

Title: Prenatal exposure to acetaminophen and childhood asthmatic symptoms in a population-based cohort in Los Angeles, California.

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Table S1. Risk ratio (RR) and 95% confidence interval (CI) for asthmatic outcomes in early childhood according to maternal prenatal acetaminophen use.

| | Never use during pregnancy (N=808) | Ever use during pregnancy (N=393) | RR (95% CI) | | |
|------------------|------------------------------------|-----------------------------------|----------------------|----------------------|----------------------|
| | | | Model A ^a | Model B ^b | Model C ^c |
| Asthma diagnosis | 71 | 47 | 1.39 (0.96, 2.00) | 1.35 (0.93, 1.95) | 1.38 (0.96, 1.98) |
| Wheezing ever | 186 | 118 | 1.25 (1.01, 1.54) | 1.22 (0.99, 1.51) | 1.25 (1.01, 1.54) |
| Dry cough ever | 147 | 96 | 1.35 (1.06, 1.73) | 1.32 (1.03, 1.69) | 1.35 (1.05, 1.73) |

a. Model A: adjusted for maternal age, parity, maternal race/ethnicity, household income, smoking, maternal high fever, and aspirin or ibuprofen during pregnancy.

b. Model B: adjusted for all in Model A and pre-pregnancy BMI, use of antibiotics, maternal alcohol intake during pregnancy.

c. Model C: adjusted for all in Model A and exposures to carbon monoxide (CO), nitrogen dioxide (NO₂), PM10 and PM2.5 during pregnancy.

Table S2. Risk ratio (RR) and 95% confidence interval (CI) for asthmatic outcomes in early childhood according to maternal prenatal acetaminophen use among Hispanic/Latinx, stratified by maternal birthplace.

| | Acetaminophen use during pregnancy | No. of all children | Asthma diagnosis | | Wheezing | | Dry cough | |
|-------------------------------------|------------------------------------|---------------------|------------------|--------------------------|----------|--------------------------|-----------|--------------------------|
| | | | N | RR ^a (95% CI) | N | RR ^a (95% CI) | N | RR ^a (95% CI) |
| U.S born Hispanic/Latinx | Never | 154 | 16 | Ref | 46 | Ref | 27 | Ref |
| | Ever | 74 | 9 | 0.95 (0.42, 2.16) | 21 | 0.96 (0.60, 1.53) | 16 | 1.18 (0.63, 2.24) |
| Foreign born Hispanic/Latinx | Never | 361 | 34 | Ref | 72 | Ref | 66 | Ref |
| | Ever | 129 | 8 | 0.68 (0.30, 1.54) | 29 | 1.11 (0.75, 1.66) | 26 | 1.17 (0.76, 1.82) |

a. Adjusted for maternal age, parity, household income, smoking, maternal high fever, and aspirin or ibuprofen during pregnancy.

Table S3. Risk ratio (RR) and 95% confidence interval (CI) for asthmatic outcomes in early childhood according to maternal acetaminophen use in each pregnancy trimester.

| | | First trimester exposure | | | | Second trimester exposure | | | | Third trimester exposure | | | |
|----------------------------|------------------|--------------------------|-----|-------------------------|--------------------------|---------------------------|-----|--------------------------|--------------------------|--------------------------|-----|--------------------------|--------------------------|
| | | No | Yes | RR ^a (95%CI) | RR ^b (95% CI) | No | Yes | RR ^a (95% CI) | RR ^b (95% CI) | No | Yes | RR ^a (95% CI) | RR ^b (95% CI) |
| Total population | Asthma diagnosis | 103 | 15 | 0.82 (0.48, 1.41) | 0.61 (0.31, 1.20) | 88 | 30 | 1.33 (0.88, 2.02) | 1.42 (0.84, 2.38) | 91 | 27 | 1.25 (0.82, 1.91) | 1.25 (0.74, 2.12) |
| | Wheezing | 249 | 55 | 1.19 (0.90, 1.56) | 1.10 (0.79, 1.54) | 232 | 72 | 1.11 (0.87, 1.41) | 0.97 (0.71, 1.33) | 231 | 73 | 1.23 (0.97, 1.56) | 1.20 (0.90, 1.62) |
| | Dry cough | 203 | 40 | 1.13 (0.81, 1.57) | 0.91 (0.61, 1.34) | 179 | 64 | 1.34 (1.02, 1.75) | 1.26 (0.90, 1.76) | 183 | 60 | 1.32 (1.00, 1.74) | 1.22 (0.87, 1.71) |
| White, not Hispanic | Asthma diagnosis | 18 | 5 | 0.70 (0.26, 1.85) | 0.48 (0.12, 1.93) | 13 | 10 | 1.20 (0.55, 2.63) | 1.33 (0.41, 4.39) | 14 | 9 | 1.23 (0.53, 2.84) | 1.40 (0.42, 4.61) |
| | Wheezing | 54 | 25 | 0.99 (0.64, 1.52) | 0.86 (0.50, 1.48) | 48 | 31 | 1.08 (0.73, 1.60) | 0.97 (0.51, 1.86) | 48 | 31 | 1.18 (0.79, 1.77) | 1.30 (0.70, 2.43) |
| | Dry cough | 44 | 17 | 0.84 (0.51, 1.37) | 0.66 (0.35, 1.24) | 37 | 24 | 1.14 (0.73, 1.79) | 1.27 (0.66, 2.45) | 39 | 22 | 1.12 (0.70, 1.79) | 1.18 (0.61, 2.30) |
| Hispanic/Latinx | Asthma diagnosis | 62 | 5 | 0.50 (0.20, 1.23) | 0.53 (0.19, 1.47) | 56 | 11 | 0.89 (0.45, 1.75) | 1.17 (0.57, 2.42) | 59 | 8 | 0.64 (0.30, 1.35) | 0.70 (0.31, 1.58) |
| | Wheezing | 146 | 22 | 1.34 (0.90, 1.97) | 1.41 (0.91, 2.19) | 139 | 29 | 1.00 (0.69, 1.46) | 0.89 (0.58, 1.36) | 140 | 28 | 1.05 (0.73, 1.52) | 1.00 (0.66, 1.51) |
| | Dry cough | 120 | 15 | 1.20 (0.72, 1.99) | 1.16 (0.65, 2.08) | 111 | 24 | 1.02 (0.66, 1.59) | 0.88 (0.53, 1.46) | 110 | 25 | 1.25 (0.83, 1.89) | 1.26 (0.81, 1.97) |
| Others^c | Asthma diagnosis | 23 | 5 | 1.87 (0.79, 4.42) | 0.86 (0.24, 3.06) | 19 | 9 | 2.76 (1.36, 5.58) | 2.00 (0.76, 5.26) | 18 | 10 | 2.93 (1.44, 5.98) | 2.33 (0.83, 6.50) |
| | Wheezing | 47 | 7 | 1.24 (0.65, 2.35) | 0.82 (0.35, 1.91) | 42 | 12 | 1.42 (0.85, 2.39) | 1.14 (0.61, 2.13) | 40 | 14 | 1.88 (1.18, 2.99) | 1.91 (1.07, 3.41) |
| | Dry cough | 38 | 8 | 1.49 (0.76, 2.95) | 0.86 (0.40, 1.88) | 30 | 16 | 2.71 (1.68, 4.35) | 2.44 (1.51, 3.93) | 33 | 13 | 2.03 (1.16, 3.55) | 1.49 (0.78, 2.85) |

a. Model A: adjusted for maternal age, parity, maternal race/ethnicity, household income, smoking, maternal high fever, and aspirin or ibuprofen during pregnancy.

b. Model B: all in Model A and mutually adjusted for first, second, and third trimester exposure in the same model.

c. Includes Black/African American, Asian/Pacific Islander, American Indian, Indian (excluding American Indian, Eskimo and Aleut), Filipino, Hawaiian, Guamanian, Samoan, Eskimo, Aleut, and other specified races.

Table S4. Risk ratio (RR) and 95% confidence interval (CI) for asthmatic outcomes in early childhood according to maternal prenatal acetaminophen use, stratified by child's sex.

| | Child's sex | Acetaminophen use during pregnancy | | RR ^a (95% CI) | Interaction p-value ^a |
|-------------------------|-------------|------------------------------------|--------------|--------------------------|----------------------------------|
| | | Never use (N) | Ever use (N) | | |
| Asthma diagnosis | Male | 43 | 33 | 1.59 (1.03, 2.45) | ref |
| | Female | 28 | 14 | 1.08 (0.55, 2.12) | 0.34 |
| Wheezing | Male | 110 | 74 | 1.35 (1.04, 1.75) | ref |
| | Female | 76 | 44 | 1.13 (0.79, 1.60) | 0.35 |
| Dry cough | Male | 87 | 53 | 1.24 (0.90, 1.71) | ref |
| | Female | 60 | 43 | 1.48 (1.01, 2.15) | 0.75 |

a. Adjusted for maternal age, parity, maternal race/ethnicity, household income, smoking, maternal high fever, and aspirin or ibuprofen during pregnancy.