI		OR**	95% CI		OR**	95% CI	
Prenatal metabolites* (n = 303)									
TCP	0.50	0.23	1.00	0.87	0.37	1.87	0.68	0.19	1.92
ETU	0.71	0.35	1.36	0.63	0.25	1.43	0.68	0.19	1.94
OHP	1.37	0.73	2.51	1.06	0.47	2.24	2.41	0.94	5.96
OHT	0.63	0.30	1.22	1.41	0.65	2.91	0.94	0.30	2.52
2.4-D	1.41	0.75	2.59	1.38	0.64	2.83	0.94	0.30	2.49
3PBA	1.22	0.64	2.26	0.62	0.24	1.41	1.59	0.58	4.04
DCCA	1.02	0.53	1.91	1.19	0.54	2.48	1.21	0.42	3.12
∑ Pyrethroid***	1.01	0.52	1.90	0.87	0.37	1.87	1.58	0.58	3.98
Child metabolites* (n = 293)									
TCP	0.93	0.47	1.76	0.63	0.24	1.42	0.92	0.29	2.47
ETU	0.52	0.24	1.04	1.37	0.64	2.83	0.29	0.05	1.05
OHP	1.35	0.70	2.52	1.17	0.52	2.45	0.66	0.18	1.88
OHT	1.19	0.62	2.21	1.58	0.74	3.12	0.29	0.05	1.03
2.4-D	1.20	0.62	2.25	1.19	0.54	2.49	1.26	0.43	3.27
3PBA	0.88	0.44	1.68	2.63	1.29	5.31	1.23	0.42	3.20
DCCA	0.77	0.38	1.49	2.05	0.99	4.15	1.20	0.41	3.10
∑ Pyrethroid***	0.87	0.43	1.67	2.65	1.30	5.33	1.55	0.57	3.91

Abbreviations: OR: Odds ratios. CI: Confidence Intervals
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile
** ∑ Pyrethroid: Sum of PBA and DCCA

Table S16: Odds ratios adjusted for maternal smoking during pregnancy and child's sex for recent environmental exposures and current **respiratory outcomes** in 293 five-year-old children from the ISA study. Matina County. Costa Rica. 2015-2016

			Current Wheeze (N = 62)			**Ever doctor-diagnosed Asthma (N= 37)**			**Current dry cough (N= 118)**			**Current LRTI (N=49)**		
	n	%	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Current maternal banana work	43	14	0.63	0.23	1.47	1.38	0.48	3.41	1.06	0.54	2.06	0.94	0.14	3.62
Maternal work in banana plantation in last 3 years	88	29	1.01	0.54	1.86	1.22	0.56	2.54	1.08	0.64	1.79	0.90	0.24	2.73
Current maternal work in agriculture	49	16	0.63	0.25	1.42	1.14	0.40	2.79	1.23	0.65	2.29	1.31	0.29	4.38
Maternal work in agriculture in last 3 years	99	33	1.00	0.54	1.80	1.17	0.55	2.40	1.19	0.72	1.95	1.05	0.32	3.04
Current paternal work in banana plantation	138	46	0.53	0.28	0.95	1.01	0.48	2.11	1.05	0.65	1.71	0.86	0.27	2.66
Paternal work in banana plantations in last 3 years	156	51	0.68	0.38	1.20	0.87	0.43	1.74	0.99	0.62	1.57	0.58	0.19	1.64
≥50 meters distance to banana plantations	232	75	0.59	0.25	1.27	0.65	0.21	1.63	1.35	0.74	2.43	0.67	0.10	2.53
Current vector control	169	56	1.17	0.65	2.13	1.03	0.50	2.19	1.77	1.08	2.91	2.78	0.84	12.53
Use of pesticides inside the house	152	50	1.40	0.78	2.55	0.99	0.47	2.07	0.96	0.60	1.54	0.50	0.15	1.50
Daily exposure to smoke of waste burning	50	17	0.53	0.20	1.20	0.34	0.08	1.04	1.28	0.68	2.38	1.27	0.28	4.24
1-HP*	74	25	1.28	0.66	2.40	1.53	0.68	3.29	1.42	0.82	2.44	0.75	0.17	2.48
2-OH-PH*	74	25	0.84	0.42	1.62	0.66	0.25	1.53	1.40	0.81	2.40	1.10	0.30	3.36

Abbreviations: OR: Odds ratios. CI: Confidence Intervals. 1-HP: 1-hydroxypyerene. 2-OH-PH: hydroxyphenanthrene
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile

Table S17: Odds ratios adjusted for maternal smoking during pregnancy and child's sex for recent environmental exposures and current allergic outcomes in 293 five-year-old children from the ISA study. Matina County. Costa Rica. 2015-2016

			Current Nasal Allergies (Allergic Rhinitis) (n = 63)			**Current Itchy Rash (Atopic Eczema) (n = 39)**			**Ever doctor-diagnosed Eczema (n = 21)**			**Current Nasal Allergies (Allergic Rhinitis) (n = 63)**		
	n	%	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Current maternal banana work	43	14	1.86	0.85	0.35	1.86	0.85	0.35	1.86	0.85	0.35	1.86	0.14	3.62
Maternal work in banana plantation in last 3 years	88	29	1.78	0.98	0.52	1.78	0.98	0.52	1.78	0.98	0.52	1.78	0.24	2.73
Current maternal work in agriculture	49	16	2.00	0.96	0.43	2.00	0.96	0.43	2.00	0.96	0.43	2.00	0.29	4.38
Maternal work in agriculture in last 3 years	99	33	1.71	0.95	0.52	1.71	0.95	0.52	1.71	0.95	0.52	1.71	0.32	3.04
Current paternal work in banana plantation	138	46	1.66	0.93	0.52	1.66	0.93	0.52	1.66	0.93	0.52	1.66	0.27	2.66
Paternal work in banana plantations in last 3 years	156	51	1.47	0.84	0.48	1.47	0.84	0.48	1.47	0.84	0.48	1.47	0.19	1.64
≥50 meters distance to banana plantations	232	75	1.84	0.92	0.42	1.84	0.92	0.42	1.84	0.92	0.42	1.84	0.10	2.53
Current vector control	169	56	1.69	0.95	0.53	1.69	0.95	0.53	1.69	0.95	0.53	1.69	0.84	12.53
Use of pesticides inside the house	152	50	2.06	1.16	0.66	2.06	1.16	0.66	2.06	1.16	0.66	2.06	0.15	1.50
Daily exposure to smoke of waste burning	50	17	2.47	1.23	0.58	2.47	1.23	0.58	2.47	1.23	0.58	2.47	0.28	4.24
1-HP*	74	25	2.99	1.62	0.86	2.99	1.62	0.86	2.99	1.62	0.86	2.99	0.17	2.48
2-OH-PH*	74	25	1.17	0.59	0.28	1.17	0.59	0.28	1.17	0.59	0.28	1.17	0.30	3.36

Abbreviations: OR: Odds ratios. CI: Confidence Intervals. 1-HP: 1-hydroxypyerene. 2-OH-PH: hydroxyphenanthrene
*Variables dichotomized at 75th percentile; Reference: Below 75th percentile