Multiple pesticides in mothers' hair and children's measurements at birth: results from the French national birth cohort (ELFE).

Supplementary files

Rémi Béranger*, Emilie M. Hardy*, Anne-Claire Binter, Marie-Aline Charles, Cécile Zaros, Brice Appenzeller**, Cécile Chevrier**.

Table of Contents:

| Figure S1. Directed acyclic graphs (DAGs) for birth weight models | (page 2) |
|---|------------------------------|
| Figure S2. Directed acyclic graphs (DAGs) for birth length models | (page 3) |
| Figure S3. Directed acyclic graphs (DAGs) for head circumference models | (page 4) |
| Table S1. Assessment of the linearity of the relations between outcomes and continuo and covariates, by using restricted cubic splines | us exposures (page 5) |
| Table S2. Population characteristics, stratified by region | (page 6) |
| Table S3 . Associations between selected pesticides and metabolites and birth weight, fpopulation (n= 300) and after stratification by sex | for the entire (page 7) |
| Table S4 . Associations between selected pesticides and metabolites and birth length, fpopulation (n= 301) and after stratification by sex | or the entire (page 8) |
| Table S5 . Associations between selected pesticides and metabolites and head circumferfor the entire population (n= 304) and after stratification by sex | erence at birth, (page 9) |
| Table S6. Sensitivity analysis: linear regression models based on the elastic net selection analyses), after exclusion of the statistical outliers | n (main (page 10) |
| Table S7. Sensitivity analysis: linear regression models stratified by region, based on th selection (main analyses). | e elastic net (page 11) |
| Table S8 . Sensitivity analysis: adding diabetes mellitus, preeclampsia, and cesarean sec circumference only) to the list of possible confounders in the elastic net regression mo | tion (head deling step |

(page 12)



DAGitty output (http://dagitty.net): Directed Acyclic Graph representing the relationships among the exposure (pesticide exposures), outcome (birth weight), and related factors. **Figure S1.** Directed acyclic graphs (DAGs) for birth weight models



DAGitty output (http://dagitty.net): Directed Acyclic Graph representing the relationships among the exposure (pesticide exposures), outcome (birth length), and related factors. **Figure S2.** Directed acyclic graphs (DAGs) for birth length models



DAGitty output (http://dagitty.net): Directed Acyclic Graph representing the relationships among the exposure (pesticide exposures), outcome (head circumference), and related factors. **Figure S3.** Directed acyclic graphs (DAGs) for head circumference models

| | Departure from linearity (<i>p</i> -value) | | | | | |
|-----------------------|---|---------------------|--------------------|--|--|--|
| Independent variable | Birth weight | Birth length | Head circumference | | | |
| EXPOSURE VARIABLES | | | | | | |
| γ-HCH (Lindane) | 0.6543 | 0.9544 | 0.7102 | | | |
| hexachlobenzene | 0.4344 | 0.8842 | 0.7089 | | | |
| Pentachlorophenol | 0.2353 | 0.1179 | 0.0227 | | | |
| α -endosulfan | 0.0664 | 0.1429 | 0.1289 | | | |
| p-nitrophenol | 0.7634 | 0.2895 | 0.7679 | | | |
| ТСРу | 0.8085 | 0.1804 | 0.6089 | | | |
| DEP | 0.8611 | 0.0322 | 0.7271 | | | |
| DETP | 0.2798 | 0.1640 | 0.1520 | | | |
| ІМРу | 0.8349 | 0.9637 | 0.4421 | | | |
| DMP | 0.3816 | 0.4924 | 0.4990 | | | |
| 3Me4NP | 0.4661 | 0.9019 | 0.6584 | | | |
| 3-PBA | 0.9893 | 0.5343 | 0.2669 | | | |
| Cl ₂ CA | 0.4207 | 0.4210 | 0.1066 | | | |
| Permethrin | 0.0120 | 0.1103 | 0.1368 | | | |
| Cypermethrin | 0.4371 | 0.5381 | 0.5391 | | | |
| Carbendazim | 0.1448 | 0.8098 | 0.9098 | | | |
| Trifluralin | 0.5836 | 0.5826 | 0.6081 | | | |
| Prosulfocarb | 0.7993 | 0.3865 | 0.3041 | | | |
| Fipronil sulfone | 0.0128 | 0.3794 | 0.1903 | | | |
| Fipronil | 0.0740 | 0.8903 | 0.2165 | | | |
| 2,4-D | 0.6057 | 0.2408 | 0.6151 | | | |
| MCPA | 0.2661 | 0.2559 | 0.9406 | | | |
| Mecoprop | 0.5555 | 0.8884 | 0.5401 | | | |
| Thiabendazole | 0.4075 | 0.6604 | 0.4513 | | | |
| Propiconazole | 0.3464 | 0.1282 | 0.2471 | | | |
| Oxadiazon | 0.4660 | 0.4332 | 0.2244 | | | |
| Terbutryn | 0.6506 | 0.0813 | 0.7610 | | | |
| Metolachlor | 0.9808 | 0.5683 | 0.9105 | | | |
| ADJUSTMENT COVARIATES | | | | | | |
| Maternal age | 0.3238 | 0.1876 | 0.6989 | | | |
| Maternal weight (log) | 0.0627 | 0.0251 | 0.6118 | | | |
| Maternal height | 0.6553 | 0.0618 | 0.5134 | | | |
| Week of gestation | 0.7965 | 0.2583 | 0.8271 | | | |

Table S1. Assessment of the linearity of the relations between outcomes and continuous exposures and covariates, by using restricted cubic splines

Abbreviations: 2,4-D, 2,4-dichlorophenoxyacetic acid; 3Me4NP, 3-methyl-4-nitrophenol; 3-PBA, 3phenoxybenzoic; Cl₂CA, cis-3-(2,2dichlorovinyl)-2,2-dimethylcyclopropane-carboxylic acid; DEP, di-ethylphosphate; DETP, di-ethyl-thiophosphate; DMP, di-methyl-phosphate; HCH, hexachlorocyclohexane; IMPy, 2isopropyl-4-methyl-6-hydroxypyrimidine; MCPA, 4-chloro-2-methylphenoxyacetic acid; TCPy, 3,5,6-trichloro-2pyridinol. Departure from linearity (p-value >0.05) was assessed with restricted cubic splines (Desquilbert and Mariotti 2010).

| Characteristics | | Southwest (n= 129) | | | Northeast (n= 182) | | | L82) |
|--------------------------------------|-----|--------------------|--------|--------------------|--------------------|-----|--------|--------------------|
| | n | % | Mean | Standard deviation | n | % | Mean | Standard deviation |
| Maternal age (years) | 129 | | 30.0 | ± 4.8 | 181 | | 30.1 | ± 5.1 |
| Prepregnancy maternal weight (kg) | 129 | | 62.5 | ± 12.4 | 181 | | 63.2 | ± 14.3 |
| Maternal height (cm) | 129 | | 164.6 | ± 5.6 | 181 | | 164.3 | ± 6.1 |
| Gestational age at birth (weeks) | 129 | | 39.4 | ± 1.2 | 180 | | 39.3 | ± 1.1 |
| Parity | | | | | | | | |
| Nulliparous | 56 | 43% | | | 77 | 42% | | |
| Parous | 73 | 57% | | | 104 | 58% | | |
| Educational level | | | | | | | | |
| High school or less | 58 | 45% | | | 82 | 45% | | |
| University | 71 | 55% | | | 99 | 55% | | |
| Tobacco consumption during pregnancy | | | | | | | | |
| No | 95 | 74% | | | 135 | 75% | | |
| Yes | 33 | 26% | | | 46 | 25% | | |
| Fish consumption during pregnancy | | | | | | | | |
| < 1 time per month | 30 | 26% | | | 63 | 39% | | |
| At least once a month | 85 | 74% | | | 97 | 61% | | |
| Child's sex | | | | | | | | |
| Boys | 60 | 47% | | | 88 | 49% | | |
| Girls | 69 | 53% | | | 93 | 51% | | |
| Cesarean section | | | | | | | | |
| No | 107 | 85% | | | 157 | 89% | | |
| Yes | 19 | 15% | | | 20 | 11% | | |
| Recruitment period | | | | | | | | |
| June 27 – July 4 | 27 | 21% | | | 50 | 27% | | |
| September 27 – October 4 | 50 | 39% | | | 61 | 34% | | |
| November 28 – December 5 | 52 | 40% | | | 71 | 39% | | |
| Birth weight (g) | 127 | | 3338.4 | ± 422.2 | 173 | | 3310.6 | ± 434.2 |
| Birth length (cm) | 124 | | 49.5 | ± 2.0 | 177 | | 49.5 | ±2.1 |
| Head circumference at birth (cm) | 127 | | 34.3 | ± 1.4 | 177 | | 34.2 | ± 1.5 |

Table S2. Population characteristics, stratified by region

| | Influence on birth weight, in g | | |
|--|---------------------------------|--------------------|-------------------------|
| Chemicals | n | $\beta_{adjusted}$ | 95% confidence interval |
| ALL (n= 300) | | | |
| β-endosulfan | | | |
| Medium (vs. low) | 91 (vs. 120) | 22 | (-78, 123) |
| High (vs. low) | 89 (vs. 120) | -80 | (-182, 23) |
| Permethrin | | | |
| Medium (vs. low) | 99 (vs. 100) | -2 | (-99, 103) |
| High (vs. low) | 101 (vs. 100) | -44 | (-152, 63) |
| Fipronil sulfone | | | |
| Medium (vs. low) | 100 (vs. 97) | 150 | (44, 255)* |
| High (vs. low) | 103 (vs. 97) | 28 | (-84, 141) |
| Mecoprop (per 2-SD increase, in log) | 300 | -54 | (-142, 35) |
| Bitertanol (detected vs. not) | 71 (vs. 229) | 82 | (-18, 182) |
| DMST (detected vs. not) | 137 (vs. 163) | 56 | (-33, 144) |
| Diflufenican (detected vs. not) | 130 (vs. 170) | -62 | (-146, 23) |
| Imidacloprid (detected vs. not) | 130 (vs. 170) | -74 | (-161, 13) |
| BOYS ONLY (n= 148) | | | |
| α -endosulfan (per 2-SD increase, in log) | 148 | -112 | (-243, 19) |
| Dieldrin | | | |
| Medium (vs. low) | 51 (vs. 43) | -22 | (-153, 108) |
| High (vs. low) | 54 (vs. 43) | 80 | (-54, 214) |
| β-endosulfan | | | |
| Medium (vs. low) | 53 (vs. 50) | -49 | (-184, 87) |
| High (vs. low) | 45 (vs. 50) | -93 | (-259, 73) |
| 3Me4NP (per 2-SD increase, in log) | 148 | 39 | (9, 239)* |
| Propoxur (detected vs. not) | 68 (vs. 80) | -261 | (-374, -147)* |
| Fipronil sulfone | | | |
| Medium (vs. low) | 46 (vs. 48) | 216 | (74, 357)* |
| High (vs. low) | 54 (vs. 48) | -114 | (-310, 82) |
| Fipronil (per 2-SD increase, in log) | 148 | 169 | (24, 314)* |
| Mecoprop (per 2-SD increase, in log) | 148 | -134 | (-249, -18)* |
| Thiabendazole (per 2-SD increase, in log) | 148 | 199 | (78, 319)* |
| Myclobutanil (detected vs. not) | 40 (vs. 108) | 80 | (-41, 200) |
| Bitertanol (detected vs. not) | 32 (vs. 116) | 0 | (-141, 141) |
| DCPMU | | | |
| Medium (vs. low) | 44 (vs. 60) | 211 | (70, 351)* |
| High (vs. low) | 44 (vs. 60) | 83 | (-51, 217) |
| Chlortoluron (detected vs. not) | 12 (vs. 136) | 108 | (-83, 299) |
| DMST (detected vs. not) | 70 (vs. 78) | 135 | (17, 254)* |
| Fenhexamid (detected vs. not) | 16 (vs. 132) | -256 | (-427, -86)* |
| GIRLS ONLY (n= 152) | | | |
| 3Me4NP (per 2-SD increase, in log) | 152 | -89 | (-196, 19) |
| Permethrin | | | |
| Medium (vs. low) | 51 (vs. 49) | 10 | (-117, 137) |
| High (vs. low) | 52 (vs. 49) | -123 | (-255, 9) |

Table S3. Associations between selected pesticides and metabolites and birth weight, for the entire population (n= 300) and after stratification by sex

Abbreviation: 3Me4NP, 3-methyl-4-nitrophenol; DCPMU, 1-(3,4-dichlorophenyl)-3-methylurea; DMST, dimethylsulftoluidide. The table presents the best predictors identified by elastic net regression modeling. Multivariable models were adjusted for parity, maternal height, prepregnancy maternal weight, gestational age at birth, tobacco consumption, alcohol consumption, and other selected exposure variables.

| · · · · · | • | Influence on birth length, in cm | | |
|--|---------------|----------------------------------|-------------------------|--|
| Chemicals | n | $\beta_{adjusted}$ | 95% confidence interval | |
| ALL (n= 301) | | | | |
| β-endosulfan | | | | |
| Medium (vs. low) | 91 (vs. 118) | -0.12 | (-0.36, 0.61) | |
| High (vs. low) | 92 (vs. 118) | -0.25 | (-0.75, 0.24) | |
| TCPy (per 2-SD increase, in log) | 301 | -0.42 | (-0.85, 0.00)* | |
| DEP | | | | |
| Medium (vs. low) | 101 (vs. 98) | -0.64 | (-1.15, -0.14)* | |
| High (vs. low) | 102 (vs. 98) | -0.13 | (-0.64, 0.38) | |
| Cypermethtin (per 2-SD increase, in log) | 301 | -0.28 | (-0.69, 0.12) | |
| Dichlorprop (detected vs. not) | 84 (vs. 217) | -0.24 | (-0.70, 0.22) | |
| Bitertanol (detected vs. not) | 68 (vs. 233) | 0.60 | (0.09, 1.10)* | |
| Fenuron (detected vs. not) | 131 (vs. 170) | -0.39 | (-0.82, 0.04) | |
| Isoproturon (detected vs. not) | 102 (vs. 199) | 0.55 | (0.11, 1.00)* | |
| BOYS ONLY (n= 141) | | | | |
| Dieldrin | | | | |
| Medium (vs. low) | 51 (vs. 40) | 0.31 | (-0.45, 1.08) | |
| High (vs. low) | 50 (vs. 40) | 0.94 | (0.14, 1.74)* | |
| β-endosulfan | | | | |
| Medium (vs. low) | 50 (vs. 47) | -0.29 | (-1.01, 0.44) | |
| High (vs. low) | 44 (vs. 40) | -0.77 | (-1.55, 0.00)* | |
| 3Me4NP (per 2-SD increase, in log) | 141 | 0.11 | (-0.09, 0.31) | |
| Bitertanol (detected vs. not) | 28 (vs. 113) | 0.04 | (-0.74, 0.83) | |
| Isoproturon (detected vs. not) | 43 (vs. 98) | 0.43 | (-0.27, 1.14) | |
| GIRLS ONLY (n= 160) | | | | |
| Dieldrin | | | | |
| Medium (vs. low) | 56 (vs. 53) | -0.11 | (-0.69, 0.47) | |
| High (vs. low) | 51 (vs. 53) | -0.54 | (-1.12, 0.03) | |
| Cypermethrin (per 2-SD increase, in log) | 160 | -0.34 | (-0.80, 0.11) | |
| Carbofuran | | | | |
| Medium (vs. low) | 50 (vs. 55) | 0.15 | (-0.44, 0.74) | |
| High (vs. low) | 55 (vs. 55) | 0.38 | (-0.21, 0.98) | |
| Dichlorprop (detected vs. not) | 45 (vs. 115) | -0.27 | (-0.81, 0.27) | |

Table S4. Associations between selected pesticides and metabolites and birth length, for the entire population (n= 301) and after stratification by sex

Abbreviation: TCPy, 3,5,6-trichloro-2-pyridinol; DEP, di-ethyl-phosphate; 3Me4NP, 3-methyl-4nitrophenol. The table presents the best predictors identified by elastic net regression modeling. Multivariable models were adjusted for parity, maternal height, prepregnancy maternal weight (squared), gestational age at birth, tobacco consumption, alcohol consumption, and other selected exposure variables.

| | | Influence on | head circumference, in cm | | |
|---|------------------|--------------------|---------------------------|--|--|
| Chemicals | n | $\beta_{adjusted}$ | 95% confidence interval | | |
| ALL (n= 304) | | | | | |
| β-endosulfan | | | | | |
| Medium (vs. low) | 92 (vs. 119) | 0.15 | (-0.24, 0.54) | | |
| High (vs. low) | 93 (vs. 119) | -0.26 | (-0.65, 0.12) | | |
| Permethrin (per 2-SD increase, in log) | 304 | -0.15 | (-0.46, 0.16) | | |
| CICF3CA | | | | | |
| Medium (vs. low) | 93 (vs. 119) | 0.39 | (-0.01, 0.78) | | |
| High (vs. low) | 92 (vs. 119) | 0.17 | (-0.20, 0.53) | | |
| Carbofuran | | | | | |
| Medium (vs. low) | 98 (vs. 206) | 0.27 | (-0.13, 0.66) | | |
| High (vs. low) | 95 (vs. 209) | -0.04 | (-0.45, 0.37) | | |
| Prosulfocarb (per 2-SD increase, in log) | 304 | -0.20 | (-0.52, 0.11) | | |
| Tebuconazole (detected vs. not) | 143 (vs. 161) | 0.31 | (0.01. 0.61)* | | |
| Prochloraz (detected vs. not) | 50 (vs. 254) | 0.57 | (0.17, 0.97)* | | |
| Imidacloprid (detected vs. not) | 131 (vs. 173) | -0.25 | (-0.56 0.06) | | |
| BOYS ONLY (n= 144) | 101 (10. 17.0) | 0.20 | (0.00, 0.00) | | |
| Pentachlorophenol | | | | | |
| Medium (vs. low) | 45 (vs. 48) | 0.16 | (-0.28, 0.60) | | |
| High (vs. low) | 51 (vs. 48) | 0.05 | (-0.54, 0.44) | | |
| Dieldrin | 51 (03. 40) | 0.05 | (0.34, 0.44) | | |
| Medium (vs. low) | 50 (vs. 43) | -0 17 | (-0.62, 0.27) | | |
| High (vs. low) | 50 (vs. 43) | 0.17 | (-0.34, 0.58) | | |
| B-endosulfan | 51 (83. 45) | 0.12 | (0.34, 0.36) | | |
| Medium (vs. low) | 52 (vs. 17) | -0.10 | (-0.57, 0.38) | | |
| High (vs. low) | $32(v_3, 47)$ | -0.51 | (-1.00, -0.02)* | | |
| B-HCH (detected vs. not) | 70 (vs 74) | -0.51 | (0.04, 0.79)* | | |
| DEB (nor 2 SD increase in log) | 111 | 0.42 | (0.04, 0.75) | | |
| DMB (per 2 SD increase, in log) | 144 | -0.50 | (0.68,0.08) | | |
| 2ModND (por 2 SD increase, in log) | 144 | -0.30 | (-0.08, 0.08) | | |
| Dermethrin (per 2-5D increase, in log) | 144 | 0.28 | (-0.14, 0.71) | | |
| CICE2CA | 144 | -0.02 | (-0.44, 0.40) | | |
| | $40 (y_{c} = 1)$ | 0.42 | | | |
| | 49 (VS. 51) | 0.42 | (-0.10, 0.88) | | |
| nigii (VS. IOW) | 44 (VS. 51) | 0.39 | (-0.10, 0.88) | | |
| Proposur (detected vs. not) | 00 (VS. 78) | -0.50 | (-0.89, -0.10)* | | |
| Dictiorprop (detected vs. not) | 42 (VS. 102) | -0.26 | (-0.70,0.18) | | |
| I niapendazoie (per 2-SD increase, in log) | 144 | 1.03 | (0.56, 1.49)* | | |
| repuconazole (detected vs. not) | 78 (VS. 66) | 0.12 | (-0.24, 0.49) | | |
| | | 0.50 | | | |
| Medium (vs. low) | 41 (vs. 59) | 0.58 | (0.09, 1.07)* | | |
| High (vs. low) | 44 (vs. 59) | -0.20 | (-0.69, 0.28) | | |
| Fenuron (detected vs. not) | 53 (vs. 91) | -0.46 | (-0.90, -0.02)* | | |
| GIRLS ONLY (n= 160) | | | | | |
| Dieldrin | | | | | |
| Medium (vs. low) | 54 (vs. 55) | 0.08 | (-0.37, 0.55) | | |
| High (vs. low) | 51 (vs. 55) | -0.39 | (-0.85, 0.08) | | |
| Prochloraz (detected vs. not) | 24 (vs. 136) | 0.72 | (0.18, 1.26)* | | |

Table S5. Associations between selected pesticides and metabolites and head circumference at birth, for the entire population (n= 304) and after stratification by sex

Abbreviation: CICF3CA, 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylic acid ; DCPMU, 1-(3,4-dichlorophenyl)-3-methylurea ; HCH, hexachlorocyclohexane ; DEP, di-ethyl-phosphate; DMP, di-methyl-phosphate. The table presents the best predictors identified by elastic net regression modeling. Multivariable models were adjusted for parity, maternal height, prepregnancy maternal weight, gestational age at birth, tobacco consumption, alcohol consumption, fish consumption, and other selected exposure variables.

| Chemicals | n | $\beta_{adjusted}$ | 95% confidence interval |
|--|---------------|--------------------|-------------------------|
| Birth weight (n=295) | | | |
| β-endosulfan | | | |
| Medium (vs. low) | 86 (vs. 120) | -27 | (-121, 68) |
| High (vs. low) | 89 (vs. 120) | -84 | (-180, 11) |
| Permethrin | | | |
| Medium (vs. low) | 98 (vs. 98) | -10 | (-104, 84) |
| High (vs. low) | 99 (vs. 98) | -69 | (-170, 31) |
| Fipronil sulfone | | | |
| Medium (vs. low) | 97 (vs. 97) | 135 | (37, 234)* |
| High (vs. low) | 101 (vs. 97) | 14 | (-90, 118) |
| Mecoprop (per 2-SD increase, in log) | 295 | -51 | (-133, 31) |
| Bitertanol (detected vs. not) | 69 (vs. 226) | 97 | (7, 193)* |
| DMST (detected vs. not) | 134 (vs. 161) | 61 | (-21, 143) |
| Diflufenican (detected vs. not) | 129 (vs. 166) | -60 | (-139, 19) |
| Imidacloprid (detected vs. not) | 127 (vs. 168) | -57 | (-138, 24) |
| Birth length (n=299) | | | |
| β-endosulfan | | | |
| Medium (vs. low) | 90 (vs. 118) | -0.19 | (-0.28, 0.67) |
| High (vs. low) | 91 (vs. 118) | -0.30 | (-0.76, 0.21) |
| TCPy (per 2-SD increase, in log) | 299 | -0.42 | (-0.84, 0.00)* |
| DEP | | | |
| Medium (vs. low) | 102 (vs. 96) | -0.61 | (-1.11, -0.12)* |
| High (vs. low) | 101 (vs. 96) | 0.04 | (-0.54, 0.46) |
| Cypermethtin (per 2-SD increase, in log) | 299 | -0.32 | (-0.72, 0.08) |
| Dichlorprop (detected vs. not) | 85 (vs. 214) | -0.29 | (-0.74, 0.16) |
| Bitertanol (detected vs. not) | 68 (vs. 231) | 0.59 | (0.09, 1.08)* |
| Fenuron (detected vs. not) | 131 (vs. 168) | -0.37 | (-0.79, 0.05) |
| Isoproturon (detected vs. not) | 102 (vs. 197) | 0.55 | (0.12, 0.99)* |
| Head Circumference (n=302) | | | |
| β-endosulfan | | | |
| Medium (vs. low) | 90 (vs. 119) | 0.05 | (-0.33, 0.43) |
| High (vs. low) | 93 (vs. 119) | -0.23 | (-0.61, 0.14) |
| Permethrin (per 2-SD increase, in log) | 302 | -0.17 | (-0.47, 0.12) |
| CICF3CA | | | |
| Medium (vs. low) | 92 (vs. 119) | 0.36 | (-0.02, 0.74) |
| High (vs. low) | 91 (vs. 119) | 0.12 | (-0.24, 0.47) |
| Carbofuran | | | |
| Medium (vs. low) | 98 (vs. 109) | 0.32 | (-0.06, 0.71) |
| High (vs. low) | 95 (vs. 109) | 0.03 | (-0.37, 0.42) |
| Prosulfocarb (per 2-SD increase, in log) | 302 | -0.26 | (-0.57, 0.05) |
| Tebuconazole (detected vs. not) | 143 (vs. 159) | 0.33 | (0.04, 0.62) |
| Prochloraz (detected vs. not) | 50 (vs. 252) | 0.49 | (-0.10, 0.88) |
| Imidacloprid (detected vs. not) | 130 (vs. 172) | -0.23 | (-0.53, 0.07) |

Table S6. Sensitivity analysis: linear regression models based on elastic net selection (main analyses), after exclusion of the statistical outliers

Abbreviation: CICF3CA, 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylic acid; DEP, di-ethyl-phosphate; DMST, dimethylsulftoluidide; TCPy, 3,5,6-trichloro-2-pyridinol. The table presents the best predictors identified by elastic net regression modeling. Statistical outliers were defined by studentized residuals with values below -2.5 or above 2.5. Multivariable models were adjusted for parity, maternal height, prepregnancy maternal weight (squared for birth length model), gestational age at birth, tobacco consumption, alcohol consumption, fish consumption (for head circumference model only), and other selected exposure variables.

| Chemicals | | Southwes | t | | Northeas | st |
|----------------------------------|--------------|--------------------|---------------|--------------|--------------------|-----------------|
| | n | $\beta_{adjusted}$ | 95% | n | $\beta_{adjusted}$ | 95% |
| | | | confidence | | | confidence |
| | | | interval | | | interval |
| Birth weight | | n= 127 | | | n= 173 | |
| Fipronil sulfone | | | | | | |
| Medium (vs. low) | 44 (vs. 35) | 38 | (-131, 208) | 56 (vs. 62) | 198 | (63, 334)* |
| High (vs. low) | 48 (vs. 35) | 31 | (-145, 209) | 55 (vs. 62) | 26 | (-116, 167) |
| Birth length | | n= 124 | | | n= 177 | |
| DEP | | | | | | |
| Medium (vs. low) | 35 (vs. 9) | 0.13 | (-1.22, 1.49) | 66 (vs. 89) | -0.87 | (-1.45, -0.29)* |
| High (vs. low) | 80 (vs. 9) | 0.30 | (-1.03, 1.63) | 22 (vs. 89) | -0.15 | (-1.01, 0.73) |
| TCPy (per 2-SD increase, in log) | 46 (vs. 78) | -0.45 | (-1.19, 0.29) | 61 (vs. 116) | -0.43 | (-0.99, 0.12) |
| Bitertanol (detected vs. not) | 31 (vs. 93) | 0.22 | (-0.59, 1.02) | 37 (vs. 140) | 0.87 | (0.20, 1.53)* |
| Isoproturon (detected vs. not) | 26 (vs. 98) | 0.84 | (-0.04, 1.73) | 76 (vs. 101) | 0.42 | (-0.11, 0.96) |
| Head Circumference | | n= 127 | | | n= 177 | |
| Tebuconazole (detected vs. not) | 62 (vs. 65) | 0.14 | (-0.35, 0.62) | 82 (vs. 95) | 0.34 | (-0.04, 0.72) |
| Prochloraz (detected vs. not) | 23 (vs. 104) | 0.21 | (-0.39, 0.82) | 27 (vs. 150) | 0.85 | (0.33, 1.37)* |

Table S7. Sensitivity analysis: linear regression models stratified by region, based on elastic netselection (main analyses).

Abbreviations: DEP, di-ethyl-phosphate; TCPy, 3,5,6-trichloro-2-pyridinol. The table presents the compounds statistically significantly associated to birth weight, birth length, and head circumference in the main analyses. Multivariable models were adjusted for parity, maternal height, prepregnancy maternal weight (squared for birth length model), gestational age at birth, tobacco consumption, alcohol consumption, fish consumption (for head circumference model only), and other selected exposure variables.

| Chemicals | n | βadjusted | 95% confidence interval |
|------------------------------------|---------------|-----------|-------------------------|
| Birth weight (n= 300) | | | |
| β-endosulfan | | | |
| Medium (vs. low) | 91 (vs. 120) | 34 | (-64, 135) |
| High (vs. low) | 89 (vs. 120) | -84 | (-187, 19) |
| Permethrin | | | |
| Medium (vs. low) | 99 (vs. 100) | -14 | (-116, 87) |
| High (vs. low) | 101 (vs. 100) | -51 | (-159 <i>,</i> 58) |
| Sum of fipronil & fipronil sulfone | | | |
| Medium (vs. low) | 99 (vs. 98) | 126 | (19, 232)* |
| High (vs. low) | 103 (vs. 98) | 58 | (-53, 169) |
| Bitertanol (detected vs. not) | 71 (vs. 229) | 76 | (-24, 176) |
| Imidacloprid (detected vs. not) | 130 (vs. 170) | -77 | (-164, 9) |
| Birth length (n= 301) | | | |
| No change | - | - | - |
| Head Circumference (n= 304) | | | |
| No change | - | - | - |

Table S8. Sensitivity analysis: replacing individual compounds by molar sum of parent compoundsand its specific metabolites, or compounds sharing common metabolites in the elastic net regressionmodeling step

The following molar sums replaced the corresponding individual analytes in the models: dialkyl phosphates (diethyl and dimethyl phosphates separately); fipronil and its metabolite (fipronil sulfone); diuron and its metabolites (DCPU and DCPMU); bifenthrin and its specific metabolite (CICF3CA); chlordanes; and DDT isomers and their metabolites. The table presents the best predictors identified by elastic net regression modeling. Multivariable models were adjusted for parity, maternal height, prepregnancy maternal weight (squared for birth length model), gestational age at birth, tobacco consumption, alcohol consumption, fish consumption (for head circumference model only), and other selected exposure variables.