Supplemental Tables

# Table S1. PAH exposure-response analysis for all jobs of case and control mothers of selected birth defects of the central nervous system and face in National Birth Defects Prevention Study 1997-2011, restricting to isolated cases

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Birth Defect** | **Exposure Level** | **Control** | **Cases** | **Crude OR (95% CI)** | **Adjusted OR (95% CI)** |
|  |  | **n** | **n** |  |  |
| Cataract†§ | None | 6064 | 190 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 383 | 13 | 1.08 (0.61-1.92) | 1.16 (0.65-2.07) |
|  | High | 383 | 17 | 1.42 (0.85-2.35) | 1.48 (0.88-2.49) |
| Glaucoma/ACD†§ | None | 6064 | 99 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 383 | 7 | 1.12 (0.52-2.43) | 1.11 (0.51-2.43) |
|  | High | 383 | 2 | n/a | n/a |
| Microphthalmia‡§ | None | 7304 | 82 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 4 | 0.87 (0.32-2.39) | 0.97 (0.35-2.68) |
|  | High | 407 | 8 | 1.75 (0.84-3.64) | 1.86 (0.88-3.93) |
| Microtia\*†§ | None | 7304 | 251 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 12 | 0.86 (0.48-1.54) | 0.92 (0.51-1.67) |
|  | High | 407 | 24 | **1.72 (1.12-2.64)** | **1.82 (1.17-2.83)** |
| Choanal atresia‡¶ | None | 7304 | 55 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 5 | 1.63 (0.65-4.09) | 2.26 (0.88-5.82) |
|  | High | 407 | 1 | n/a | n/a |
| Cerebellar hypoplasia‡§ | None | 7304 | 22 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 2 | n/ae | n/ae |
|  | High | 407 | 3 | 2.45 (0.73-8.21) | 2.00 (0.58-6.91) |
| Dandy Walker‡§ | None | 7304 | 66 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 1 | n/a | n/a |
|  | High | 407 | 9 | **2.45 (1.21-4.95)** | **2.09 (1.02-4.29)** |
| Holoprosencephaly\*‡§ | None | 7304 | 54 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 8 | **2.65 (1.25-5.61)** | **2.71 (1.26-5.81)** |
|  | High | 407 | 7 | **2.33 (1.05-5.15)** | **2.45 (1.09-5.49)** |
| Hydrocephaly‡§ | None | 7304 | 198 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 408 | 27 | **2.44 (1.61-3.69)** | **2.32 (1.52-3.54)** |
|  | High | 407 | 13 | 1.18 (0.67-2.08) | 1.11 (0.62-1.98) |

PAH = polycyclic aromatic hydrocarbon; B1 = one month prior to conception; P3 = three months after conception; isolated case = no other major defects or multiple major defects only within the same organ system; SHS = secondhand-smoke; n/a = not available, the number of exposed cases was too low for meaningful analysis (n<3).

\*Trend analysis p-value ≤ 0.05

† Exposure levels correspond to none (0 µg/m3-hours), low (0< exp ≤45.26 µg/m3-hours), and high (>45.26µg/m3-hours)

‡ Exposure levels correspond to none (0 µg/m3-hours), low (0<exp ≤51.43 µg/m3-hours), and high (exp >51.43 µg/m3-hours)

§ Adjusted for study center, maternal smoking, and any SHS at home or work during B1-P3

¶ Adjusted for study center, maternal age, maternal race, maternal smoking, and any SHS at home or work during B1-P3

# Table S2. Exposure-response analysis excluding jobs with low confidence for exposure assessment among case and control mothers of selected birth defects of the central nervous system and face, National Birth Defects Prevention Study 1997-2011

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Birth Defect** | **Exposure Level** | **Control** | **Cases** | **Crude OR (95% CI)** | **Adjusted OR (95% CI)** |
|  |  | **n** | **n** |  |  |
| Cataract\*†§ | None | 6014 | 212 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 312 | 13 | 1.18 (0.67-2.09) | 1.24 (0.69-2.21) |
|  | High | 345 | 21 | **1.73 (1.09-2.74)** | **1.80 (1.12-2.90)** |
| Glaucoma/ACD†§ | None | 6014 | 121 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 312 | 6 | 0.96 (0.42-2.19) | 0.96 (0.41-2.21) |
|  | High | 345 | 5 | 0.72 (0.29-1.77) | 0.73 (0.29-1.81) |
| Microphthalmia\*‡§ | None | 7254 | 138 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 4 | 0.63 (0.23-1.71) | 0.58 (0.21-1.58) |
|  | High | 370 | 14 | **1.99 (1.14-3.48)** | **1.81 (1.02-3.20)** |
| Microtia\*‡§ | None | 7254 | 359 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 13 | 0.78 (0.45-1.38) | 0.82 (0.46-1.44) |
|  | High | 370 | 31 | **1.69 (1.16-2.48)** | **1.74 (1.18-2.57)** |
| Choanal atresia‡¶ | None | 7254 | 106 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 3 | 0.61 (0.19-1.94) | 0.87 (0.27-2.79) |
|  | High | 370 | 4 | 0.74 (0.27-2.02) | 1.34 (0.48-3.79) |
| Cerebellar hypoplasia‡§ | None | 7254 | 37 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 4 | 2.34 (0.83-6.61) | 1.99 (0.69-5.71) |
|  | High | 370 | 4 | 2.12 (0.75-5.98) | 1.79 (0.62-5.15) |
| Dandy Walker‡§ | None | 7254 | 107 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 6 | 1.21 (0.53-2.78) | 1.07 (0.46-2.47) |
|  | High | 370 | 11 | **2.02 (1.08-3.78)** | 1.73 (0.91-3.28) |
| Holoprosencephaly\*‡§ | None | 7254 | 77 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 9 | **2.53 (1.26-5.09)** | **2.44 (1.20-4.98)** |
|  | High | 370 | 11 | **2.80 (1.48-5.31)** | **2.70 (1.40-5.20)** |
| Hydrocephaly‡§ | None | 7254 | 275 | 1.0 (reference) | 1.0 (reference) |
|  | Low | 335 | 31 | **2.44 (1.66-3.60)** | **2.31 (1.56-3.43)** |
|  | High | 370 | 18 | 1.28 (0.79-2.09) | 1.21 (0.74-1.98) |

PAH = polycyclic aromatic hydrocarbon; B1 = one month prior to conception; P3 = three months after conception; SHS = secondhand-smoke

\* Trend analysis p-value ≤ 0.05

† Exposure levels correspond to none (0 µg/m3-hours), low (0< exp ≤45.26 µg/m3-hours), and high (>45.26µg/m3-hours)

‡ Exposure levels correspond to none (0 µg/m3-hours), low (0< exp ≤51.43 µg/m3-hours), and high (exp >51.43 µg/m3-hours)

§ Adjusted for study center, maternal smoking, and any SHS at home or work during B1-P3

¶ Adjusted for study center, maternal age, maternal race, maternal smoking, and any SHS at home or work during B1-P3

# Table S3. Stratified odds ratios (ORs) by BMI for the association between maternal occupational exposure to PAHs and selected birth defects, National Birth Defects Prevention Study 1997-2011

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Birth Defect** | **Underweight/Normal Weight** | | | | **Overweight/Obese** | | | |  |
|  | **Control** | **Cases** | **Crude OR**  **(95% CI)** | **Adjusted OR**  **(95% CI)** | **Control** | **Cases** | **Crude OR**  **(95% CI)** | **Adjusted OR**  **(95% CI)** | **Breslow-Day** |
|  | **n** | **n** |  |  | **n** | **n** |  |  | **p-value** |
| Cataract† |  |  |  |  |  |  |  |  | 0.10 |
| not exposed | 3425 | 120 | 1.0 (reference) | 1.0 (reference) | 2514 | 93 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 415 | 26 | **1.79 (1.16-2.77)** | **2.09 (1.32-3.30)** | 318 | 11 | 0.94 (0.50-1.77) | 0.86 (0.45-1.65) |  |
| Glaucoma/ACD† |  |  |  |  |  |  |  |  | 0.73 |
| not exposed | 3425 | 66 | 1.0 (reference) | 1.0 (reference) | 2514 | 51 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 415 | 6 | 0.75 (0.32-1.74) | 0.74 (0.31-1.75) | 318 | 6 | 0.93 (0.40-2.19) | 0.94 (0.39-2.26) |  |
| Microphthalmia† |  |  |  |  |  |  |  |  | 0.99 |
| not exposed | 4223 | 73 | 1.0 (reference) | 1.0 (reference) | 2936 | 64 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 10 | 1.32 (0.68-2.58) | 1.05 (0.53-2.11) | 345 | 10 | 1.33 (0.68-2.61) | 1.33 (0.67-2.65) |  |
| Microtia† |  |  |  |  |  |  |  |  | 0.65 |
| not exposed | 4223 | 189 | 1.0 (reference) | 1.0 (reference) | 2936 | 150 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 23 | 1.18 (0.75-1.83) | 1.21 (0.77-1.92) | 345 | 24 | 1.36 (0.87-2.13) | 1.41 (0.90-2.23) |  |
| Choanal atresia‡ |  |  |  |  |  |  |  |  | 0.68 |
| not exposed | 4223 | 63 | 1.0 (reference) | 1.0 (reference) | 2936 | 42 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 5 | 0.77 (0.31-1.92) | 1.16 (0.45-3.00) | 345 | 5 | 1.01 (0.40-2.58) | 1.43 (0.54-3.75) |  |
| Cerebellar hypoplasia† |  |  |  |  |  |  |  |  | n/a |
| not exposed | 4223 | 18 | 1.0 (reference) | 1.0 (reference) | 2936 | 20 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 6 | **3.22 (1.27-8.16)** | **2.73 (1.03-7.20)** | 345 | 2 | n/ac | n/ac |  |
| Dandy Walker† |  |  |  |  |  |  |  |  | 0.19 |
| not exposed | 4223 | 46 | 1.0 (reference) | 1.0 (reference) | 2936 | 57 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 10 | **2.10 (1.05-4.19)** | 1.72 (0.84-3.53) | 345 | 7 | 1.05 (0.47-2.31) | 0.99 (0.44-2.23) |  |
| Holoprosencephaly† |  |  |  |  |  |  |  |  | 0.42 |
| not exposed | 4223 | 45 | 1.0 (reference) | 1.0 (reference) | 2936 | 32 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 9 | 1.93 (0.94-3.98) | 1.87 (0.88-3.96) | 345 | 11 | **2.93 (1.46-5.86)** | **2.87 (1.41-5.88)** |  |
| Hydrocephaly† |  |  |  |  |  |  |  |  | 0.29 |
| not exposed | 4223 | 145 | 1.0 (reference) | 1.0 (reference) | 2936 | 124 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 437 | 29 | **1.93 (1.28-2.91)** | **1.88 (1.23-2.88)** | 345 | 20 | 1.37 (0.84-2.23) | 1.34 (0.82-2.20) |  |

PAH = polycyclic aromatic hydrocarbon; B1 = one month prior to conception; P3 = three months after conception; SHS = secondhand-smoke; n/a = not available, the number of exposed cases was too low for meaningful analysis (n<3).

† Adjusted for study center, maternal smoking, and any SHS at home or work during B1-P3

‡ Adjusted for study center, maternal age, maternal race, maternal smoking, and any SHS at home or work during B1-P3

# Table S4. Stratified odds ratios (ORs) by maternal age for the association between maternal occupational exposure to PAHs and selected birth defects, National Birth Defects Prevention Study 1997-2011

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Birth Defect** | **Younger (under 30 years old)** | | | | **Older (30 years old or older)** | | | |  |
|  | **Control** | **Cases** | **Crude OR (95% CI)** | **Adjusted OR (95% CI)** | **Control** | **Cases** | **Crude OR (95% CI)** | **Adjusted OR (95% CI)** | **Breslow-Day** |
|  | **n** | **n** |  |  | **n** | **n** |  |  | **p-value** |
| Cataracta |  |  |  |  |  |  |  |  | 0.34 |
| not exposed | 3396 | 123 | 1.0 (reference) | 1.0 (reference) | 2667 | 92 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 590 | 33 | **1.54 (1.04-2.29)** | **1.61 (1.07-2.42)** | 177 | 6 | 0.98 (0.42-2.28) | 0.98 (0.42-2.30) |  |
| Glaucoma/ACDa |  |  |  |  |  |  |  |  | 0.11 |
| not exposed | 3396 | 74 | 1.0 (reference) | 1.0 (reference) | 2667 | 47 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 590 | 8 | 0.62 (0.30-1.30) | 0.62 (0.29-1.31) | 177 | 5 | 1.60 (0.63-4.08) | 1.63 (0.63-4.23) |  |
| Microphthalmiaa |  |  |  |  |  |  |  |  | 0.49 |
| not exposed | 4078 | 87 | 1.0 (reference) | 1.0 (reference) | 3225 | 52 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 15 | 1.12 (0.64-1.95) | 1.04 (0.59-1.83) | 189 | 5 | 1.64 (0.65-4.16) | 1.58 (0.61-4.07) |  |
| Microtiaa |  |  |  |  |  |  |  |  | 0.44 |
| not exposed | 4078 | 209 | 1.0 (reference) | 1.0 (reference) | 3225 | 151 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 39 | 1.21 (0.85-1.73) | 1.31 (0.91-1.87) | 189 | 14 | 1.58 (0.90-2.79) | 1.58 (0.88-2.82) |  |
| Choanal atresiab |  |  |  |  |  |  |  |  | 0.76 |
| not exposed | 4078 | 45 | 1.0 (reference) | 1.0 (reference) | 3225 | 63 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 7 | 1.01 (0.45-2.25) | 1.25 (0.55-2.83) | 189 | 3 | 0.81 (0.25-2.61) | 1.14 (0.35-3.72) |  |
| Cerebellar hypoplasiaa |  |  |  |  |  |  |  |  | 0.57 |
| not exposed | 4078 | 20 | 1.0 (reference) | 1.0 (reference) | 3225 | 20 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 5 | 1.63 (0.61-4.35) | 1.39 (0.51-3.79) | 189 | 3 | 2.56 (0.75-8.69) | 2.30 (0.66-8.04) |  |
| Dandy Walkera |  |  |  |  |  |  |  |  | 0.92 |
| not exposed | 4078 | 64 | 1.0 (reference) | 1.0 (reference) | 3225 | 45 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 14 | 1.42 (0.79-2.55) | 1.33 (0.73-2.41) | 189 | 4 | 1.52 (0.54-4.26) | 1.23 (0.43-3.54) |  |
| Holoprosencephalya |  |  |  |  |  |  |  |  | 0.74 |
| not exposed | 4078 | 47 | 1.0 (reference) | 1.0 (reference) | 3225 | 32 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 16 | **2.21 (1.25-3.93)** | **2.17 (1.21-3.89)** | 189 | 5 | **2.67 (1.03-6.92)** | 2.44 (0.91-6.54) |  |
| Hydrocephalya |  |  |  |  |  |  |  |  | 0.25 |
| not exposed | 4078 | 173 | 1.0 (reference) | 1.0 (reference) | 3225 | 107 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 627 | 40 | **1.50 (1.06-2.14)** | **1.45 (1.01-2.09)** | 189 | 14 | **2.23 (1.26-3.97)** | **2.21 (1.23-3.98)** |  |

PAH = polycyclic aromatic hydrocarbon; B1 = one month prior to conception; P3 = three months after conception; SHS = secondhand-smoke

† Adjusted for study center, maternal smoking, and any SHS at home or work during B1-P3

‡ Adjusted for study center, maternal age, maternal race, maternal smoking, and any SHS at home or work during B1-P3

# Table S5. Stratified odds ratios (ORs) by infant gender for the association between maternal occupational exposure to PAHs and selected birth defects, National Birth Defects Prevention Study 1997-2011

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Birth Defect** | **Male** | | | | | **Female** | | | |  |
|  | **Control n** | **Cases n** | **Crude OR**  **(95% CI)** | **Adjusted OR**  **(95% CI)** | **Control n** | | **Cases n** | **Crude OR**  **(95% CI)** | **Adjusted OR**  **(95% CI)** | **Breslow-Day p-value** |
| Cataract† |  |  |  |  |  | |  |  |  | 0.87 |
| not exposed | 3095 | 94 | 1.0 (reference) | 1.0 (reference) | 2964 | | 121 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 422 | 18 | 1.40 (0.84-2.35) | 1.33 (0.78-2.27) | 345 | | 21 | 1.49 (0.93-2.40) | **1.71 (1.04-2.80)** |  |
| Glaucoma/ACD† |  |  |  |  |  | |  |  |  | 0.13 |
| not exposed | 3095 | 62 | 1.0 (reference) | 1.0 (reference) | 2964 | | 59 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 422 | 10 | 1.18 (0.60-2.32) | 1.23 (0.62-2.47) | 345 | | 3 | 0.44 (0.14-1.40) | 0.43 (0.13-1.38) |  |
| Microphthalmia† |  |  |  |  |  | |  |  |  | 0.34 |
| not exposed | 3699 | 68 | 1.0 (reference) | 1.0 (reference) | 3600 | | 70 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 13 | 1.58 (0.86-2.87) | 1.51 (0.81-2.80) | 367 | | 7 | 0.98 (0.45-2.15) | 0.85 (0.38-1.88) |  |
| Microtia† |  |  |  |  |  | |  |  |  | 0.66 |
| not exposed | 3699 | 207 | 1.0 (reference) | 1.0 (reference) | 3600 | | 153 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 31 | 1.23 (0.84-1.82) | 1.27 (0.85-1.90) | 367 | | 22 | 1.41 (0.89-2.23) | 1.43 (0.89-2.29) |  |
| Choanal atresia‡ |  |  |  |  |  | |  |  |  | 0.53 |
| not exposed | 3699 | 39 | 1.0 (reference) | 1.0 (reference) | 3600 | | 69 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 3 | 0.63 (0.20-2.06) | 1.03 (0.31-3.47) | 367 | | 7 | 1.00 (0.45-2.18) | 1.51 (0.66-3.43) |  |
| Cerebellar hypoplasia† |  |  |  |  |  | |  |  |  | 0.72 |
| not exposed | 3699 | 26 | 1.0 (reference) | 1.0 (reference) | 3600 | | 14 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 5 | 1.58 (0.61-4.15) | 1.44 (0.53-3.87) | 367 | | 3 | 2.10 (0.60-7.35) | 1.74 (0.48-6.28) |  |
| Dandy Walker† |  |  |  |  |  | |  |  |  | 0.34 |
| not exposed | 3699 | 57 | 1.0 (reference) | 1.0 (reference) | 3600 | | 52 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 8 | 1.16 (0.55-2.44) | 1.05 (0.49-2.25) | 367 | | 10 | 1.89 (0.95-3.74) | 1.63 (0.80-3.29) |  |
| Holoprosencephaly† |  |  |  |  |  | |  |  |  | 0.26 |
| not exposed | 3699 | 33 | 1.0 (reference) | 1.0 (reference) | 3600 | | 44 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 7 | 1.75 (0.77-3.97) | 1.56 (0.67-3.63) | 367 | | 14 | **3.12 (1.69-5.75)** | **3.12 (1.66-5.87)** |  |
| Hydrocephaly† |  |  |  |  |  | |  |  |  | 0.37 |
| not exposed | 3699 | 152 | 1.0 (reference) | 1.0 (reference) | 3600 | | 128 | 1.0 (reference) | 1.0 (reference) |  |
| exposed | 449 | 28 | **1.52 (1.00-2.30)** | 1.52 (0.99-2.33) | 367 | | 26 | **1.99 (1.29-3.08)** | **1.84 (1.17-2.87)** |  |

PAH = polycyclic aromatic hydrocarbon; B1 = one month prior to conception; P3 = three months after conception; SHS = secondhand-smoke

† Adjusted for study center, maternal smoking, and any SHS at home or work during B1-P3

‡ Adjusted for maternal age, maternal race, study center, maternal smoking, and any