**SUPPLEMENTAL MATERIAL (ONLINE ONLY)**

**Supplemental Table 1:** All results for cardiac defects (including sub-classifications) and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 2:** Isolated cardiac defects and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 3:** Simple isolated cardiac defects and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 4:** All results for non-cardiac defects (including sub-classifications) and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 5:** Isolated non-cardiac defects and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 6:** Number of days exposed to antihistamines during one-month prior pregnancy through first trimester, among significant positive associations presented in Tables 3 and 4. National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 7:** Sensitivity analyses: Birth defects adversely associated with exposure to antihistamines during month four through month six of pregnancy (trimester two), among those not exposed to the antihistamine of interest during one-month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

**Supplement Figure 1:** Daily distribution of cases and controls exposed to antihistamines during one month prior to pregnancy through first trimester (among the 20 positive findings reported in Tables 3 and 4). National Birth Defects Prevention Study, 1997-2011.

**Supplemental Table 1:** All results for cardiac defects (including sub-classifications) and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine**  Birth defect   * Defect sub-classification | **Controls** | | **Cases** | | **Odds Ratios (95% CI)** | |
| **Not Exposed** | **Exposed** | **Not Exposed** | **Exposed** | **Crude** | **Adjusted** |
| **Any Antihistamine** |  |  |  |  |  |  |
| Heart defect (any) | 9622 (87.02) | 1435 (12.98) | 10294 (87.33) | 1493 (12.67) | 0.97 (0.90,1.05) | 0.96 (0.89,1.04) |
| Anomalous pulmonary venous return | 9622 (87.02) | 1435 (12.98) | 327 (89.59) | 38 (10.41) | 0.78 (0.55,1.10) | 0.84 (0.60,1.19) |
| Atrioventricular septal defect | 9622 (87.02) | 1435 (12.98) | 309 (86.55) | 48 (13.45) | 1.04 (0.77,1.42) | 0.97 (0.71,1.33) |
| Conotruncal defects | 9622 (87.02) | 1435 (12.98) | 2161 (86.61) | 334 (13.39) | 1.04 (0.91,1.18) | 1.07 (0.94,1.22) |
| * Truncus Arteriosus | 9622 (87.02) | 1435 (12.98) | 105 (81.40) | 24 (18.60) | 1.53 (0.98,2.40) | 1.54 (0.97,2.45) |
| * IAA (type B) | 9622 (87.02) | 1435 (12.98) | 38 (80.85) | 9 (19.15) | 1.59 (0.77,3.29) | 1.46 (0.69,3.10) |
| * Tetralogy of Fallot | 9622 (87.02) | 1435 (12.98) | 984 (85.19) | 171 (14.81) | 1.17 (0.98,1.38) | 1.19 (1.00,1.42) |
| * TGA | 9622 (87.02) | 1435 (12.98) | 654 (88.26) | 87 (11.74) | 0.89 (0.71,1.12) | 0.89 (0.71,1.13) |
| * Double outlet right ventricle + TGA | 9622 (87.02) | 1435 (12.98) | 161 (89.44) | 19 (10.56) | 0.79 (0.49,1.28) | 0.84 (0.51,1.37) |
| * Double outlet right ventricle (other) | 9622 (87.02) | 1435 (12.98) | 100 (87.72) | 14 (12.28) | 0.94 (0.54,1.65) | 1.13 (0.64,2.02) |
| * VSD conoventricular | 9622 (87.02) | 1435 (12.98) | 125 (89.29) | 15 (10.71) | 0.80 (0.47,1.38) | 0.97 (0.56,1.68) |
| LVOTO | 9622 (87.02) | 1435 (12.98) | 1863 (87.14) | 275 (12.86) | 0.99 (0.86,1.14) | 0.92 (0.80,1.06) |
| * HLHS | 9622 (87.02) | 1435 (12.98) | 543 (85.92) | 89 (14.08) | 1.10 (0.87,1.38) | 1.06 (0.83,1.34) |
| * Coarctation of the aorta (COA) | 9622 (87.02) | 1435 (12.98) | 985 (88.10) | 133 (11.90) | 0.91 (0.75,1.09) | 0.85 (0.70,1.03) |
| * Aortic stenosis | 9622 (87.02) | 1435 (12.98) | 418 (86.01) | 68 (13.99) | 1.09 (0.84,1.42) | 0.96 (0.73,1.25) |
| RVOTO | 9622 (87.02) | 1435 (12.98) | 1759 (88.04) | 239 (11.96) | 0.91 (0.79,1.05) | 0.87 (0.75,1.01) |
| * Pulmonary atresia | 9622 (87.02) | 1435 (12.98) | 234 (92.49) | 19 (7.51) | 0.54 (0.34,0.87) | 0.59 (0.37,0.96) |
| * Pulmonary valve stenosis (PVS) | 9222 (86.88) | 1393 (13.12) | 1295 (87.56) | 184 (12.44) | 0.94 (0.80,1.11) | 0.87 (0.73,1.03) |
| * Ebstein anomaly | 9622 (87.02) | 1435 (12.98) | 151 (88.82) | 19 (11.18) | 0.84 (0.52,1.36) | 0.89 (0.54,1.45) |
| * Tricuspid atresia | 9622 (87.02) | 1435 (12.98) | 141 (85.98) | 23 (14.02) | 1.09 (0.70,1.71) | 1.31 (0.83,2.07) |
| Septal defect | 9622 (87.02) | 1435 (12.98) | 3977 (87.75) | 555 (12.25) | 0.94 (0.84,1.04) | 0.92 (0.83,1.03) |
| * VSD perimembranous | 9622 (87.02) | 1435 (12.98) | 1431 (88.94) | 178 (11.06) | 0.83 (0.71,0.98) | 0.85 (0.71,1.00) |
| * VSD + COA | 9622 (87.02) | 1435 (12.98) | 257 (87.71) | 36 (12.29) | 0.94 (0.66,1.34) | 0.89 (0.62,1.28) |
| * VSD + PVS | 9622 (87.02) | 1435 (12.98) | 137 (93.20) | 10 (6.80) | 0.49 (0.26,0.93) | 0.53 (0.27,1.02) |
| * ASD + PVS | 9622 (87.02) | 1435 (12.98) | 210 (86.78) | 32 (13.22) | 1.02 (0.70,1.49) | 0.92 (0.62,1.35) |
| * VSD + ASD | 9622 (87.02) | 1435 (12.98) | 639 (86.94) | 96 (13.06) | 1.01 (0.81,1.26) | 1.03 (0.82,1.29) |
| * ASD secundum or ASD NOS | 9622 (87.02) | 1435 (12.98) | 2544 (87.15) | 375 (12.85) | 0.99 (0.88,1.12) | 0.95 (0.84,1.08) |
| **Cetirizine** |  |  |  |  |  |  |
| Heart defect (any) | 10897 (98.55) | 160 (1.45) | 11649 (98.83) | 138 (1.17) | 0.81 (0.64,1.02) | 0.82 (0.65,1.03) |
| Anomalous pulmonary venous return | 10897 (98.55) | 160 (1.45) | 359 (98.36) | 6 (1.64) | 1.14 (0.50,2.59) | * 1. (0.59,3.08) |
| Conotruncal defect | 10897 (98.55) | 160 (1.45) | 2450 (98.20) | 45 (1.80) | 1.25 (0.90,1.75) | * 1. (0.94,1.85) |
| * Truncus Arteriosus | **10897 (98.55)** | **160 (1.45)** | **123 (95.35)** | **6 (4.65)** | **3.32 (1.44,7.65)** | * 1. **(1.40,7.69)** |
| * Tetralogy of Fallot | **10897 (98.55)** | **160 (1.45)** | **1129 (97.75)** | **26 (2.25)** | **1.57 (1.03,2.39)** | **1.64 (1.07,2.50)** |
| * TGA | 10897 (98.55) | 160 (1.45) | 731 (98.65) | 10 (1.35) | 0.93 (0.49,1.77) | 0.95 (0.50,1.82) |
| LVOTO | 10897 (98.55) | 160 (1.45) | 2116 (98.97) | 22 (1.03) | 0.71 (0.45,1.11) | 0.63 (0.40,0.98) |
| * HLHS | 10897 (98.55) | 160 (1.45) | 626 (99.05) | 6 (0.95) | 0.65 (0.29,1.48) | 0.61 (0.27,1.39) |
| * Coarctation of the aorta (COA) | 10897 (98.55) | 160 (1.45) | 1112 (99.46) | 6 (0.54) | 0.37 (0.16,0.83) | 0.32 (0.14,0.73) |
| * Aortic stenosis | 10897 (98.55) | 160 (1.45) | 475 (97.74) | 11 (2.26) | 1.58 (0.85,2.92) | 1.28 (0.68,2.39) |
| RVOTO | 10897 (98.55) | 160 (1.45) | 1969 (98.55) | 29 (1.45) | 1.00 (0.67,1.49) | 0.97 (0.65,1.45) |
| * Pulmonary valve stenosis (PVS) | 10455 (98.49) | 160 (1.51) | 1456 (98.44) | 23 (1.56) | 1.03 (0.67,1.60) | 0.96 (0.62,1.51) |
| Septal defect | 10897 (98.55) | 160 (1.45) | 4496 (99.21) | 36 (0.79) | 0.55 (0.38,0.78) | 0.55 (0.38,0.79) |
| * VSD perimembranous | 10897 (98.55) | 160 (1.45) | 1601 (99.50) | 8 (0.50) | 0.34 (0.17,0.69) | 0.36 (0.18,0.73) |
| * ASD + PVS | 10897 (98.55) | 160 (1.45) | 236 (97.52) | 6 (2.48) | 1.73 (0.76,3.95) | 1.57 (0.68,3.64) |
| * VSD + ASD | 10897 (98.55) | 160 (1.45) | 729 (99.18) | 6 (0.82) | 0.56 (0.25,1.27) | 0.57 (0.25,1.31) |
| * ASD secundum or ASD NOS | 10897 (98.55) | 160 (1.45) | 2889 (98.97) | 30 (1.03) | 0.71 (0.48,1.05) | 0.69 (0.46,1.04) |
| **Clemastine** |  |  |  |  |  |  |
| Heart defect (any) | 11051 (99.95) | 6 (0.05) | 11780 (99.94) | 7 (0.06) | 1.09 (0.37,3.26) | 1.04 (0.35,3.12) |
| **Dimenhydrinate** |  |  |  |  |  |  |
| Heart defect (any) | 11037 (99.82) | 20 (0.18) | 11758 (99.75) | 29 (0.25) | 1.36 (0.77,2.41) | 1.33 (0.75,2.35) |
| Conotruncal defect | 11037 (99.82) | 20 (0.18) | 2488 (99.72) | 7 (0.28) | 1.55 (0.66,3.68) | 1.56 (0.66,3.71) |
| Septal defect | 11037 (99.82) | 20 (0.18) | 4521 (99.76) | 11 (0.24) | 1.34 (0.64,2.81) | 1.37 (0.65,2.90) |
| * ASD secundum or ASD NOS | 11037 (99.82) | 20 (0.18) | 2910 (99.69) | 9 (0.31) | 1.71 (0.78,3.76) | 1.84 (0.82,4.12) |
| **Diphenhydramine** |  |  |  |  |  |  |
| Heart defect (any) | 10814 (97.80) | 243 (2.20) | 11513 (97.68) | 274 (2.32) | 1.06 (0.89,1.26) | 1.04 (0.88,1.25) |
| Anomalous pulmonary venous return | 10814 (97.80) | 243 (2.20) | 355 (97.26) | 10 (2.74) | 1.25 (0.66,2.38) | 1.30 (0.68,2.49) |
| Atrioventricular septal defect | 10814 (97.80) | 243 (2.20) | 347 (97.20) | 10 (2.80) | 1.28 (0.68,2.43) | 1.18 (0.62,2.25) |
| Conotruncal defect | 10814 (97.80) | 243 (2.20) | 2441 (97.84) | 54 (2.16) | 0.99 (0.73,1.33) | 0.97 (0.72,1.31) |
| * Tetralogy of Fallot | 10814 (97.80) | 243 (2.20) | 1126 (97.49) | 29 (2.51) | 1.15 (0.78,1.69) | 1.12 (0.76,1.66) |
| * TGA | 10814 (97.80) | 243 (2.20) | 727 (98.11) | 14 (1.89) | 0.86 (0.50,1.48) | 0.83 (0.48,1.43) |
| LVOTO | 10814 (97.80) | 243 (2.20) | 2092 (97.85) | 46 (2.15) | 0.98 (0.71,1.35) | 0.93 (0.68,1.29) |
| * HLHS | 10814 (97.80) | 243 (2.20) | 614 (97.15) | 18 (2.85) | 1.31 (0.80,2.12) | 1.26 (0.77,2.06) |
| * Coarctation of the aorta (COA) | 10814 (97.80) | 243 (2.20) | 1096 (98.03) | 22 (1.97) | 0.89 (0.58,1.39) | 0.86 (0.55,1.34) |
| * Aortic stenosis | 10814 (97.80) | 243 (2.20) | 478 (98.35) | 8 (1.65) | 0.75 (0.37,1.52) | 0.68 (0.34,1.40) |
| RVOTO | 10814 (97.80) | 243 (2.20) | 1952 (97.70) | 46 (2.30) | 1.05 (0.76,1.44) | * 1. (0.74,1.41) |
| * Pulmonary atresia | 10814 (97.80) | 243 (2.20) | 246 (97.23) | 7 (2.77) | 1.27 (0.59,2.71) | 1.38 (0.64,3.00) |
| * Pulmonary valve stenosis (PVS) | 10383 (97.81) | 232 (2.19) | 1449 (97.97) | 30 (2.03) | 0.93 (0.63,1.36) | 0.87 (0.59,1.28) |
| * Tricuspid atresia | **10814 (97.80)** | **243 (2.20)** | **156 (95.12)** | **8 (4.88)** | **2.28 (1.11,4.70)** | **2.67 (1.28,5.55)** |
| Septal defect | 10814 (97.80) | 243 (2.20) | 4430 (97.75) | 102 (2.25) | 1.03 (0.81,1.30) | 1.01 (0.80,1.29) |
| * VSD perimembranous | 10814 (97.80) | 243 (2.20) | 1571 (97.64) | 38 (2.36) | 1.08 (0.76,1.52) | 1.07 (0.76,1.52) |
| * VSD + COA | 10814 (97.80) | 243 (2.20) | 283 (96.59) | 10 (3.41) | 1.57 (0.83,3.00) | 1.62 (0.85,3.10) |
| * VSD + ASD | 10814 (97.80) | 243 (2.20) | 714 (97.14) | 21 (2.86) | 1.31 (0.83,2.06) | 1.36 (0.86,2.15) |
| * ASD secundum or ASD NOS | 10814 (97.80) | 243 (2.20) | 2858 (97.91) | 61 (2.09) | 0.95 (0.72,1.26) | 0.94 (0.71,1.27) |
| **Doxylamine** |  |  |  |  |  |  |
| Heart defect (any) | 10870 (98.31) | 187 (1.69) | 11576 (98.21) | 211 (1.79) | 1.06 (0.87,1.29) | 1.06 (0.87,1.30) |
| Conotruncal defect | 10870 (98.31) | 187 (1.69) | 2449 (98.16) | 46 (1.84) | 1.09 (0.79,1.51) | 1.20 (0.86,1.67) |
| * Tetralogy of Fallot | 10870 (98.31) | 187 (1.69) | 1138 (98.53) | 17 (1.47) | 0.87 (0.53,1.43) | 0.97 (0.59,1.61) |
| * TGA | 10870 (98.31) | 187 (1.69) | 724 (97.71) | 17 (2.29) | 1.37 (0.83,2.26) | 1.40 (0.84,2.32) |
| LVOTO | 10870 (98.31) | 187 (1.69) | 2091 (97.80) | 47 (2.20) | 1.31 (0.95,1.81) | * 1. (0.77,1.48) |
| * HLHS | **10870 (98.31)** | **187 (1.69)** | **611 (96.68)** | **21 (3.32)** | **2.00 (1.26,3.16)** | **1.73 (1.09,2.76)** |
| * Coarctation of the aorta (COA) | 10870 (98.31) | 187 (1.69) | 1101 (98.48) | 17 (1.52) | 0.90 (0.54,1.48) | 0.75 (0.45,1.24) |
| * Aortic stenosis | 10870 (98.31) | 187 (1.69) | 473 (97.33) | 13 (2.67) | 1.60 (0.90,2.82) | 1.11 (0.62,1.98) |
| RVOTO | 10870 (98.31) | 187 (1.69) | 1969 (98.55) | 29 (1.45) | 0.86 (0.58,1.27) | 0.78 (0.52,1.16) |
| * Pulmonary valve stenosis (PVS) | 10437 (98.32) | 178 (1.68) | 1458 (98.58) | 21 (1.42) | 0.85 (0.54,1.33) | 0.72 (0.45,1.14) |
| Septal defect | 10870 (98.31) | 187 (1.69) | 4454 (98.28) | 78 (1.72) | 1.02 (0.78,1.33) | 1.09 (0.83,1.43) |
| * VSD perimembranous | 10870 (98.31) | 187 (1.69) | 1588 (98.69) | 21 (1.31) | 0.77 (0.49,1.21) | 0.87 (0.55,1.38) |
| * VSD + ASD | 10870 (98.31) | 187 (1.69) | 722 (98.23) | 13 (1.77) | 1.05 (0.59,1.85) | 1.19 (0.67,2.11) |
| * ASD secundum or ASD NOS | 10870 (98.31) | 187 (1.69) | 2864 (98.12) | 55 (1.88) | 1.11 (0.82,1.51) | 1.130 (0.83,1.54) |
| **Fexofenadine** |  |  |  |  |  |  |
| Heart defect (any) | 10964 (99.16) | 93 (0.84) | 11699 (99.25) | 88 (0.75) | 0.89 (0.66,1.19) | 0.90 (0.67,1.21) |
| Conotruncal defect | 10964 (99.16) | 93 (0.84) | 2475 (99.20) | 20 (0.80) | 0.95 (0.59,1.55) | 0.97 (0.60,1.58) |
| * Tetralogy of Fallot | 10964 (99.16) | 93 (0.84) | 1146 (99.22) | 9 (0.78) | 0.93 (0.47,1.84) | 0.94 (0.47,1.87) |
| LVOTO | 10964 (99.16) | 93 (0.84) | 2119 (99.11) | 19 (0.89) | 1.06 (0.64,1.74) | 1.01 (0.61,1.66) |
| * Coarctation of the aorta (COA) | 10964 (99.16) | 93 (0.84) | 1103 (98.66) | 15 (1.34) | 1.60 (0.93,2.78) | 1.49 (0.86,2.60) |
| RVOTO | 10964 (99.16) | 93 (0.84) | 1986 (99.40) | 12 (0.60) | 0.71 (0.39,1.30) | 0.70 (0.38,1.29) |
| * Pulmonary valve stenosis (PVS) | 10527 (99.17) | 88 (0.83) | 1471 (99.46) | 8 (0.54) | 0.65 (0.32,1.35) | 0.61 (0.29,1.28) |
| Septal defect | 10964 (99.16) | 93 (0.84) | 4498 (99.25) | 34 (0.75) | 0.89 (0.60,1.32) | 0.94 (0.63,1.40) |
| * VSD perimembranous | 10964 (99.16) | 93 (0.84) | 1598 (99.32) | 11 (0.68) | 0.81 (0.43,1.52) | 0.87 (0.46,1.63) |
| * VSD + COA | 10964 (99.16) | 93 (0.84) | 287 (97.95) | 6 (2.05) | 2.47 (1.07,5.67) | 2.32 (1.00,5.37) |
| * VSD + ASD | 10964 (99.16) | 93 (0.84) | 729 (99.18) | 6 (0.82) | 0.97 (0.42,2.22) | 0.94 (0.41,2.18) |
| * ASD secundum or ASD NOS | 10964 (99.16) | 93 (0.84) | 2899 (99.31) | 20 (0.69) | 0.81 (0.50,1.32) | 0.81 (0.49,1.32) |
| **Hydroxyzine** |  |  |  |  |  |  |
| Heart defect (any) | 11050 (99.94) | 7 (0.06) | 11770 (99.86) | 17 (0.14) | 2.28 (0.95,5.50) | 2.17 (0.90,5.25) |
| Conotruncal defect | **11050 (99.94)** | **7 (0.06)** | **2489 (99.76)** | **6 (0.24)** | **3.81 (1.28,11.33)** | **3.75 (1.25,11.26)** |
| Septal defect | 11050 (99.94) | 7 (0.06) | 4524 (99.82) | 8 (0.18) | 2.79 (1.01,7.69) | 2.73 (0.98,7.61) |
| **Loratadine** |  |  |  |  |  |  |
| Heart defect (any) | 10775 (97.45) | 282 (2.55) | 11503 (97.59) | 284 (2.41) | 0.94 (0.80,1.12) | 0.97 (0.82,1.15) |
| Anomalous pulmonary venous return | 10775 (97.45) | 282 (2.55) | 354 (96.99) | 11 (3.01) | 1.19 (0.64,2.19) | 1.32 (0.71,2.44) |
| Atrioventricular septal defect | 10775 (97.45) | 282 (2.55) | 349 (97.76) | 8 (2.24) | 0.88 (0.43,1.78) | 0.82 (0.40,1.68) |
| Conotruncal defect | 10775 (97.45) | 282 (2.55) | 2415 (96.79) | 80 (3.21) | 1.27 (0.98,1.63) | * 1. (0.97,1.61) |
| * Truncus Arteriosus | **10775 (97.45)** | **282 (2.55)** | **121 (93.80)** | **8 (6.20)** | **2.53 (1.22,5.22)** | * 1. **(1.27,5.56)** |
| * Tetralogy of Fallot | 10775 (97.45) | 282 (2.55) | 1114 (96.45) | 41 (3.55) | 1.41 (1.01,1.96) | 1.33 (0.95,1.86) |
| * TGA | 10775 (97.45) | 282 (2.55) | 721 (97.30) | 20 (2.70) | 1.06 (0.67,1.68) | 1.03 (0.65,1.64) |
| LVOTO | 10775 (97.45) | 282 (2.55) | 2083 (97.43) | 55 (2.57) | 1.01 (0.75,1.35) | 0.99 (0.74,1.33) |
| * HLHS | 10775 (97.45) | 282 (2.55) | 618 (97.78) | 14 (2.22) | 0.87 (0.50,1.49) | 0.89 (0.51,1.53) |
| * Coarctation of the aorta (COA) | 10775 (97.45) | 282 (2.55) | 1087 (97.23) | 31 (2.77) | 1.09 (0.75,1.59) | 1.05 (0.72,1.53) |
| * Aortic stenosis | 10775 (97.45) | 282 (2.55) | 470 (96.71) | 16 (3.29) | 1.30 (0.78,2.17) | 1.27 (0.76,2.14) |
| RVOTO | 10775 (97.45) | 282 (2.55) | 1955 (97.85) | 43 (2.15) | 0.84 (0.61,1.16) | 0.88 (0.63,1.22) |
| * Pulmonary valve stenosis (PVS) | 10343 (97.44) | 272 (2.56) | 1450 (98.04) | 29 (1.96) | 0.76 (0.52,1.12) | 0.80 (0.54,1.18) |
| * Tricuspid atresia | 10775 (97.45) | 282 (2.55) | 158 (96.34) | 6 (3.66) | 1.45 (0.64,3.31) | 1.61 (0.70,3.70) |
| Septal defect | 10775 (97.45) | 282 (2.55) | 4454 (98.28) | 78 (1.72) | 0.67 (0.52,0.86) | 0.71 (0.55,0.92) |
| * VSD perimembranous | 10775 (97.45) | 282 (2.55) | 1592 (98.94) | 17 (1.06) | 0.41 (0.25,0.67) | 0.42 (0.26,0.69) |
| * VSD + ASD | 10775 (97.45) | 282 (2.55) | 725 (98.64) | 10 (1.36) | 0.53 (0.28,0.99) | 0.54 (0.28,1.02) |
| * ASD secundum or ASD NOS | 10775 (97.45) | 282 (2.55) | 2860 (97.98) | 59 (2.02) | 0.79 (0.59,1.05) | 0.85 (0.64,1.14) |
| **Meclizine** |  |  |  |  |  |  |
| Heart defect (any) | 11050 (99.94) | 7 (0.06) | 11777 (99.92) | 10 (0.08) | 1.34 (0.51,3.51) | 1.30 (0.49,3.41) |
| **Pheniramine** |  |  |  |  |  |  |
| Heart defect (any) | 10871 (98.32) | 186 (1.68) | 11586 (98.29) | 201 (1.71) | 1.01 (0.83,1.24) | 1.02 (0.83,1.25) |
| Atrioventricular septal defect | 10871 (98.32) | 186 (1.68) | 346 (96.92) | 11 (3.08) | 1.86 (1.00,3.45) | 1.80 (0.97,3.35) |
| Conotruncal defect | 10871 (98.32) | 186 (1.68) | 2455 (98.40) | 40 (1.60) | 0.95 (0.68,1.35) | 1.00 (0.71,1.41) |
| * Tetralogy of Fallot | 10871 (98.32) | 186 (1.68) | 1138 (98.53) | 17 (1.47) | 0.87 (0.53,1.44) | 0.89 (0.54,1.47) |
| * TGA | 10871 (98.32) | 186 (1.68) | 730 (98.52) | 11 (1.48) | 0.88 (0.48,1.63) | 0.93 (0.50,1.72) |
| LVOTO | 10871 (98.32) | 186 (1.68) | 2105 (98.46) | 33 (1.54) | 0.91 (0.63,1.33) | * 1. (0.66,1.39) |
| * HLHS | 10871 (98.32) | 186 (1.68) | 625 (98.89) | 7 (1.11) | 0.66 (0.31,1.40) | 0.71 (0.33,1.52) |
| * Coarctation of the aorta (COA) | 10871 (98.32) | 186 (1.68) | 1099 (98.30) | 19 (1.70) | 1.01 (0.63,1.63) | 1.04 (0.65,1.69) |
| * Aortic stenosis | 10871 (98.32) | 186 (1.68) | 478 (98.35) | 8 (1.65) | 0.98 (0.48,2.00) | 1.04 (0.50,2.13) |
| RVOTO | 10871 (98.32) | 186 (1.68) | 1969 (98.55) | 29 (1.45) | 0.86 (0.58,1.28) | 0.88 (0.59,1.31) |
| * Pulmonary valve stenosis (PVS) | 10433 (98.29) | 182 (1.71) | 1456 (98.44) | 23 (1.56) | 0.91 (0.59,1.40) | 0.92 (0.59,1.43) |
| Septal defect | 10871 (98.32) | 186 (1.68) | 4455 (98.30) | 77 (1.70) | 1.01 (0.77,1.32) | 0.98 (0.75,1.29) |
| * VSD perimembranous | 10871 (98.32) | 186 (1.68) | 1585 (98.51) | 24 (1.49) | 0.89 (0.58,1.36) | 0.89 (0.58,1.36) |
| * VSD + ASD | 10871 (98.32) | 186 (1.68) | 720 (97.96) | 15 (2.04) | 1.22 (0.72,2.07) | 1.21 (0.70,2.06) |
| * ASD secundum or ASD NOS | 10871 (98.32) | 186 (1.68) | 2867 (98.22) | 52 (1.78) | 1.06 (0.78,1.45) | 1.01 (0.73,1.39) |
| **Promethazine** |  |  |  |  |  |  |
| Heart defect (any) | 10652 (96.34) | 405 (3.66) | 11348 (96.28) | 439 (3.72) | 1.02 (0.89,1.17) | 0.96 (0.83,1.10) |
| Anomalous pulmonary venous return | 10652 (96.34) | 405 (3.66) | 357 (97.81) | 8 (2.19) | 0.59 (0.29,1.20) | 0.60 (0.29,1.23) |
| Atrioventricular septal defect | 10652 (96.34) | 405 (3.66) | 345 (96.64) | 12 (3.36) | 0.92 (0.51,1.64) | 0.82 (0.45,1.48) |
| Conotruncal defect | 10652 (96.34) | 405 (3.66) | 2412 (96.67) | 83 (3.33) | 0.91 (0.71,1.15) | 0.97 (0.76,1.24) |
| * Tetralogy of Fallot | 10652 (96.34) | 405 (3.66) | 1105 (95.67) | 50 (4.33) | 1.19 (0.88,1.61) | 1.29 (0.95,1.75) |
| * TGA | 10652 (96.34) | 405 (3.66) | 721 (97.30) | 20 (2.70) | 0.73 (0.46,1.15) | 0.77 (0.48,1.22) |
| LVOTO | 10652 (96.34) | 405 (3.66) | 2060 (96.35) | 78 (3.65) | 1.00 (0.78,1.28) | 0.93 (0.72,1.20) |
| * HLHS | 10652 (96.34) | 405 (3.66) | 607 (96.04) | 25 (3.96) | 1.08 (0.72,1.64) | 1.01 (0.66,1.53) |
| * Coarctation of the aorta (COA) | 10652 (96.34) | 405 (3.66) | 1080 (96.60) | 38 (3.40) | 0.92 (0.66,1.30) | 0.90 (0.63,1.26) |
| * Aortic stenosis | 10652 (96.34) | 405 (3.66) | 469 (96.50) | 17 (3.50) | 0.95 (0.58,1.56) | 0.82 (0.49,1.35) |
| RVOTO | 10652 (96.34) | 405 (3.66) | 1920 (96.10) | 78 (3.90) | 1.07 (0.83,1.37) | 0.92 (0.72,1.19) |
| * Pulmonary valve stenosis (PVS) | 10216 (96.24) | 399 (3.76) | 1414 (95.61) | 65 (4.39) | 1.18 (0.90,1.54) | 0.98 (0.74,1.29) |
| Septal defect | 10652 (96.34) | 405 (3.66) | 4350 (95.98) | 182 (4.02) | 1.10 (0.92,1.32) | 0.98 (0.81,1.18) |
| * VSD perimembranous | 10652 (96.34) | 405 (3.66) | 1546 (96.08) | 63 (3.92) | 1.07 (0.82,1.41) | 1.03 (0.78,1.36) |
| * VSD + COA | 10652 (96.34) | 405 (3.66) | 282 (96.25) | 11 (3.75) | 1.03 (0.56,1.89) | 0.96 (0.52,1.79) |
| * ASD + PVS | 10652 (96.34) | 405 (3.66) | 229 (94.63) | 13 (5.37) | 1.49 (0.85,2.63) | 1.08 (0.60,1.94) |
| * VSD + ASD | 10652 (96.34) | 405 (3.66) | 706 (96.05) | 29 (3.95) | 1.08 (0.74,1.59) | 1.06 (0.71,1.57) |
| * ASD secundum or ASD NOS | 10652 (96.34) | 405 (3.66) | 2796 (95.79) | 123 (4.21) | 1.16 (0.94,1.42) | 0.97 (0.79,1.21) |
| **Triprolidine** |  |  |  |  |  |  |
| Heart defect (any) | 11042 (99.86) | 15 (0.14) | 11770 (99.86) | 17 (0.14) | 1.06 (0.53,2.13) | 1.05 (0.52,2.11) |
| Septal defect | 11042 (99.86) | 15 (0.14) | 4526 (99.87) | 6 (0.13) | 0.98 (0.38,2.52) | 1.02 (0.39,2.64) |
| HLHS = Hypoplastic left heart syndrome, LVOTO = Left ventricular outflow tract obstruction, RVOTO = Right ventricular outflow tract obstruction, TGA = DTransposition of the great arteries, VSD = Ventricular septal defect. Note: Inconsistencies in the number of controls due to no controls for PVS from CA prior to 2002.  Logistic regression models adjusted for: maternal age, maternal race, maternal education, parity, folic acid use, prenatal care (time of entry), smoking and alcohol status, and study site (see Table 2 for categorizations). | | | | | | |

**Supplemental Table 2:** Isolated cardiac defects and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine**  Birth defect   * Defect sub-classification | **Controls** | | **Cases** | | **Odds Ratios (95% CI)** | |
| **Not Exposed** | **Exposed** | **Not Exposed** | **Exposed** | **Crude** | **Adjusted** |
| **Any Antihistamine** |  |  |  |  |  |  |
| Heart defect (any) | 9622 (87.02) | 1435 (12.98) | 8596 (87.20) | 1262 (12.80) | 0.98 (0.91,1.07) | 0.96 (0.88,1.04) |
| Anomalous pulmonary venous return | 9622 (87.02) | 1435 (12.98) | 289 (89.20) | 35 (10.80) | 0.81 (0.57,1.16) | 0.90 (0.62,1.29) |
| Atrioventricular septal defect | 9622 (87.02) | 1435 (12.98) | 229 (85.77) | 38 (14.23) | 1.11 (0.79,1.58) | 1.03 (0.72,1.48) |
| Conotruncal defects | 9622 (87.02) | 1435 (12.98) | 1801 (86.50) | 281 (13.50) | 1.05 (0.91,1.20) | 1.07 (0.93,1.24) |
| * Truncus Arteriosus | 9622 (87.02) | 1435 (12.98) | 85 (83.33) | 17 (16.67) | 1.34 (0.79,2.26) | 1.31 (0.76,2.24) |
| * IAA (type B) | 9622 (87.02) | 1435 (12.98) | 27 (81.82) | 6 (18.18) | 1.49 (0.61,3.62) | 1.39 (0.56,3.46) |
| * Tetralogy of Fallot | **9622 (87.02)** | **1435 (12.98)** | **783 (84.65)** | **142 (15.35)** | **1.22 (1.01,1.47)** | **1.23 (1.02,1.49)** |
| * TGA | 9622 (87.02) | 1435 (12.98) | 604 (88.43) | 79 (11.57) | 0.88 (0.69,1.12) | 0.88 (0.69,1.12) |
| * Double outlet right ventricle + TGA | 9622 (87.02) | 1435 (12.98) | 136 (90.67) | 14 (9.33) | 0.69 (0.40,1.20) | 0.71 (0.40,1.25) |
| * Double outlet right ventricle (other) | 9622 (87.02) | 1435 (12.98) | 73 (84.88) | 13 (15.12) | 1.19 (0.66,2.16) | 1.47 (0.80,2.70) |
| * VSD conoventricular | 9622 (87.02) | 1435 (12.98) | 98 (88.29) | 13 (11.71) | 0.89 (0.50,1.59) | 1.09 (0.60,1.98) |
| LVOTO | 9622 (87.02) | 1435 (12.98) | 1656 (87.25) | 242 (12.75) | 0.98 (0.85,1.13) | 0.90 (0.78,1.05) |
| * HLHS | 9622 (87.02) | 1435 (12.98) | 496 (86.26) | 79 (13.74) | 1.07 (0.84,1.36) | 1.02 (0.79,1.30) |
| * Coarctation of the aorta (COA) | 9622 (87.02) | 1435 (12.98) | 850 (88.27) | 113 (11.73) | 0.89 (0.73,1.09) | 0.83 (0.67,1.02) |
| * Aortic stenosis | 9622 (87.02) | 1435 (12.98) | 387 (86.00) | 63 (14.00) | 1.09 (0.83,1.43) | 0.96 (0.72,1.27) |
| RVOTO | 9622 (87.02) | 1435 (12.98) | 1609 (87.78) | 224 (12.22) | 0.93 (0.80,1.08) | 0.89 (0.76,1.03) |
| * Pulmonary atresia | 9622 (87.02) | 1435 (12.98) | 215 (92.27) | 18 (7.73) | 0.56 (0.35,0.91) | 0.62 (0.38,1.01) |
| * Pulmonary valve stenosis (PVS) | 9222 (86.88) | 1393 (13.12) | 1190 (87.18) | 175 (12.82) | 0.97 (0.82,1.15) | 0.89 (0.75,1.06) |
| * Ebstein anomaly | 9622 (87.02) | 1435 (12.98) | 138 (89.61) | 16 (10.39) | 0.78 (0.46,1.31) | 0.81 (0.48,1.38) |
| * Tricuspid atresia | 9622 (87.02) | 1435 (12.98) | 125 (86.21) | 20 (13.79) | 1.07 (0.67,1.73) | 1.31 (0.80,2.14) |
| Septal defect | 9622 (87.02) | 1435 (12.98) | 3293 (87.65) | 464 (12.35) | 0.94 (0.84,1.06) | 0.92 (0.82,1.03) |
| * VSD perimembranous | 9622 (87.02) | 1435 (12.98) | 1192 (88.69) | 152 (11.31) | 0.86 (0.72,1.02) | 0.86 (0.71,1.03) |
| * VSD + COA | 9622 (87.02) | 1435 (12.98) | 210 (87.87) | 29 (12.13) | 0.93 (0.63,1.37) | 0.88 (0.59,1.32) |
| * VSD + PVS | 9622 (87.02) | 1435 (12.98) | 115 (92.00) | 10 (8.00) | 0.58 (0.31,1.12) | 0.65 (0.33,1.25) |
| * ASD + PVS | 9622 (87.02) | 1435 (12.98) | 184 (86.79) | 28 (13.21) | 1.02 (0.68,1.52) | 0.89 (0.59,1.35) |
| * VSD + ASD | 9622 (87.02) | 1435 (12.98) | 494 (86.06) | 80 (13.94) | 1.09 (0.85,1.38) | 1.11 (0.86,1.42) |
| * ASD secundum or ASD NOS | 9622 (87.02) | 1435 (12.98) | 2062 (87.04) | 307 (12.96) | 1.00 (0.87,1.14) | 0.95 (0.83,1.09) |
| **Cetirizine** |  |  |  |  |  |  |
| Heart defect (any) | 10897 (98.55) | 160 (1.45) | 9740 (98.80) | 118 (1.20) | 0.83 (0.65,1.05) | 0.82 (0.64,1.04) |
| Conotruncal defect | 10897 (98.55) | 160 (1.45) | 2045 (98.22) | 37 (1.78) | 1.23 (0.86,1.77) | 1.30 (0.90,1.87) |
| * Tetralogy of Fallot | 10897 (98.55) | 160 (1.45) | 905 (97.84) | 20 (2.16) | 1.51 (0.94,2.41) | 1.56 (0.97,2.51) |
| * TGA | 10897 (98.55) | 160 (1.45) | 674 (98.68) | 9 (1.32) | 0.91 (0.46,1.79) | 0.94 (0.48,1.85) |
| LVOTO | 10897 (98.55) | 160 (1.45) | 1878 (98.95) | 20 (1.05) | 0.73 (0.45,1.16) | 0.63 (0.39,1.01) |
| * HLHS | 10897 (98.55) | 160 (1.45) | 569 (98.96) | 6 (1.04) | 0.72 (0.32,1.63) | 0.66 (0.29,1.50) |
| * Aortic stenosis | 10897 (98.55) | 160 (1.45) | 439 (97.56) | 11 (2.44) | 1.71 (0.92,3.17) | 1.39 (0.74,2.60) |
| RVOTO | 10897 (98.55) | 160 (1.45) | 1805 (98.47) | 28 (1.53) | 1.06 (0.71,1.58) | 1.01 (0.67,1.52) |
| * Pulmonary valve stenosis (PVS) | 10455 (98.49) | 160 (1.51) | 1343 (98.39) | 22 (1.61) | 1.07 (0.68,1.68) | 1.00 (0.63,1.57) |
| Septal defect | 10897 (98.55) | 160 (1.45) | 3727 (99.20) | 30 (0.80) | 0.55 (0.37,0.81) | 0.54 (0.36,0.80) |
| * ASD secundum or ASD NOS | 10897 (98.55) | 160 (1.45) | 2344 (98.94) | 25 (1.06) | 0.73 (0.48,1.11) | 0.69 (0.45,1.07) |
| **Clemastine** |  |  |  |  |  |  |
| Heart defect (any) | 11051 (99.95) | 6 (0.05) | 9851 (99.93) | 7 (0.07) | 1.31 (0.44,3.90) | 1.21 (0.41,3.64) |
| **Dimenhydrinate** |  |  |  |  |  |  |
| Heart defect (any) | 11037 (99.82) | 20 (0.18) | 9833 (99.75) | 25 (0.25) | 1.40 (0.78,2.53) | 1.34 (0.74,2.41) |
| Conotruncal defect | 11037 (99.82) | 20 (0.18) | 2076 (99.71) | 6 (0.29) | 1.60 (0.64,3.98) | 1.56 (0.62,3.92) |
| Septal defect | 11037 (99.82) | 20 (0.18) | 3748 (99.76) | 9 (0.24) | 1.33 (0.60,2.91) | 1.32 (0.59,2.94) |
| * ASD secundum or ASD NOS | 11037 (99.82) | 20 (0.18) | 2362 (99.70) | 7 (0.30) | 1.64 (0.69,3.88) | 1.70 (0.70,4.11) |
| **Diphenhydramine** |  |  |  |  |  |  |
| Heart defect (any) | 10814 (97.80) | 243 (2.20) | 9639 (97.78) | 219 (2.22) | 1.01 (0.84,1.22) | 0.98 (0.82,1.18) |
| Anomalous pulmonary venous return | 10814 (97.80) | 243 (2.20) | 315 (97.22) | 9 (2.78) | 1.27 (0.65,2.50) | 1.33 (0.67,2.63) |
| Atrioventricular septal defect | 10814 (97.80) | 243 (2.20) | 261 (97.75) | 6 (2.25) | 1.02 (0.45,2.32) | 0.93 (0.41,2.11) |
| Conotruncal defect | 10814 (97.80) | 243 (2.20) | 2039 (97.93) | 43 (2.07) | 0.94 (0.68,1.30) | 0.91 (0.66,1.27) |
| * Tetralogy of Fallot | 10814 (97.80) | 243 (2.20) | 902 (97.51) | 23 (2.49) | 1.13 (0.74,1.75) | 1.09 (0.70,1.69) |
| * TGA | 10814 (97.80) | 243 (2.20) | 671 (98.24) | 12 (1.76) | 0.80 (0.44,1.43) | 0.76 (0.42,1.37) |
| LVOTO | 10814 (97.80) | 243 (2.20) | 1859 (97.95) | 39 (2.05) | 0.93 (0.66,1.31) | 0.88 (0.63,1.25) |
| * HLHS | 10814 (97.80) | 243 (2.20) | 559 (97.22) | 16 (2.78) | 1.27 (0.76,2.13) | 1.22 (0.73,2.05) |
| * Coarctation of the aorta (COA) | 10814 (97.80) | 243 (2.20) | 945 (98.13) | 18 (1.87) | 0.85 (0.52,1.37) | 0.81 (0.50,1.32) |
| * Aortic stenosis | 10814 (97.80) | 243 (2.20) | 443 (98.44) | 7 (1.56) | 0.70 (0.33,1.50) | 0.65 (0.30,1.38) |
| RVOTO | 10814 (97.80) | 243 (2.20) | 1791 (97.71) | 42 (2.29) | 1.04 (0.75,1.45) | 1.01 (0.72,1.41) |
| * Pulmonary atresia | 10814 (97.80) | 243 (2.20) | 227 (97.42) | 6 (2.58) | 1.18 (0.52,2.67) | 1.30 (0.57,2.97) |
| * Pulmonary valve stenosis (PVS) | 10383 (97.81) | 232 (2.19) | 1337 (97.95) | 28 (2.05) | 0.94 (0.63,1.39) | 0.87 (0.58,1.30) |
| * Tricuspid atresia | **10814 (97.80)** | **243 (2.20)** | **138 (95.17)** | **7 (4.83)** | **2.26 (1.05,4.87)** | **2.72 (1.24,5.94)** |
| Septal defect | 10814 (97.80) | 243 (2.20) | 3678 (97.90) | 79 (2.10) | 0.96 (0.74,1.24) | 0.94 (0.72,1.22) |
| * VSD perimembranous | 10814 (97.80) | 243 (2.20) | 1311 (97.54) | 33 (2.46) | 1.12 (0.78,1.62) | 1.10 (0.76,1.60) |
| * VSD + COA | 10814 (97.80) | 243 (2.20) | 233 (97.49) | 6 (2.51) | 1.15 (0.50,2.60) | 1.16 (0.51,2.65) |
| * VSD + ASD | 10814 (97.80) | 243 (2.20) | 559 (97.39) | 15 (2.61) | 1.19 (0.70,2.03) | 1.26 (0.74,2.15) |
| * ASD secundum or ASD NOS | 10814 (97.80) | 243 (2.20) | 2325 (98.14) | 44 (1.86) | 0.84 (0.61,1.16) | 0.84 (0.60,1.17) |
| **Doxylamine** |  |  |  |  |  |  |
| Heart defect (any) | 10870 (98.31) | 187 (1.69) | 9680 (98.19) | 178 (1.81) | 1.07 (0.87,1.31) | 1.06 (0.86,1.31) |
| Conotruncal defect | 10870 (98.31) | 187 (1.69) | 2044 (98.17) | 38 (1.83) | 1.08 (0.76,1.54) | 1.18 (0.83,1.69) |
| * Tetralogy of Fallot | 10870 (98.31) | 187 (1.69) | 910 (98.38) | 15 (1.62) | 0.96 (0.56,1.63) | 1.08 (0.63,1.85) |
| * TGA | 10870 (98.31) | 187 (1.69) | 669 (97.95) | 14 (2.05) | 1.22 (0.70,2.11) | 1.24 (0.71,2.17) |
| LVOTO | 10870 (98.31) | 187 (1.69) | 1858 (97.89) | 40 (2.11) | 1.25 (0.89,1.77) | 1.00 (0.70,1.42) |
| * HLHS | 10870 (98.31) | 187 (1.69) | 558 (97.04) | 17 (2.96) | 1.77 (1.07,2.93) | 1.48 (0.88,2.47) |
| * Coarctation of the aorta (COA) | 10870 (98.31) | 187 (1.69) | 949 (98.55) | 14 (1.45) | 0.86 (0.50,1.48) | 0.71 (0.41,1.24) |
| * Aortic stenosis | 10870 (98.31) | 187 (1.69) | 438 (97.33) | 12 (2.67) | 1.59 (0.88,2.88) | 1.08 (0.59,1.97) |
| RVOTO | 10870 (98.31) | 187 (1.69) | 1806 (98.53) | 27 (1.47) | 0.87 (0.58,1.31) | 0.79 (0.53,1.20) |
| * Pulmonary valve stenosis (PVS) | 10437 (98.32) | 178 (1.68) | 1346 (98.61) | 19 (1.39) | 0.83 (0.51,1.33) | 0.71 (0.44,1.15) |
| Septal defect | 10870 (98.31) | 187 (1.69) | 3692 (98.27) | 65 (1.73) | 1.02 (0.77,1.36) | 1.11 (0.83,1.48) |
| * VSD perimembranous | 10870 (98.31) | 187 (1.69) | 1326 (98.66) | 18 (1.34) | 0.79 (0.48,1.28) | 0.89 (0.55,1.46) |
| * VSD + ASD | 10870 (98.31) | 187 (1.69) | 561 (97.74) | 13 (2.26) | 1.35 (0.76,2.38) | 1.54 (0.87,2.75) |
| * ASD secundum or ASD NOS | 10870 (98.31) | 187 (1.69) | 2323 (98.06) | 46 (1.94) | 1.15 (0.83,1.59) | 1.18 (0.85,1.65) |
| **Fexofenadine** |  |  |  |  |  |  |
| Heart defect (any) | 10964 (99.16) | 93 (0.84) | 9780 (99.21) | 78 (0.79) | 0.94 (0.70,1.27) | 0.94 (0.70,1.28) |
| Conotruncal defect | 10964 (99.16) | 93 (0.84) | 2065 (99.18) | 17 (0.82) | 0.97 (0.58,1.63) | 0.98 (0.58,1.66) |
| * Tetralogy of Fallot | 10964 (99.16) | 93 (0.84) | 918 (99.24) | 7 (0.76) | 0.90 (0.42,1.94) | 0.89 (0.41,1.94) |
| LVOTO | 10964 (99.16) | 93 (0.84) | 1881 (99.10) | 17 (0.90) | 1.07 (0.63,1.79) | 1.00 (0.59,1.70) |
| * Coarctation of the aorta (COA) | 10964 (99.16) | 93 (0.84) | 948 (98.44) | 15 (1.56) | 1.87 (1.08,3.23) | 1.73 (0.99,3.01) |
| RVOTO | 10964 (99.16) | 93 (0.84) | 1822 (99.40) | 11 (0.60) | 0.71 (0.38,1.33) | 0.70 (0.37,1.32) |
| * Pulmonary valve stenosis (PVS) | 10527 (99.17) | 88 (0.83) | 1358 (99.49) | 7 (0.51) | 0.62 (0.29,1.33) | 0.58 (0.27,1.26) |
| Septal defect | 10964 (99.16) | 93 (0.84) | 3723 (99.10) | 34 (0.90) | 1.08 (0.73,1.60) | 1.14 (0.76,1.70) |
| * VSD perimembranous | 10964 (99.16) | 93 (0.84) | 1333 (99.18) | 11 (0.82) | 0.97 (0.52,1.82) | 1.03 (0.55,1.94) |
| * VSD + COA | **10964 (99.16)** | **93 (0.84)** | **233 (97.49)** | **6 (2.51)** | **3.04 (1.32,7.00)** | **2.88 (1.24,6.68)** |
| * VSD + ASD | 10964 (99.16) | 93 (0.84) | 568 (98.95) | 6 (1.05) | 1.25 (0.54,2.86) | 1.22 (0.53,2.83) |
| * ASD secundum or ASD NOS | 10964 (99.16) | 93 (0.84) | 2349 (99.16) | 20 (0.84) | 1.00 (0.62,1.63) | 1.00 (0.61,1.64) |
| **Hydroxyzine** |  |  |  |  |  |  |
| Heart defect (any) | 11050 (99.94) | 7 (0.06) | 9844 (99.86) | 14 (0.14) | 2.24 (0.91,5.56) | 2.11 (0.85,5.26) |
| Conotruncal defect | **11050 (99.94)** | **7 (0.06)** | **2076 (99.71)** | **6 (0.29)** | **4.56 (1.53,13.59)** | **4.50 (1.50,13.55)** |
| **Loratadine** |  |  |  |  |  |  |
| Heart defect (any) | 10775 (97.45) | 282 (2.55) | 9617 (97.56) | 241 (2.44) | 0.96 (0.80,1.14) | 0.98 (0.82,1.17) |
| Anomalous pulmonary venous return | 10775 (97.45) | 282 (2.55) | 315 (97.22) | 9 (2.78) | 1.09 (0.56,2.14) | 1.22 (0.62,2.40) |
| Conotruncal defect | 10775 (97.45) | 282 (2.55) | 2014 (96.73) | 68 (3.27) | 1.29 (0.99,1.69) | 1.26 (0.96,1.65) |
| * Truncus Arteriosus | **10775 (97.45)** | **282 (2.55)** | **96 (94.12)** | **6 (5.88)** | **2.39 (1.04,5.49)** | **2.42 (1.04,5.64)** |
| * Tetralogy of Fallot | 10775 (97.45) | 282 (2.55) | 892 (96.43) | 33 (3.57) | 1.42 (0.98,2.04) | 1.32 (0.91,1.91) |
| * TGA | 10775 (97.45) | 282 (2.55) | 664 (97.22) | 19 (2.78) | 1.09 (0.68,1.75) | 1.06 (0.66,1.71) |
| LVOTO | 10775 (97.45) | 282 (2.55) | 1849 (97.42) | 49 (2.58) | 1.01 (0.74,1.38) | 0.98 (0.72,1.34) |
| * HLHS | 10775 (97.45) | 282 (2.55) | 563 (97.91) | 12 (2.09) | 0.81 (0.45,1.46) | 0.82 (0.46,1.48) |
| * Coarctation of the aorta (COA) | 10775 (97.45) | 282 (2.55) | 935 (97.09) | 28 (2.91) | 1.14 (0.77,1.70) | 1.09 (0.73,1.62) |
| * Aortic stenosis | 10775 (97.45) | 282 (2.55) | 435 (96.67) | 15 (3.33) | 1.32 (0.78,2.24) | 1.28 (0.75,2.19) |
| RVOTO | 10775 (97.45) | 282 (2.55) | 1793 (97.82) | 40 (2.18) | 0.85 (0.61,1.19) | 0.89 (0.63,1.25) |
| * Pulmonary valve stenosis (PVS) | 10343 (97.44) | 272 (2.56) | 1337 (97.95) | 28 (2.05) | 0.80 (0.54,1.18) | 0.83 (0.56,1.24) |
| Septal defect | 10775 (97.45) | 282 (2.55) | 3690 (98.22) | 67 (1.78) | 0.69 (0.53,0.91) | 0.74 (0.56,0.97) |
| * VSD perimembranous | 10775 (97.45) | 282 (2.55) | 1331 (99.03) | 13 (0.97) | 0.37 (0.21,0.65) | 0.38 (0.22,0.67) |
| * VSD + ASD | 10775 (97.45) | 282 (2.55) | 566 (98.61) | 8 (1.39) | 0.54 (0.27,1.10) | 0.55 (0.27,1.13) |
| * ASD secundum or ASD NOS | 10775 (97.45) | 282 (2.55) | 2319 (97.89) | 50 (2.11) | 0.82 (0.61,1.12) | 0.89 (0.65,1.21) |
| **Meclizine** |  |  |  |  |  |  |
| Heart defect (any) | 11050 (99.94) | 7 (0.06) | 9852 (99.94) | 6 (0.06) | 0.96 (0.32,2.86) | 0.96 (0.32,2.87) |
| **Pheniramine** |  |  |  |  |  |  |
| Heart defect (any) | 10871 (98.32) | 186 (1.68) | 9691 (98.31) | 167 (1.69) | 1.01 (0.82,1.24) | 1.00 (0.81,1.24) |
| Atrioventricular septal defect | **10871 (98.32)** | **186 (1.68)** | **257 (96.25)** | **10 (3.75)** | **2.27 (1.19,4.35)** | **2.23 (1.16,4.29)** |
| Conotruncal defect | 10871 (98.32) | 186 (1.68) | 2049 (98.41) | 33 (1.59) | 0.94 (0.65,1.37) | 0.99 (0.68,1.43) |
| * Tetralogy of Fallot | 10871 (98.32) | 186 (1.68) | 910 (98.38) | 15 (1.62) | 0.96 (0.57,1.64) | 0.97 (0.57,1.66) |
| * TGA | 10871 (98.32) | 186 (1.68) | 673 (98.54) | 10 (1.46) | 0.87 (0.46,1.65) | 0.92 (0.48,1.75) |
| LVOTO | 10871 (98.32) | 186 (1.68) | 1872 (98.63) | 26 (1.37) | 0.81 (0.54,1.23) | 0.85 (0.56,1.28) |
| * HLHS | 10871 (98.32) | 186 (1.68) | 568 (98.78) | 7 (1.22) | 0.72 (0.34,1.54) | 0.78 (0.37,1.68) |
| * Coarctation of the aorta (COA) | 10871 (98.32) | 186 (1.68) | 951 (98.75) | 12 (1.25) | 0.74 (0.41,1.33) | 0.76 (0.42,1.38) |
| * Aortic stenosis | 10871 (98.32) | 186 (1.68) | 442 (98.22) | 8 (1.78) | 1.06 (0.52,2.16) | 1.13 (0.55,2.32) |
| RVOTO | 10871 (98.32) | 186 (1.68) | 1804 (98.42) | 29 (1.58) | 0.94 (0.63,1.40) | 0.95 (0.64,1.42) |
| * Pulmonary valve stenosis (PVS) | 10433 (98.29) | 182 (1.71) | 1342 (98.32) | 23 (1.68) | 0.98 (0.63,1.52) | 0.99 (0.64,1.54) |
| Septal defect | 10871 (98.32) | 186 (1.68) | 3695 (98.35) | 62 (1.65) | 0.98 (0.73,1.31) | 0.93 (0.69,1.25) |
| * VSD perimembranous | 10871 (98.32) | 186 (1.68) | 1327 (98.74) | 17 (1.26) | 0.75 (0.45,1.23) | 0.74 (0.45,1.22) |
| * VSD + ASD | 10871 (98.32) | 186 (1.68) | 562 (97.91) | 12 (2.09) | 1.25 (0.69,2.25) | 1.22 (0.67,2.21) |
| * ASD secundum or ASD NOS | 10871 (98.32) | 186 (1.68) | 2328 (98.27) | 41 (1.73) | 1.03 (0.73,1.45) | 0.97 (0.68,1.37) |
| **Promethazine** |  |  |  |  |  |  |
| Heart defect (any) | 10652 (96.34) | 405 (3.66) | 9479 (96.16) | 379 (3.84) | 1.05 (0.91,1.21) | 0.97 (0.84,1.13) |
| Anomalous pulmonary venous return | 10652 (96.34) | 405 (3.66) | 316 (97.53) | 8 (2.47) | 0.67 (0.33,1.35) | 0.71 (0.35,1.46) |
| Atrioventricular septal defect | 10652 (96.34) | 405 (3.66) | 258 (96.63) | 9 (3.37) | 0.92 (0.47,1.80) | 0.80 (0.40,1.59) |
| Conotruncal defect | 10652 (96.34) | 405 (3.66) | 2007 (96.40) | 75 (3.60) | 0.98 (0.76,1.26) | 1.05 (0.81,1.35) |
| * Tetralogy of Fallot | **10652 (96.34)** | **405 (3.66)** | **879 (95.03)** | **46 (4.97)** | **1.38 (1.01,1.88)** | **1.47 (1.07,2.03)** |
| * TGA | 10652 (96.34) | 405 (3.66) | 664 (97.22) | 19 (2.78) | 0.75 (0.47,1.20) | 0.79 (0.49,1.27) |
| LVOTO | 10652 (96.34) | 405 (3.66) | 1827 (96.26) | 71 (3.74) | 1.02 (0.79,1.32) | 0.96 (0.74,1.25) |
| * HLHS | 10652 (96.34) | 405 (3.66) | 551 (95.83) | 24 (4.17) | 1.15 (0.75,1.74) | 1.07 (0.70,1.65) |
| * Coarctation of the aorta (COA) | 10652 (96.34) | 405 (3.66) | 931 (96.68) | 32 (3.32) | 0.90 (0.63,1.30) | 0.88 (0.60,1.27) |
| * Aortic stenosis | 10652 (96.34) | 405 (3.66) | 434 (96.44) | 16 (3.56) | 0.97 (0.58,1.61) | 0.85 (0.50,1.42) |
| RVOTO | 10652 (96.34) | 405 (3.66) | 1758 (95.91) | 75 (4.09) | 1.12 (0.87,1.44) | 0.96 (0.74,1.25) |
| * Pulmonary valve stenosis (PVS) | 10216 (96.24) | 399 (3.76) | 1301 (95.31) | 64 (4.69) | 1.26 (0.96,1.65) | 1.04 (0.79,1.38) |
| Septal defect | 10652 (96.34) | 405 (3.66) | 3603 (95.90) | 154 (4.10) | 1.12 (0.93,1.36) | 0.98 (0.81,1.19) |
| * VSD perimembranous | 10652 (96.34) | 405 (3.66) | 1289 (95.91) | 55 (4.09) | 1.12 (0.84,1.50) | 1.05 (0.78,1.41) |
| * VSD + COA | 10652 (96.34) | 405 (3.66) | 231 (96.65) | 8 (3.35) | 0.91 (0.45,1.86) | 0.87 (0.42,1.80) |
| * ASD + PVS | 10652 (96.34) | 405 (3.66) | 199 (93.87) | 13 (6.13) | 1.72 (0.97,3.04) | 1.19 (0.66,2.14) |
| * VSD + ASD | 10652 (96.34) | 405 (3.66) | 549 (95.64) | 25 (4.36) | 1.20 (0.79,1.81) | 1.15 (0.75,1.75) |
| * ASD secundum or ASD NOS | 10652 (96.34) | 405 (3.66) | 2265 (95.61) | 104 (4.39) | 1.21 (0.97,1.51) | 0.99 (0.79,1.25) |
| **Triprolidine** |  |  |  |  |  |  |
| Heart defect (any) | 11042 (99.86) | 15 (0.14) | 9843 (99.85) | 15 (0.15) | 1.12 (0.55,2.30) | 1.12 (0.55,2.31) |
| Septal defect | 11042 (99.86) | 15 (0.14) | 3751 (99.84) | 6 (0.16) | 1.18 (0.46,3.04) | 1.25 (0.48,3.25) |
| HLHS = Hypoplastic left heart syndrome, LVOTO = Left ventricular outflow tract obstruction, RVOTO = Right ventricular outflow tract obstruction, TGA = DTransposition of the great arteries, VSD = Ventricular septal defect. Note: Inconsistencies in the number of controls due to no controls for PVS from CA prior to 2002.  Logistic regression models adjusted for: maternal age, maternal race, maternal education, parity, folic acid use, prenatal care (time of entry), smoking and alcohol status, and study site (see Table 2 for categorizations). | | | | | | |

**Supplemental Table 3:** Simple isolated cardiac defects and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine**  Birth defect   * Defect sub-classification | **Controls** | | **Cases** | | **Odds Ratios (95% CI)** | |
| **Not Exposed** | **Exposed** | **Not Exposed** | **Exposed** | **Crude** | **Adjusted** |
| **Any Antihistamine** |  |  |  |  |  |  |
| Heart defect (any) | 9622 (87.02) | 1435 (12.98) | 6502 (87.15) | 959 (12.85) | 0.99 (0.91,1.08) | 0.95 (0.87,1.04) |
| Anomalous pulmonary venous return | 9622 (87.02) | 1435 (12.98) | 255 (89.16) | 31 (10.84) | 0.82 (0.56,1.19) | 0.93 (0.63,1.36) |
| Atrioventricular septal defect | 9622 (87.02) | 1435 (12.98) | 141 (84.43) | 26 (15.57) | 1.24 (0.81,1.89) | 1.11 (0.72,1.71) |
| Conotruncal defects | 9622 (87.02) | 1435 (12.98) | 1470 (86.07) | 238 (13.93) | 1.09 (0.94,1.26) | 1.11 (0.95,1.29) |
| * Truncus Arteriosus | 9622 (87.02) | 1435 (12.98) | 74 (85.06) | 13 (14.94) | 1.18 (0.65,2.13) | 1.15 (0.63,2.12) |
| * Tetralogy of Fallot | **9622 (87.02)** | **1435 (12.98)** | **773 (84.57)** | **141 (15.43)** | **1.22 (1.01,1.48)** | **1.24 (1.02,1.50)** |
| * TGA | 9622 (87.02) | 1435 (12.98) | 484 (88.00) | 66 (12.00) | 0.91 (0.70,1.19) | 0.93 (0.71,1.21) |
| * Double outlet right ventricle (other) | **9622 (87.02)** | **1435 (12.98)** | **23 (76.67)** | **7 (23.33)** | **2.04 (0.87,4.77)** | **3.17 (1.30,7.72)** |
| * VSD conoventricular | 9622 (87.02) | 1435 (12.98) | 46 (86.79) | 7 (13.21) | 1.02 (0.46,2.26) | 1.29 (0.57,2.93) |
| LVOTO | 9622 (87.02) | 1435 (12.98) | 1252 (87.00) | 187 (13.00) | 1.00 (0.85,1.18) | 0.91 (0.77,1.08) |
| * HLHS | 9622 (87.02) | 1435 (12.98) | 485 (86.30) | 77 (13.70) | 1.06 (0.83,1.36) | 1.01 (0.79,1.30) |
| * Coarctation of the aorta (COA) | 9622 (87.02) | 1435 (12.98) | 476 (88.48) | 62 (11.52) | 0.87 (0.67,1.14) | 0.80 (0.60,1.05) |
| * Aortic stenosis | 9622 (87.02) | 1435 (12.98) | 273 (85.05) | 48 (14.95) | 1.18 (0.86,1.61) | 0.99 (0.72,1.36) |
| RVOTO | 9622 (87.02) | 1435 (12.98) | 1155 (87.24) | 169 (12.76) | 0.98 (0.83,1.16) | 0.91 (0.76,1.08) |
| * Pulmonary atresia | 9622 (87.02) | 1435 (12.98) | 145 (91.77) | 13 (8.23) | 0.60 (0.34,1.06) | 0.61 (0.34,1.09) |
| * Pulmonary valve stenosis (PVS) | 9222 (86.88) | 1393 (13.12) | 863 (86.56) | 134 (13.44) | 1.03 (0.85,1.24) | 0.93 (0.77,1.13) |
| * Ebstein anomaly | 9622 (87.02) | 1435 (12.98) | 92 (89.32) | 11 (10.68) | 0.80 (0.43,1.50) | 0.83 (0.44,1.57) |
| * Tricuspid atresia | 9622 (87.02) | 1435 (12.98) | 54 (83.08) | 11 (16.92) | 1.37 (0.71,2.62) | 1.54 (0.79,3.02) |
| Septal defect | 9622 (87.02) | 1435 (12.98) | 2225 (87.81) | 309 (12.19) | 0.93 (0.82,1.06) | 0.90 (0.79,1.04) |
| * VSD perimembranous | 9622 (87.02) | 1435 (12.98) | 769 (88.19) | 103 (11.81) | 0.90 (0.73,1.11) | 0.90 (0.73,1.12) |
| * ASD secundum or ASD NOS | 9622 (87.02) | 1435 (12.98) | 1292 (87.24) | 189 (12.76) | 0.98 (0.83,1.15) | 0.92 (0.78,1.10) |
| **Cetirizine** |  |  |  |  |  |  |
| Heart defect (any) | 10897 (98.55) | 160 (1.45) | 7369 (98.77) | 92 (1.23) | 0.85 (0.66,1.10) | 0.83 (0.64,1.07) |
| Conotruncal defect | 10897 (98.55) | 160 (1.45) | 1674 (98.01) | 34 (1.99) | 1.38 (0.95,2.01) | 1.44 (0.99,2.10) |
| * Tetralogy of Fallot | 10897 (98.55) | 160 (1.45) | 894 (97.81) | 20 (2.19) | 1.52 (0.95,2.44) | 1.57 (0.98,2.53) |
| * TGA | 10897 (98.55) | 160 (1.45) | 542 (98.55) | 8 (1.45) | 1.01 (0.49,2.06) | 1.04 (0.51,2.15) |
| LVOTO | 10897 (98.55) | 160 (1.45) | 1421 (98.75) | 18 (1.25) | 0.86 (0.53,1.41) | 0.73 (0.45,1.20) |
| * HLHS | 10897 (98.55) | 160 (1.45) | 556 (98.93) | 6 (1.07) | 0.74 (0.32,1.67) | 0.67 (0.30,1.54) |
| * Aortic stenosis | 10897 (98.55) | 160 (1.45) | 311 (96.88) | 10 (3.12) | 2.19 (1.15,4.19) | 1.69 (0.87,3.27) |
| RVOTO | 10897 (98.55) | 160 (1.45) | 1305 (98.56) | 19 (1.44) | 0.99 (0.61,1.60) | 0.91 (0.56,1.48) |
| * Pulmonary valve stenosis (PVS) | 10455 (98.49) | 160 (1.51) | 983 (98.60) | 14 (1.40) | 0.93 (0.54,1.61) | 0.84 (0.48,1.46) |
| Septal defect | 10897 (98.55) | 160 (1.45) | 2517 (99.33) | 17 (0.67) | 0.46 (0.28,0.76) | 0.45 (0.27,0.75) |
| * ASD secundum or ASD NOS | 10897 (98.55) | 160 (1.45) | 1465 (98.92) | 16 (1.08) | 0.74 (0.44,1.25) | 0.70 (0.41,1.18) |
| **Dimenhydrinate** |  |  |  |  |  |  |
| Heart defect (any) | 11037 (99.82) | 20 (0.18) | 7442 (99.75) | 19 (0.25) | 1.41 (0.75,2.64) | 1.31 (0.70,2.47) |
| Septal defect | 11037 (99.82) | 20 (0.18) | 2528 (99.76) | 6 (0.24) | 1.31 (0.53,3.27) | 1.25 (0.49,3.17) |
| **Diphenhydramine** |  |  |  |  |  |  |
| Heart defect (any) | 10814 (97.80) | 243 (2.20) | 7287 (97.67) | 174 (2.33) | 1.06 (0.87,1.29) | 1.02 (0.84,1.24) |
| Anomalous pulmonary venous return | 10814 (97.80) | 243 (2.20) | 278 (97.20) | 8 (2.80) | 1.28 (0.63,2.62) | 1.36 (0.66,2.81) |
| Conotruncal defect | 10814 (97.80) | 243 (2.20) | 1669 (97.72) | 39 (2.28) | 1.04 (0.74,1.46) | 1.01 (0.72,1.43) |
| * Tetralogy of Fallot | 10814 (97.80) | 243 (2.20) | 891 (97.48) | 23 (2.52) | 1.15 (0.75,1.77) | 1.10 (0.71,1.71) |
| * TGA | 10814 (97.80) | 243 (2.20) | 540 (98.18) | 10 (1.82) | 0.82 (0.44,1.56) | 0.80 (0.42,1.52) |
| LVOTO | 10814 (97.80) | 243 (2.20) | 1409 (97.92) | 30 (2.08) | 0.95 (0.65,1.39) | 0.88 (0.60,1.29) |
| * HLHS | 10814 (97.80) | 243 (2.20) | 546 (97.15) | 16 (2.85) | 1.30 (0.78,2.18) | 1.25 (0.75,2.10) |
| * Coarctation of the aorta (COA) | 10814 (97.80) | 243 (2.20) | 528 (98.14) | 10 (1.86) | 0.84 (0.45,1.60) | 0.78 (0.41,1.48) |
| RVOTO | 10814 (97.80) | 243 (2.20) | 1288 (97.28) | 36 (2.72) | 1.24 (0.87,1.77) | 1.18 (0.82,1.68) |
| * Pulmonary valve stenosis (PVS) | 10383 (97.81) | 232 (2.19) | 972 (97.49) | 25 (2.51) | 1.15 (0.76,1.75) | 1.05 (0.69,1.60) |
| Septal defect | 10814 (97.80) | 243 (2.20) | 2478 (97.79) | 56 (2.21) | 1.01 (0.75,1.35) | 0.97 (0.72,1.31) |
| * VSD perimembranous | 10814 (97.80) | 243 (2.20) | 844 (96.79) | 28 (3.21) | 1.48 (0.99,2.20) | 1.44 (0.96,2.16) |
| * ASD secundum or ASD NOS | 10814 (97.80) | 243 (2.20) | 1454 (98.18) | 27 (1.82) | 0.83 (0.55,1.23) | 0.80 (0.53,1.22) |
| **Doxylamine** |  |  |  |  |  |  |
| Heart defect (any) | 10870 (98.31) | 187 (1.69) | 7321 (98.12) | 140 (1.88) | 1.11 (0.89,1.39) | 1.10 (0.88,1.37) |
| Conotruncal defect | 10870 (98.31) | 187 (1.69) | 1674 (98.01) | 34 (1.99) | 1.18 (0.82,1.71) | 1.30 (0.89,1.89) |
| * Tetralogy of Fallot | 10870 (98.31) | 187 (1.69) | 899 (98.36) | 15 (1.64) | 0.97 (0.57,1.65) | 1.09 (0.64,1.86) |
| * TGA | 10870 (98.31) | 187 (1.69) | 537 (97.64) | 13 (2.36) | 1.41 (0.80,2.49) | 1.48 (0.83,2.64) |
| LVOTO | 10870 (98.31) | 187 (1.69) | 1406 (97.71) | 33 (2.29) | 1.36 (0.94,1.98) | 1.07 (0.73,1.57) |
| * HLHS | 10870 (98.31) | 187 (1.69) | 545 (96.98) | 17 (3.02) | 1.81 (1.10,3.00) | 1.51 (0.90,2.52) |
| * Coarctation of the aorta (COA) | 10870 (98.31) | 187 (1.69) | 531 (98.70) | 7 (1.30) | 0.77 (0.36,1.64) | 0.62 (0.29,1.33) |
| * Aortic stenosis | 10870 (98.31) | 187 (1.69) | 312 (97.20) | 9 (2.80) | 1.68 (0.85,3.30) | 1.06 (0.53,2.11) |
| RVOTO | 10870 (98.31) | 187 (1.69) | 1302 (98.34) | 22 (1.66) | 0.98 (0.63,1.53) | 0.88 (0.56,1.38) |
| * Pulmonary valve stenosis (PVS) | 10437 (98.32) | 178 (1.68) | 981 (98.40) | 16 (1.60) | 0.96 (0.57,1.60) | 0.81 (0.48,1.36) |
| Septal defect | 10870 (98.31) | 187 (1.69) | 2489 (98.22) | 45 (1.78) | 1.05 (0.76,1.46) | 1.19 (0.85,1.67) |
| * VSD perimembranous | 10870 (98.31) | 187 (1.69) | 859 (98.51) | 13 (1.49) | 0.88 (0.50,1.55) | 1.03 (0.58,1.84) |
| * ASD secundum or ASD NOS | 10870 (98.31) | 187 (1.69) | 1453 (98.11) | 28 (1.89) | 1.12 (0.75,1.67) | 1.19 (0.79,1.80) |
| **Fexofenadine** |  |  |  |  |  |  |
| Heart defect (any) | 10964 (99.16) | 93 (0.84) | 7402 (99.21) | 59 (0.79) | 0.94 (0.68,1.30) | 0.94 (0.67,1.30) |
| Conotruncal defect | 10964 (99.16) | 93 (0.84) | 1691 (99.00) | 17 (1.00) | 1.19 (0.70,1.99) | 1.19 (0.70,2.00) |
| * Tetralogy of Fallot | 10964 (99.16) | 93 (0.84) | 907 (99.23) | 7 (0.77) | 0.91 (0.42,1.97) | 0.90 (0.42,1.96) |
| LVOTO | 10964 (99.16) | 93 (0.84) | 1429 (99.31) | 10 (0.69) | 0.83 (0.43,1.59) | 0.77 (0.40,1.50) |
| * Coarctation of the aorta (COA) | 10964 (99.16) | 93 (0.84) | 530 (98.51) | 8 (1.49) | 1.78 (0.86,3.68) | 1.63 (0.78,3.38) |
| RVOTO | 10964 (99.16) | 93 (0.84) | 1316 (99.40) | 8 (0.60) | 0.72 (0.35,1.48) | 0.68 (0.33,1.42) |
| Septal defect | 10964 (99.16) | 93 (0.84) | 2514 (99.21) | 20 (0.79) | 0.94 (0.58,1.52) | 1.01 (0.62,1.66) |
| * VSD perimembranous | 10964 (99.16) | 93 (0.84) | 865 (99.20) | 7 (0.80) | 0.95 (0.44,2.06) | 1.05 (0.48,2.28) |
| * ASD secundum or ASD NOS | 10964 (99.16) | 93 (0.84) | 1468 (99.12) | 13 (0.88) | 1.04 (0.58,1.87) | 1.09 (0.60,1.98) |
| **Hydroxyzine** |  |  |  |  |  |  |
| Heart defect (any) | 11050 (99.94) | 7 (0.06) | 7450 (99.85) | 11 (0.15) | 2.33 (0.90,6.01) | 2.19 (0.85,5.70) |
| **Loratadine** |  |  |  |  |  |  |
| Heart defect (any) | 10775 (97.45) | 282 (2.55) | 7276 (97.52) | 185 (2.48) | 0.97 (0.81,1.17) | 0.99 (0.82,1.19) |
| Anomalous pulmonary venous return | 10775 (97.45) | 282 (2.55) | 278 (97.20) | 8 (2.80) | 1.10 (0.54,2.24) | 1.26 (0.61,2.58) |
| Conotruncal defect | 10775 (97.45) | 282 (2.55) | 1650 (96.60) | 58 (3.40) | 1.34 (1.01,1.79) | 1.29 (0.96,1.72) |
| * Tetralogy of Fallot | 10775 (97.45) | 282 (2.55) | 881 (96.39) | 33 (3.61) | 1.43 (0.99,2.07) | 1.33 (0.92,1.93) |
| * TGA | 10775 (97.45) | 282 (2.55) | 533 (96.91) | 17 (3.09) | 1.22 (0.74,2.00) | 1.18 (0.72,1.95) |
| LVOTO | 10775 (97.45) | 282 (2.55) | 1402 (97.43) | 37 (2.57) | 1.01 (0.71,1.43) | 0.98 (0.69,1.39) |
| * HLHS | 10775 (97.45) | 282 (2.55) | 550 (97.86) | 12 (2.14) | 0.83 (0.46,1.50) | 0.84 (0.47,1.51) |
| * Coarctation of the aorta (COA) | 10775 (97.45) | 282 (2.55) | 522 (97.03) | 16 (2.97) | 1.17 (0.70,1.95) | 1.10 (0.66,1.85) |
| * Aortic stenosis | 10775 (97.45) | 282 (2.55) | 312 (97.20) | 9 (2.80) | 1.10 (0.56,2.16) | 1.06 (0.54,2.10) |
| RVOTO | 10775 (97.45) | 282 (2.55) | 1293 (97.66) | 31 (2.34) | 0.92 (0.63,1.33) | 0.93 (0.64,1.36) |
| * Pulmonary valve stenosis (PVS) | 10343 (97.44) | 272 (2.56) | 974 (97.69) | 23 (2.31) | 0.90 (0.58,1.38) | 0.91 (0.59,1.41) |
| Septal defect | 10775 (97.45) | 282 (2.55) | 2485 (98.07) | 49 (1.93) | 0.75 (0.55,1.02) | 0.81 (0.59,1.11) |
| * VSD perimembranous | 10775 (97.45) | 282 (2.55) | 863 (98.97) | 9 (1.03) | 0.40 (0.20,0.78) | 0.42 (0.21,0.81) |
| * ASD secundum or ASD NOS | 10775 (97.45) | 282 (2.55) | 1444 (97.50) | 37 (2.50) | 0.98 (0.69,1.39) | 1.09 (0.76,1.55) |
| **Pheniramine** |  |  |  |  |  |  |
| Heart defect (any) | 10871 (98.32) | 186 (1.68) | 7339 (98.36) | 122 (1.64) | 0.97 (0.77,1.22) | 0.96 (0.76,1.21) |
| Atrioventricular septal defect | **10871 (98.32)** | **186 (1.68)** | **160 (95.81)** | **7 (4.19)** | **2.56 (1.18,5.53)** | **2.53 (1.16,5.51)** |
| Conotruncal defect | 10871 (98.32) | 186 (1.68) | 1683 (98.54) | 25 (1.46) | 0.87 (0.57,1.32) | 0.90 (0.59,1.38) |
| * Tetralogy of Fallot | 10871 (98.32) | 186 (1.68) | 899 (98.36) | 15 (1.64) | 0.98 (0.57,1.66) | 0.99 (0.58,1.68) |
| * TGA | 10871 (98.32) | 186 (1.68) | 543 (98.73) | 7 (1.27) | 0.75 (0.35,1.61) | 0.80 (0.37,1.72) |
| LVOTO | 10871 (98.32) | 186 (1.68) | 1417 (98.47) | 22 (1.53) | 0.91 (0.58,1.42) | 0.95 (0.60,1.48) |
| * HLHS | 10871 (98.32) | 186 (1.68) | 555 (98.75) | 7 (1.25) | 0.74 (0.35,1.58) | 0.80 (0.37,1.72) |
| * Coarctation of the aorta (COA) | 10871 (98.32) | 186 (1.68) | 530 (98.51) | 8 (1.49) | 0.88 (0.43,1.80) | 0.91 (0.44,1.86) |
| * Aortic stenosis | 10871 (98.32) | 186 (1.68) | 314 (97.82) | 7 (2.18) | 1.30 (0.61,2.80) | 1.38 (0.64,2.99) |
| RVOTO | 10871 (98.32) | 186 (1.68) | 1302 (98.34) | 22 (1.66) | 0.99 (0.63,1.54) | 0.98 (0.63,1.54) |
| * Pulmonary valve stenosis (PVS) | 10433 (98.29) | 182 (1.71) | 979 (98.19) | 18 (1.81) | 1.06 (0.65,1.72) | 1.05 (0.64,1.71) |
| Septal defect | 10871 (98.32) | 186 (1.68) | 2491 (98.30) | 43 (1.70) | 1.01 (0.72,1.41) | 0.94 (0.67,1.32) |
| * VSD perimembranous | 10871 (98.32) | 186 (1.68) | 861 (98.74) | 11 (1.26) | 0.75 (0.41,1.38) | 0.72 (0.39,1.34) |
| * ASD secundum or ASD NOS | 10871 (98.32) | 186 (1.68) | 1456 (98.31) | 25 (1.69) | 1.00 (0.66,1.53) | 0.91 (0.59,1.39) |
| **Promethazine** |  |  |  |  |  |  |
| Heart defect (any) | 10652 (96.34) | 405 (3.66) | 7178 (96.21) | 283 (3.79) | 1.04 (0.89,1.21) | 0.95 (0.81,1.11) |
| Anomalous pulmonary venous return | 10652 (96.34) | 405 (3.66) | 279 (97.55) | 7 (2.45) | 0.66 (0.31,1.41) | 0.72 (0.33,1.56) |
| Atrioventricular septal defect | 10652 (96.34) | 405 (3.66) | 161 (96.41) | 6 (3.59) | 0.98 (0.43,2.23) | 0.80 (0.34,1.83) |
| Conotruncal defect | 10652 (96.34) | 405 (3.66) | 1645 (96.31) | 63 (3.69) | 1.01 (0.77,1.32) | 1.08 (0.82,1.42) |
| * Tetralogy of Fallot | **10652 (96.34)** | **405 (3.66)** | **869 (95.08)** | **45 (4.92)** | **1.36 (0.99,1.87)** | **1.45 (1.05,2.01)** |
| * TGA | 10652 (96.34) | 405 (3.66) | 535 (97.27) | 15 (2.73) | 0.74 (0.44,1.24) | 0.80 (0.47,1.36) |
| LVOTO | 10652 (96.34) | 405 (3.66) | 1384 (96.18) | 55 (3.82) | 1.05 (0.78,1.39) | 0.97 (0.72,1.30) |
| * HLHS | 10652 (96.34) | 405 (3.66) | 540 (96.09) | 22 (3.91) | 1.07 (0.69,1.66) | 1.01 (0.65,1.58) |
| * Coarctation of the aorta (COA) | 10652 (96.34) | 405 (3.66) | 519 (96.47) | 19 (3.53) | 0.96 (0.60,1.54) | 0.93 (0.58,1.50) |
| * Aortic stenosis | 10652 (96.34) | 405 (3.66) | 307 (95.64) | 14 (4.36) | 1.20 (0.70,2.07) | 0.99 (0.57,1.73) |
| RVOTO | 10652 (96.34) | 405 (3.66) | 1271 (96.00) | 53 (4.00) | 1.10 (0.82,1.47) | 0.93 (0.69,1.25) |
| * Pulmonary valve stenosis (PVS) | 10216 (96.24) | 399 (3.76) | 951 (95.39) | 46 (4.61) | 1.24 (0.91,1.69) | 1.03 (0.74,1.41) |
| Septal defect | 10652 (96.34) | 405 (3.66) | 2435 (96.09) | 99 (3.91) | 1.07 (0.85,1.34) | 0.91 (0.72,1.14) |
| * VSD perimembranous | 10652 (96.34) | 405 (3.66) | 836 (95.87) | 36 (4.13) | 1.13 (0.80,1.60) | 1.05 (0.73,1.50) |
| * ASD secundum or ASD NOS | 10652 (96.34) | 405 (3.66) | 1421 (95.95) | 60 (4.05) | 1.11 (0.84,1.46) | 0.86 (0.65,1.15) |
| **Triprolidine** |  |  |  |  |  |  |
| Heart defect (any) | 11042 (99.86) | 15 (0.14) | 7452 (99.88) | 9 (0.12) | 0.89 (0.39,2.04) | 0.87 (0.38,1.99) |
| HLHS = Hypoplastic left heart syndrome, LVOTO = Left ventricular outflow tract obstruction, RVOTO = Right ventricular outflow tract obstruction, TGA = DTransposition of the great arteries, VSD = Ventricular septal defect. Note: Inconsistencies in the number of controls due to no controls for PVS from CA prior to 2002.  Logistic regression models adjusted for: maternal age, maternal race, maternal education, parity, folic acid use, prenatal care (time of entry), smoking and alcohol status, and study site (see Table 2 for categorizations). | | | | | | |

**Supplemental Table 4:** All results for non-cardiac defects (including sub-classifications) and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine**  Birth defect   * Defect sub-classification | **Controls** | | **Cases** | | **Odds Ratios (95% CI)** | |
| **Not Exposed** | **Exposed** | **Not Exposed** | **Exposed** | **Crude** | **Adjusted** |
| **Any Antihistamine** |  |  |  |  |  |  |
| ABS-LBW | 9622 (87.02) | 1435 (12.98) | 261 (86.14) | 42 (13.86) | 1.08 (0.78,1.50) | 1.18 (0.84,1.66) |
| * Limb anomalies only | 9622 (87.02) | 1435 (12.98) | 163 (84.46) | 30 (15.54) | 1.23 (0.83,1.83) | 1.37 (0.91,2.06) |
| * Craniofacial disruptions +/- limb def. | 9622 (87.02) | 1435 (12.98) | 54 (88.52) | 7 (11.48) | 0.87 (0.39,1.91) | 1.03 (0.46,2.33) |
| Anorectal atresia/stenosis | 9622 (87.02) | 1435 (12.98) | 911 (89.84) | 103 (10.16) | 0.76 (0.61,0.94) | 0.81 (0.66,1.01) |
| Anotia/microtia | 9622 (87.02) | 1435 (12.98) | 606 (91.82) | 54 (8.18) | 0.60 (0.45,0.80) | 0.78 (0.58,1.04) |
| Bilateral renal agenesis or hypoplasia | 9622 (87.02) | 1435 (12.98) | 149 (84.18) | 28 (15.82) | 1.26 (0.84,1.90) | 1.32 (0.86,2.01) |
| Biliary atresia | 9622 (87.02) | 1435 (12.98) | 167 (87.89) | 23 (12.11) | 0.92 (0.60,1.43) | 0.94 (0.60,1.47) |
| Bladder exstrophy | 9622 (87.02) | 1435 (12.98) | 63 (85.14) | 11 (14.86) | 1.17 (0.62,2.23) | 1.23 (0.64,2.38) |
| Cerebellar hypoplasia | 9622 (87.02) | 1435 (12.98) | 53 (88.33) | 7 (11.67) | 0.89 (0.40,1.95) | 0.76 (0.34,1.69) |
| Choanal atresia | 9622 (87.02) | 1435 (12.98) | 132 (85.16) | 23 (14.84) | 1.17 (0.75,1.83) | 1.15 (0.73,1.81) |
| Colonic atresia/stenosis | 9622 (87.02) | 1435 (12.98) | 43 (84.31) | 8 (15.69) | 1.25 (0.59,2.66) | 1.58 (0.72,3.48) |
| Craniosynostosis | **9622 (87.02)** | **1435 (12.98)** | **1282 (83.46)** | **254 (16.54)** | **1.33 (1.15,1.54)** | **1.17 (1.01,1.36)** |
| Dandy Walker Malformation | 9622 (87.02) | 1435 (12.98) | 149 (85.63) | 25 (14.37) | 1.13 (0.73,1.73) | 1.24 (0.80,1.93) |
| Diaphragmatic hernia | 9622 (87.02) | 1435 (12.98) | 706 (85.27) | 122 (14.73) | 1.16 (0.95,1.42) | 1.16 (0.95,1.43) |
| Duodenal atresia/stenosis | **9622 (87.02)** | **1435 (12.98)** | **190 (82.61)** | **40 (17.39)** | **1.41 (1.00,1.99)** | **1.51 (1.06,2.15)** |
| Esophageal atresia | 9622 (87.02) | 1435 (12.98) | 644 (88.10) | 87 (11.90) | 0.91 (0.72,1.14) | 0.89 (0.71,1.13) |
| Gastroschisis | 9622 (87.02) | 1435 (12.98) | 1150 (87.32) | 167 (12.68) | 0.97 (0.82,1.16) | 1.13 (0.93,1.36) |
| Holoprosencephaly | 9622 (87.02) | 1435 (12.98) | 142 (88.75) | 18 (11.25) | 0.85 (0.52,1.39) | 1.05 (0.63,1.74) |
| Hypospadias | 4907 (87.44) | 705 (12.56) | 2097 (85.17) | 365 (14.83) | 1.21 (1.06,1.39) | 1.10 (0.95,1.27) |
| Intestinal atresia/stenosis | 9622 (87.02) | 1435 (12.98) | 390 (86.67) | 60 (13.33) | 1.03 (0.78,1.36) | 1.24 (0.93,1.64) |
| Limb deficiencies | 9622 (87.02) | 1435 (12.98) | 1040 (87.25) | 152 (12.75) | 0.98 (0.82,1.17) | * 1. (0.86,1.23) |
| * Longitudinal limb deficiency | 9622 (87.02) | 1435 (12.98) | 401 (87.17) | 59 (12.83) | 0.99 (0.75,1.30) | 1.01 (0.76,1.34) |
| * Transverse limb deficiency | 9622 (87.02) | 1435 (12.98) | 600 (87.59) | 85 (12.41) | 0.95 (0.75,1.20) | 1.02 (0.80,1.30) |
| * Intercalary limb deficiency | 9622 (87.02) | 1435 (12.98) | 53 (85.48) | 9 (14.52) | 1.14 (0.56,2.31) | 1.09 (0.53,2.26) |
| Neural tube defects | **9622 (87.02)** | **1435 (12.98)** | **1711 (85.04)** | **301 (14.96)** | **1.18 (1.03,1.35)** | **1.22 (1.06,1.40)** |
| * Anencephaly and craniorachischisis | **9622 (87.02)** | **1435 (12.98)** | **498 (83.70)** | **97 (16.30)** | **1.31 (1.04,1.64)** | **1.31 (1.04,1.66)** |
| * Spina bifida | **9622 (87.02)** | **1435 (12.98)** | **1025 (85.13)** | **179 (14.87)** | **1.17 (1.00,1.39)** | **1.22 (1.02,1.45)** |
| * Encephalocele | 9622 (87.02) | 1435 (12.98) | 188 (88.26) | 25 (11.74) | 0.89 (0.59,1.36) | 0.97 (0.63,1.50) |
| Omphalocele | 9622 (87.02) | 1435 (12.98) | 359 (85.07) | 63 (14.93) | 1.18 (0.90,1.55) | 1.16 (0.88,1.54) |
| Oral Clefts | 9505 (87.00) | 1420 (13.00) | 3915 (87.29) | 570 (12.71) | 0.98 (0.88,1.08) | 0.99 (0.89,1.10) |
| * Cleft palate (CP) | 9505 (87.00) | 1420 (13.00) | 1337 (87.33) | 194 (12.67) | 0.97 (0.83,1.14) | 0.96 (0.82,1.13) |
| * Cleft Lip (CL) w/wo CP | 9505 (87.00) | 1420 (13.00) | 2578 (87.27) | 376 (12.73) | 0.98 (0.86,1.10) | 1.00 (0.88,1.13) |
| * CL with CP | 9505 (87.00) | 1420 (13.00) | 1662 (87.34) | 241 (12.66) | 0.97 (0.84,1.12) | 1.03 (0.89,1.20) |
| * CL without CP | 9505 (87.00) | 1420 (13.00) | 916 (87.16) | 135 (12.84) | 0.99 (0.82,1.19) | 0.95 (0.78,1.15) |
| Sacral agenesis or caudal dysplasia | 9622 (87.02) | 1435 (12.98) | 91 (90.10) | 10 (9.90) | 0.74 (0.38,1.50) | 0.83 (0.42,1.62) |
| **Cetirizine** |  |  |  |  |  |  |
| Anorectal atresia/stenosis | 10897 (98.55) | 160 (1.45) | 1008 (99.41) | 6 (0.59) | 0.41 (0.18,0.92) | 0.46 (0.20,1.05) |
| Craniosynostosis | 10897 (98.55) | 160 (1.45) | 1505 (97.98) | 31 (2.02) | 1.40 (0.95,2.07) | 1.08 (0.73,1.60) |
| Diaphragmatic hernia | 10897 (98.55) | 160 (1.45) | 818 (98.79) | 10 (1.21) | 0.84 (0.44,1.58) | 0.84 (0.44,1.60) |
| Esophageal atresia | 10897 (98.55) | 160 (1.45) | 717 (98.08) | 14 (1.92) | 1.33 (0.77,2.31) | 1.27 (0.73,2.22) |
| Gastroschisis | 10897 (98.55) | 160 (1.45) | 1304 (99.01) | 13 (0.99) | 0.68 (0.39,1.20) | 1.03 (0.56,1.90) |
| Hypospadias | 5535 (98.63) | 77 (1.37) | 2408 (97.81) | 54 (2.19) | 1.61 (1.14,2.29) | 1.40 (0.97,2.02) |
| Limb deficiencies | 10897 (98.55) | 160 (1.45) | 1175 (98.57) | 17 (1.43) | 0.99 (0.60,1.63) | 1.07 (0.65,1.79) |
| * Longitudinal limb deficiency | 10897 (98.55) | 160 (1.45) | 451 (98.04) | 9 (1.96) | 1.36 (0.69,2.68) | 1.50 (0.76,2.98) |
| * Transverse limb deficiency | 10897 (98.55) | 160 (1.45) | 677 (98.83) | 8 (1.17) | 0.80 (0.39,1.64) | 0.87 (0.42,1.78) |
| Neural tube defects | 10897 (98.55) | 160 (1.45) | 1982 (98.51) | 30 (1.49) | 1.03 (0.60,1.53) | 1.07 (0.72,1.60) |
| * Anencephaly and craniorachischisis | 10897 (98.55) | 160 (1.45) | 586 (98.49) | 9 (1.51) | 1.05 (0.53,2.06) | 1.03 (0.52,2.04) |
| * Spina bifida | 10897 (98.55) | 160 (1.45) | 1186 (98.50) | 18 (1.50) | 1.03 (0.63,1.69) | 1.08 (0.66,1.77) |
| Oral Clefts | 10766 (98.54) | 159 (1.46) | 4425 (98.66) | 60 (1.34) | 0.92 (0.68,1.24) | 0.96 (0.71,1.29) |
| * Cleft palate (CP) | 10766 (98.54) | 159 (1.46) | 1507 (98.43) | 24 (1.57) | 1.08 (0.70,1.66) | 1.09 (0.70,1.68) |
| * Cleft Lip (CL) w/wo CP | 10766 (98.54) | 159 (1.46) | 2918 (98.78) | 36 (1.22) | 0.84 (0.58,1.20) | 0.88 (0.61,1.28) |
| * CL with CP | 10766 (98.54) | 159 (1.46) | 1880 (98.79) | 23 (1.21) | 0.83 (0.53,1.29) | 0.93 (0.59,1.45) |
| * CL without CP | 10766 (98.54) | 159 (1.46) | 1038 (98.76) | 13 (1.24) | 0.85 (0.48,1.50) | 0.82 (0.46,1.45) |
| **Dimenhydrinate** |  |  |  |  |  |  |
| Oral Clefts | 10906 (99.83) | 19 (0.17) | 4475 (99.78) | 10 (0.22) | 1.28 (0.60,2.76) | 1.26 (0.58,2.73) |
| * CL w/wo CP | 10906 (99.83) | 19 (0.17) | 2948 (99.80) | 6 (0.20) | 1.17 (0.47,2.93) | 1.14 (0.45,2.89) |
| **Diphenhydramine** |  |  |  |  |  |  |
| ABS-LBW | 10814 (97.80) | 243 (2.20) | 295 (97.36) | 8 (2.64) | 1.21 (0.59,2.46) | 1.20 (0.58,2.48) |
| * Limb anomalies only | 10814 (97.80) | 243 (2.20) | 187 (96.89) | 6 (3.11) | 1.43 (0.63,3.25) | 1.37 (0.59,3.16) |
| Anorectal atresia/stenosis | 10814 (97.80) | 243 (2.20) | 992 (97.83) | 22 (2.17) | 0.99 (0.63,1.53) | 1.04 (0.67,1.62) |
| Anotia/microtia | 10814 (97.80) | 243 (2.20) | 645 (97.73) | 15 (2.27) | 1.04 (0.61,1.76) | 1.35 (0.79,2.31) |
| Craniosynostosis | **10814 (97.80)** | **243 (2.20)** | **1485 (96.68)** | **51 (3.32)** | **1.53 (1.13,2.08)** | **1.43 (1.04,1.95)** |
| Diaphragmatic hernia | 10814 (97.80) | 243 (2.20) | 801 (96.74) | 27 (3.26) | 1.50 (1.00,2.25) | 1.48 (0.99,2.23) |
| Duodenal atresia/stenosis | 10814 (97.80) | 243 (2.20) | 222 (96.52) | 8 (3.48) | 1.60 (0.78,3.28) | 1.73 (0.84,3.56) |
| Esophageal atresia | 10814 (97.80) | 243 (2.20) | 717 (98.08) | 14 (1.92) | 0.87 (0.50,1.50) | 0.84 (0.48,1.45) |
| Gastroschisis | 10814 (97.80) | 243 (2.20) | 1282 (97.34) | 35 (2.66) | 1.22 (0.85,1.74) | 1.33 (0.90,1.98) |
| Hypospadias | 5491 (97.84) | 121 (2.16) | 2399 (97.44) | 63 (2.56) | 1.19 (0.88,1.62) | 1.09 (0.79,1.51) |
| Intestinal atresia/stenosis | 10814 (97.80) | 243 (2.20) | 440 (97.78) | 10 (2.22) | 1.01 (0.53,1.92) | 1.17 (0.61,2.23) |
| Limb deficiencies | 10814 (97.80) | 243 (2.20) | 1159 (97.23) | 33 (2.77) | 1.27 (0.88,1.83) | 1.33 (0.92,1.93) |
| * Longitudinal limb deficiency | 10814 (97.80) | 243 (2.20) | 444 (96.52) | 16 (3.48) | 1.60 (0.96,2.68) | 1.62 (0.96,2.73) |
| * Transverse limb deficiency | 10814 (97.80) | 243 (2.20) | 670 (97.81) | 15 (2.19) | 1.00 (0.59,1.69) | 1.09 (0.64,1.85) |
| Neural tube defects | 10814 (97.80) | 243 (2.20) | 1959 (97.37) | 53 (2.63) | 1.20 (0.89,1.63) | 1.23 (0.91,1.67) |
| * Anencephaly and craniorachischisis | **10814 (97.80)** | **243 (2.20)** | **573 (96.30)** | **22 (3.70)** | **1.71 (1.10,2.66)** | **1.70 (1.08,2.68)** |
| * Spina bifida | 10814 (97.80) | 243 (2.20) | 1177 (97.76) | 27 (2.24) | 1.02 (0.68,1.53) | 1.07 (0.71,1.60) |
| Omphalocele | 10814 (97.80) | 243 (2.20) | 410 (97.16) | 12 (2.84) | 1.30 (0.72,2.35) | 1.22 (0.68,2.21) |
| Oral Clefts | 10685 (97.80) | 240 (2.20) | 4384 (97.75) | 101 (2.25) | 1.03 (0.81,1.30) | 1.04 (0.82,1.32) |
| * Cleft palate (CP) | 10685 (97.80) | 240 (2.20) | 1505 (98.30) | 26 (1.70) | 0.77 (0.51,1.16) | 0.75 (0.50,1.14) |
| * Cleft Lip (CL) w/wo CP | 10685 (97.80) | 240 (2.20) | 2879 (97.46) | 75 (2.54) | 1.16 (0.89,1.51) | 1.19 (0.91,1.55) |
| * CL with CP | 10685 (97.80) | 240 (2.20) | 1854 (97.43) | 49 (2.57) | 1.18 (0.86,1.61) | 1.24 (0.90,1.70) |
| * CL without CP | 10685 (97.80) | 240 (2.20) | 1025 (97.53) | 26 (2.47) | 1.13 (0.75,1.70) | 1.09 (0.72,1.64) |
| **Doxylamine** |  |  |  |  |  |  |
| ABS-LBW | 10870 (98.31) | 187 (1.69) | 293 (96.70) | 10 (3.30) | 1.98 (1.04,3.79) | 1.94 (1.00,3.77) |
| * Limb anomalies only | **10870 (98.31)** | **187 (1.69)** | **186 (96.37)** | **7 (3.63)** | **2.19 (1.01,4.72)** | **2.32 (1.05,5.12)** |
| Anorectal atresia/stenosis | 10870 (98.31) | 187 (1.69) | 1001 (98.72) | 13 (1.28) | 0.76 (0.43,1.33) | 0.86 (0.49,1.52) |
| Anotia/microtia | 10870 (98.31) | 187 (1.69) | 650 (98.48) | 10 (1.52) | 0.89 (0.47,1.70) | 1.02 (0.53,1.96) |
| Craniosynostosis | 10870 (98.31) | 187 (1.69) | 1506 (98.05) | 30 (1.95) | 1.16 (0.78,1.71) | 0.83 (0.56,1.24) |
| Diaphragmatic hernia | 10870 (98.31) | 187 (1.69) | 810 (97.83) | 18 (2.17) | 1.29 (0.79,2.11) | 1.23 (0.75,2.03) |
| Esophageal atresia | 10870 (98.31) | 187 (1.69) | 720 (98.50) | 11 (1.50) | 0.89 (0.48,1.64) | 0.89 (0.48,1.66) |
| Gastroschisis | 10870 (98.31) | 187 (1.69) | 1295 (98.33) | 22 (1.67) | 0.99 (0.63,1.54) | 1.04 (0.64,1.68) |
| Hypospadias | 5523 (98.41) | 89 (1.59) | 2419 (98.25) | 43 (1.75) | 1.10 (0.76,1.59) | 1.04 (0.71,1.51) |
| Intestinal atresia/stenosis | 10870 (98.31) | 187 (1.69) | 439 (97.56) | 11 (2.44) | 1.46 (0.79,2.70) | 1.71 (0.92,3.21) |
| Limb deficiencies | 10870 (98.31) | 187 (1.69) | 1169 (98.07) | 23 (1.93) | 1.14 (0.74,1.77) | 1.08 (0.69,1.68) |
| * Longitudinal limb deficiency | 10870 (98.31) | 187 (1.69) | 451 (98.04) | 9 (1.96) | 1.16 (0.59,2.28) | 1.10 (0.56,2.18) |
| * Transverse limb deficiency | 10870 (98.31) | 187 (1.69) | 672 (98.10) | 13 (1.90) | 1.12 (0.64,1.99) | 1.09 (0.61,1.94) |
| Neural tube defects | 10870 (98.31) | 187 (1.69) | 1968 (97.81) | 44 (2.19) | 1.30 (0.93,1.81) | 1.28 (0.91,1.80) |
| * Anencephaly and craniorachischisis | 10870 (98.31) | 187 (1.69) | 582 (97.82) | 13 (2.18) | 1.30 (0.74,2.29) | 1.29 (0.73,2.31) |
| * Spina bifida | 10870 (98.31) | 187 (1.69) | 1179 (97.92) | 25 (2.08) | 1.23 (0.81,1.88) | 1.18 (0.77,1.81) |
| * Encephalocele | 10870 (98.31) | 187 (1.69) | 207 (97.18) | 6 (2.82) | 1.69 (0.74,3.84) | 1.90 (0.82,4.39) |
| Omphalocele | **10870 (98.31)** | **187 (1.69)** | **408 (96.68)** | **14 (3.32)** | **2.00 (1.15,3.46)** | **2.02 (1.15,3.55)** |
| Oral Clefts | 10745 (98.35) | 180 (1.65) | 4412 (98.37) | 73 (1.63) | 0.99 (0.75,1.30) | 0.95 (0.72,1.25) |
| * Cleft palate (CP) | 10745 (98.35) | 180 (1.65) | 1503 (98.17) | 28 (1.83) | 1.11 (0.74,1.66) | 1.13 (0.75,1.70) |
| * Cleft Lip (CL) w/wo CP | 10745 (98.35) | 180 (1.65) | 2909 (98.48) | 45 (1.52) | 0.92 (0.66,1.28) | 0.86 (0.62,1.20) |
| * CL with CP | 10745 (98.35) | 180 (1.65) | 1872 (98.37) | 31 (1.63) | 0.99 (0.67,1.45) | 0.98 (0.66,1.44) |
| * CL without CP | 10745 (98.35) | 180 (1.65) | 1037 (98.67) | 14 (1.33) | 0.81 (0.47,1.39) | 0.69 (0.39,1.19) |
| **Fexofenadine** |  |  |  |  |  |  |
| Anorectal atresia/stenosis | 10964 (99.16) | 93 (0.84) | 1008 (99.41) | 6 (0.59) | 0.70 (0.31,1.61) | 0.75 (0.33,1.72) |
| Bilateral renal agenesis or hypoplasia | **10964 (99.16)** | **93 (0.84)** | **171 (96.61)** | **6 (3.39)** | **4.14 (1.79,9.58)** | **4.34 (1.85,10.22)** |
| Craniosynostosis | 10964 (99.16) | 93 (0.84) | 1517 (98.76) | 19 (1.24) | 1.48 (0.90,2.43) | 1.27 (0.77,2.11) |
| Gastroschisis | 10964 (99.16) | 93 (0.84) | 1309 (99.39) | 8 (0.61) | 0.72 (0.35,1.49) | 0.86 (0.40,1.84) |
| Hypospadias | 5569 (99.23) | 43 (0.77) | 2427 (98.58) | 35 (1.42) | 1.87 (1.19,2.93) | 1.47 (0.93,2.34) |
| Limb deficiencies | 10964 (99.16) | 93 (0.84) | 1186 (99.50) | 6 (0.50) | 0.60 (0.26,1.36) | 0.63 (0.27,1.44) |
| Neural tube defects | 10964 (99.16) | 93 (0.84) | 1989 (98.86) | 23 (1.14) | 1.36 (0.86,2.16) | 1.43 (0.90,2.28) |
| * Anencephaly and craniorachischisis | 10964 (99.16) | 93 (0.84) | 589 (98.99) | 6 (1.01) | 1.20 (0.52,2.75) | 1.21 (0.52,2.80) |
| * Spina bifida | 10964 (99.16) | 93 (0.84) | 1189 (98.75) | 15 (1.25) | 1.49 (0.86,2.58) | 1.56 (0.90,2.71) |
| Oral Clefts | 10833 (99.16) | 92 (0.84) | 4448 (99.18) | 37 (0.82) | 0.98 (0.67,1.44) | 0.98 (0.67,1.44) |
| * Cleft palate (CP) | 10833 (99.16) | 92 (0.84) | 1517 (99.09) | 14 (0.91) | 1.09 (0.62,1.91) | 1.07 (0.61,1.89) |
| * Cleft Lip (CL) w/wo CP | 10833 (99.16) | 92 (0.84) | 2931 (99.22) | 23 (0.78) | 0.93 (0.59,1.46) | 0.94 (0.59,1.49) |
| * CL with CP | 10833 (99.16) | 92 (0.84) | 1886 (99.11) | 17 (0.89) | 1.06 (0.63,1.79) | 1.11 (0.66,1.88) |
| * CL without CP | 10833 (99.16) | 92 (0.84) | 1045 (99.43) | 6 (0.57) | 0.68 (0.30,1.55) | 0.64 (0.28,1.48) |
| **Hydroxyzine** |  |  |  |  |  |  |
| Oral Clefts | 10918 (99.94) | 7 (0.06) | 4479 (99.87) | 6 (0.13) | 2.09 (0.70,6.22) | 1.77 (0.59,5.31) |
| * CL w/wo CP | 10918 (99.94) | 7 (0.06) | 2948 (99.80) | 6 (0.20) | 3.17 (1.06,9.44) | 2.74 (0.91,8.26) |
| **Loratadine** |  |  |  |  |  |  |
| ABS-LBW | 10775 (97.45) | 282 (2.55) | 294 (97.03) | 9 (2.97) | 1.17 (0.60,2.29) | 1.29 (0.65,2.55) |
| * Limb anomalies only | 10775 (97.45) | 282 (2.55) | 187 (96.89) | 6 (3.11) | 1.23 (0.54,2.79) | 1.33 (0.58,3.05) |
| Anorectal atresia/stenosis | 10775 (97.45) | 282 (2.55) | 985 (97.14) | 29 (2.86) | 1.12 (0.76,1.66) | 1.18 (0.80,1.75) |
| Anotia/microtia | 10775 (97.45) | 282 (2.55) | 649 (98.33) | 11 (1.67) | 0.65 (0.35,1.19) | 0.78 (0.42,1.44) |
| Bilateral renal agenesis or hypoplasia | **10775 (97.45)** | **282 (2.55)** | **167 (94.35)** | **10 (5.65)** | **2.29 (1.20,4.38)** | **2.56 (1.32,4.96)** |
| Craniosynostosis | 10775 (97.45) | 282 (2.55) | 1496 (97.40) | 40 (2.60) | 1.02 (0.73,1.43) | 0.96 (0.68,1.34) |
| Dandy Walker Malformation | 10775 (97.45) | 282 (2.55) | 167 (95.98) | 7 (4.02) | 1.60 (0.75,3.44) | 1.69 (0.78,3.66) |
| Diaphragmatic hernia | 10775 (97.45) | 282 (2.55) | 799 (96.50) | 29 (3.50) | 1.39 (0.94,2.05) | 1.38 (0.93,2.04) |
| Duodenal atresia/stenosis | **10775 (97.45)** | **282 (2.55)** | **218 (94.78)** | **12 (5.22)** | **2.10 (1.16,3.81)** | **2.08 (1.14,3.80)** |
| Esophageal atresia | 10775 (97.45) | 282 (2.55) | 713 (97.54) | 18 (2.46) | 0.97 (0.60,1.56) | 0.88 (0.54,1.43) |
| Gastroschisis | 10775 (97.45) | 282 (2.55) | 1286 (97.65) | 31 (2.35) | 0.92 (0.63,1.34) | 1.23 (0.82,1.85) |
| Hypospadias | 5466 (97.40) | 146 (2.60) | 2366 (96.10) | 96 (3.90) | 1.52 (1.17,1.97) | 1.32 (1.00,1.73) |
| Intestinal atresia/stenosis | 10775 (97.45) | 282 (2.55) | 438 (97.33) | 12 (2.67) | 1.05 (0.58,1.88) | 1.18 (0.66,2.14) |
| Limb deficiencies | 10775 (97.45) | 282 (2.55) | 1159 (97.23) | 33 (2.77) | 1.09 (0.75,1.57) | 1.14 (0.79,1.65) |
| * Longitudinal limb deficiency | 10775 (97.45) | 282 (2.55) | 448 (97.39) | 12 (2.61) | 1.02 (0.57,1.84) | 1.10 (0.61,1.99) |
| * Transverse limb deficiency | 10775 (97.45) | 282 (2.55) | 664 (96.93) | 21 (3.07) | 1.21 (0.77,1.90) | 1.25 (0.79,1.97) |
| Neural tube defects | 10775 (97.45) | 282 (2.55) | 1949 (96.87) | 63 (3.13) | 1.24 (0.94,1.63) | 1.30 (0.98,1.73) |
| * Anencephaly and craniorachischisis | 10775 (97.45) | 282 (2.55) | 576 (96.81) | 19 (3.19) | 1.26 (0.79,2.02) | 1.32 (0.82,2.14) |
| * Spina bifida | 10775 (97.45) | 282 (2.55) | 1169 (97.09) | 35 (2.91) | 1.14 (0.80,1.63) | 1.19 (0.83,1.72) |
| * Encephalocele | 10775 (97.45) | 282 (2.55) | 204 (95.77) | 9 (4.23) | 1.69 (0.86,3.32) | 1.88 (0.95,3.74) |
| Omphalocele | 10775 (97.45) | 282 (2.55) | 409 (96.92) | 13 (3.08) | 1.21 (0.69,2.14) | 1.15 (0.65,2.03) |
| Oral Clefts | 10644 (97.43) | 281 (2.57) | 4366 (97.35) | 119 (2.65) | 1.03 (0.83,1.28) | 1.04 (0.84,1.30) |
| * Cleft palate (CP) | 10644 (97.43) | 281 (2.57) | 1491 (97.39) | 40 (2.61) | 1.02 (0.73,1.42) | 0.98 (0.70,1.38) |
| * Cleft Lip (CL) w/wo CP | 10644 (97.43) | 281 (2.57) | 2875 (97.33) | 79 (2.67) | 1.04 (0.81,1.34) | 1.08 (0.84,1.40) |
| * CL with CP | 10644 (97.43) | 281 (2.57) | 1855 (97.48) | 48 (2.52) | 0.98 (0.72,1.34) | 1.07 (0.78,1.46) |
| * CL without CP | 10644 (97.43) | 281 (2.57) | 1020 (97.05) | 31 (2.95) | 1.15 (0.79,1.68) | 1.13 (0.77,1.65) |
| **Meclizine** |  |  |  |  |  |  |
| Oral Clefts | 10918 (99.94) | 7 (0.06) | 4478 (99.84) | 7 (0.16) | 2.44 (0.85,6.95) | 2.30 (0.80,6.62) |
| **Pheniramine** |  |  |  |  |  |  |
| Anorectal atresia/stenosis | 10871 (98.32) | 186 (1.68) | 1002 (98.82) | 12 (1.18) | 0.70 (0.39,1.26) | 0.74 (0.41,1.33) |
| Choanal atresia | **10871 (98.32)** | **186 (1.68)** | **149 (96.13)** | **6 (3.87)** | **2.35 (1.03,5.39)** | **2.49 (1.08,5.74)** |
| Craniosynostosis | 10871 (98.32) | 186 (1.68) | 1511 (98.37) | 25 (1.63) | 0.97 (0.64,1.47) | 1.00 (0.65,1.53) |
| Diaphragmatic hernia | 10871 (98.32) | 186 (1.68) | 819 (98.91) | 9 (1.09) | 0.64 (0.33,1.26) | 0.68 (0.35,1.33) |
| Esophageal atresia | 10871 (98.32) | 186 (1.68) | 720 (98.50) | 11 (1.50) | 0.89 (0.48,1.65) | 0.92 (0.50,1.71) |
| Gastroschisis | 10871 (98.32) | 186 (1.68) | 1296 (98.41) | 21 (1.59) | 0.95 (0.60,1.49) | 1.14 (0.70,1.85) |
| Hypospadias | 5527 (98.49) | 85 (1.51) | 2421 (98.33) | 41 (1.67) | 1.10 (0.76,1.60) | 1.10 (0.74,1.64) |
| Intestinal atresia/stenosis | 10871 (98.32) | 186 (1.68) | 443 (98.44) | 7 (1.56) | 0.92 (0.43,1.98) | 1.05 (0.49,2.26) |
| Limb deficiencies | 10871 (98.32) | 186 (1.68) | 1173 (98.41) | 19 (1.59) | 0.95 (0.59,1.53) | 1.01 (0.63,1.63) |
| * Longitudinal limb deficiency | 10871 (98.32) | 186 (1.68) | 453 (98.48) | 7 (1.52) | 0.90 (0.42,1.93) | 0.95 (0.44,2.03) |
| * Transverse limb deficiency | 10871 (98.32) | 186 (1.68) | 675 (98.54) | 10 (1.46) | 0.87 (0.46,1.64) | 0.95 (0.50,1.82) |
| Neural tube defects | 10871 (98.32) | 186 (1.68) | 1976 (98.21) | 36 (1.79) | 1.07 (0.74,1.53) | 1.16 (0.81,1.67) |
| * Anencephaly and craniorachischisis | 10871 (98.32) | 186 (1.68) | 585 (98.32) | 10 (1.68) | 1.00 (0.53,1.90) | 1.08 (0.57,2.07) |
| * Spina bifida | 10871 (98.32) | 186 (1.68) | 1180 (98.01) | 24 (1.99) | 1.19 (0.77,1.83) | 1.30 (0.84,2.00) |
| Omphalocele | 10871 (98.32) | 186 (1.68) | 416 (98.58) | 6 (1.42) | 0.84 (0.37,1.91) | 0.88 (0.38,1.99) |
| Oral Clefts | 10740 (98.31) | 185 (1.69) | 4401 (98.13) | 84 (1.87) | 1.11 (0.85,1.44) | 1.20 (0.92,1.56) |
| * Cleft palate (CP) | 10740 (98.31) | 185 (1.69) | 1501 (98.04) | 30 (1.96) | 1.16 (0.79,1.71) | 1.23 (0.83,1.83) |
| * Cleft Lip (CL) w/wo CP | 10740 (98.31) | 185 (1.69) | 2900 (98.17) | 54 (1.83) | 1.08 (0.80,1.47) | 1.19 (0.87,1.62) |
| * CL with CP | 10740 (98.31) | 185 (1.69) | 1866 (98.06) | 37 (1.94) | 1.15 (0.81,1.64) | 1.29 (0.90,1.84) |
| * CL without CP | 10740 (98.31) | 185 (1.69) | 1034 (98.38) | 17 (1.62) | 0.96 (0.58,1.58) | 1.03 (0.62,1.71) |
| **Promethazine** |  |  |  |  |  |  |
| ABS-LBW | 10652 (96.34) | 405 (3.66) | 292 (96.37) | 11 (3.63) | 0.99 (0.54,1.82) | 1.08 (0.58,2.02) |
| * Limb anomalies only | 10652 (96.34) | 405 (3.66) | 185 (95.85) | 8 (4.15) | 1.14 (0.56,2.32) | 1.23 (0.61,2.67) |
| Anorectal atresia/stenosis | 10652 (96.34) | 405 (3.66) | 992 (97.83) | 22 (2.17) | 0.58 (0.38,0.90) | 0.61 (0.39,0.95) |
| Anotia/microtia | 10652 (96.34) | 405 (3.66) | 649 (98.33) | 11 (1.67) | 0.45 (0.24,0.82) | 0.67 (0.36,1.23) |
| Bilateral renal agenesis or hypoplasia | 10652 (96.34) | 405 (3.66) | 167 (94.35) | 10 (5.65) | 1.57 (0.83,3.00) | 1.51 (0.77,2.93) |
| Biliary atresia | 10652 (96.34) | 405 (3.66) | 184 (96.84) | 6 (3.16) | 0.86 (0.38,1.95) | 0.90 (0.39,2.07) |
| Craniosynostosis | **10652 (96.34)** | **405 (3.66)** | **1451 (94.47)** | **85 (5.53)** | **1.54 (1.21,1.96)** | **1.37 (1.07,1.76)** |
| Dandy Walker Malformation | 10652 (96.34) | 405 (3.66) | 168 (96.55) | 6 (3.45) | 0.94 (0.41,2.13) | 0.96 (0.41,2.22) |
| Diaphragmatic hernia | 10652 (96.34) | 405 (3.66) | 798 (96.38) | 30 (3.62) | 0.99 (0.68,1.44) | 1.00 (0.68,1.48) |
| Duodenal atresia/stenosis | 10652 (96.34) | 405 (3.66) | 219 (95.22) | 11 (4.78) | 1.32 (0.72,2.44) | 1.47 (0.78,2.76) |
| Esophageal atresia | 10652 (96.34) | 405 (3.66) | 709 (96.99) | 22 (3.01) | 0.82 (0.53,1.26) | 0.90 (0.58,1.40) |
| Gastroschisis | 10652 (96.34) | 405 (3.66) | 1263 (95.90) | 54 (4.10) | 1.12 (0.84,1.50) | 1.08 (0.79,1.49) |
| Hypospadias | 5418 (96.54) | 194 (3.46) | 2382 (96.75) | 80 (3.25) | 0.94 (0.72,1.22) | 0.93 (0.70,1.22) |
| Intestinal atresia/stenosis | 10652 (96.34) | 405 (3.66) | 435 (96.67) | 15 (3.33) | 0.91 (0.54,1.53) | 1.09 (0.64,1.86) |
| Limb deficiencies | 10652 (96.34) | 405 (3.66) | 1157 (97.06) | 35 (2.94) | 0.80 (0.56,1.13) | 0.83 (0.58,1.19) |
| * Longitudinal limb deficiency | 10652 (96.34) | 405 (3.66) | 446 (96.96) | 14 (3.04) | 0.83 (0.48,1.42) | 0.80 (0.46,1.39) |
| * Transverse limb deficiency | 10652 (96.34) | 405 (3.66) | 665 (97.08) | 20 (2.92) | 0.79 (0.50,1.25) | 0.90 (0.57,1.44) |
| Neural tube defects | 10652 (96.34) | 405 (3.66) | 1937 (96.27) | 75 (3.73) | 1.02 (0.79,1.31) | 0.98 (0.76,1.27) |
| * Anencephaly and craniorachischisis | 10652 (96.34) | 405 (3.66) | 574 (96.47) | 21 (3.53) | 0.96 (0.62,1.50) | 0.86 (0.54,1.35) |
| * Spina bifida | 10652 (96.34) | 405 (3.66) | 1152 (95.68) | 52 (4.32) | 1.19 (0.88,1.60) | 1.19 (0.88,1.61) |
| Omphalocele | 10652 (96.34) | 405 (3.66) | 409 (96.92) | 13 (3.08) | 0.84 (0.48,1.47) | 0.83 (0.47,1.47) |
| Oral Clefts | 10521 (96.30) | 404 (3.70) | 4339 (96.74) | 146 (3.26) | 0.88 (0.72,1.06) | 0.88 (0.72,1.07) |
| * Cleft palate (CP) | 10521 (96.30) | 404 (3.70) | 1483 (96.86) | 48 (3.14) | 0.84 (0.62,1.14) | 0.83 (0.61,1.13) |
| * Cleft Lip (CL) w/wo CP | 10521 (96.30) | 404 (3.70) | 2856 (96.68) | 98 (3.32) | 0.89 (0.71,1.12) | 0.90 (0.72,1.14) |
| * CL with CP | 10521 (96.30) | 404 (3.70) | 1845 (96.95) | 58 (3.05) | 0.82 (0.62,1.08) | 0.84 (0.63,1.12) |
| * CL without CP | 10521 (96.30) | 404 (3.70) | 1011 (96.19) | 40 (3.81) | 1.03 (0.74,1.44) | 1.01 (0.72,1.42) |
| ABS-LBW = Amniotic band syndrome and limb body wall complex. Note: inconsistencies in the number of controls due to 1) hypospadias - males only, 2) no controls for clefts from Utah in 2003. Logistic regression models adjusted for: maternal age, maternal race, maternal education, parity, folic acid use, prenatal care (time of entry), smoking and alcohol status, and study site (see Table 2 for categorizations). | | | | | | |

**Supplemental Table 5:** Isolated Non-Cardiac defects and exposure to antihistamines during one month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine**  Birth defect   * Defect sub-classification | **Controls** | | **Cases** | | **Odds Ratios (95% CI)** | |
| **Not Exposed** | **Exposed** | **Not Exposed** | **Exposed** | **Crude** | **Adjusted** |
| **Any Antihistamine** |  |  |  |  |  |  |
| ABS-LBW | 9622 (87.02) | 1435 (12.98) | 220 (85.94) | 36 (14.06) | 1.10 (0.77,1.57) | 1.19 (0.82,1.72) |
| * Limb anomalies only | 9622 (87.02) | 1435 (12.98) | 142 (84.02) | 27 (15.98) | 1.28 (0.84,1.93) | 1.43 (0.93,2.19) |
| Anorectal atresia/stenosis | 9622 (87.02) | 1435 (12.98) | 402 (90.74) | 41 (9.26) | 0.68 (0.49,0.95) | 0.72 (0.52,1.01) |
| Anotia/microtia | 9622 (87.02) | 1435 (12.98) | 417 (91.45) | 39 (8.55) | 0.63 (0.45,0.87) | 0.84 (0.60,1.19) |
| Bilateral renal agenesis or hypoplasia | 9622 (87.02) | 1435 (12.98) | 109 (86.51) | 17 (13.49) | 1.05 (0.63,1.75) | 1.03 (0.61,1.75) |
| Biliary atresia | 9622 (87.02) | 1435 (12.98) | 143 (88.27) | 19 (11.73) | 0.89 (0.55,1.44) | 0.91 (0.55,1.48) |
| Bladder exstrophy | 9622 (87.02) | 1435 (12.98) | 48 (87.27) | 7 (12.73) | 0.98 (0.44,2.17) | 1.08 (0.48,2.43) |
| Colonic atresia/stenosis | 9622 (87.02) | 1435 (12.98) | 65 (81.25) | 15 (18.75) | 1.55 (0.88,2.72) | 1.62 (0.91,2.89) |
| Craniosynostosis | 9622 (87.02) | 1435 (12.98) | 1163 (83.37) | 232 (16.63) | 1.34 (1.15,1.56) | 1.16 (1.00,1.36) |
| Dandy Walker Malformation | 9622 (87.02) | 1435 (12.98) | 92 (85.98) | 15 (14.02) | 1.09 (0.63,1.89) | 1.20 (0.68,2.12) |
| Diaphragmatic hernia | 9622 (87.02) | 1435 (12.98) | 540 (85.44) | 92 (14.56) | 1.14 (0.91,1.43) | 1.14 (0.90,1.43) |
| Duodenal atresia/stenosis | **9622 (87.02)** | **1435 (12.98)** | **117 (81.25)** | **27 (18.75)** | **1.55 (1.01,2.36)** | **1.66 (1.07,2.57)** |
| Esophageal atresia | 9622 (87.02) | 1435 (12.98) | 267 (86.97) | 40 (13.03) | 1.00 (0.72,1.41) | 0.97 (0.69,1.36) |
| Gastroschisis | 9622 (87.02) | 1435 (12.98) | 1045 (87.23) | 153 (12.77) | 0.98 (0.82,1.17) | 1.14 (0.94,1.39) |
| Holoprosencephaly | 9622 (87.02) | 1435 (12.98) | 105 (90.52) | 11 (9.48) | 0.70 (0.38,1.31) | 0.85 (0.45,1.60) |
| Hypospadias | 4907 (87.44) | 705 (12.56) | 1882 (85.24) | 326 (14.76) | 1.21 (1.05,1.39) | 1.09 (0.94,1.26) |
| Intestinal atresia/stenosis | 9622 (87.02) | 1435 (12.98) | 333 (86.95) | 50 (13.05) | 1.01 (0.74,1.36) | 1.20 (0.88,1.64) |
| Limb deficiencies | 9622 (87.02) | 1435 (12.98) | 760 (86.96) | 114 (13.04) | 1.01 (0.82,1.23) | 1.03 (0.84,1.27) |
| * Longitudinal limb deficiency | 9622 (87.02) | 1435 (12.98) | 225 (86.54) | 35 (13.46) | 1.04 (0.73,1.50) | 1.01 (0.70,1.46) |
| * Transverse limb deficiency | 9622 (87.02) | 1435 (12.98) | 502 (87.15) | 74 (12.85) | 0.99 (0.77,1.27) | 1.05 (0.81,1.36) |
| Neural tube defects | **9622 (87.02)** | **1435 (12.98)** | **1493 (85.22)** | **259 (14.78)** | **1.16 (1.01,1.34)** | **1.19 (1.03,1.38)** |
| * Anencephaly and craniorachischisis | **9622 (87.02)** | **1435 (12.98)** | **444 (83.77)** | **86 (16.23)** | **1.30 (1.02,1.65)** | **1.29 (1.01,1.65)** |
| * Spina bifida | 9622 (87.02) | 1435 (12.98) | 908 (85.50) | 154 (14.50) | 1.14 (0.95,1.36) | 1.18 (0.98,1.42) |
| * Encephalocele | 9622 (87.02) | 1435 (12.98) | 141 (88.13) | 19 (11.88) | 0.90 (0.56,1.46) | 0.96 (0.59,1.58) |
| Omphalocele | 9622 (87.02) | 1435 (12.98) | 218 (87.55) | 31 (12.45) | 0.95 (0.65,1.39) | 0.94 (0.64,1.39) |
| Oral Clefts | 9505 (87.00) | 1420 (13.00) | 3328 (87.01) | 497 (12.99) | 1.00 (0.90,1.12) | 1.00 (0.89,1.12) |
| * Cleft palate (CP) | 9505 (87.00) | 1420 (13.00) | 1072 (87.15) | 158 (12.85) | 0.99 (0.83,1.18) | 0.96 (0.81,1.16) |
| * Cleft Lip (CL) w/wo CP | 9505 (87.00) | 1420 (13.00) | 2256 (86.94) | 339 (13.06) | 1.01 (0.89,1.14) | 1.02 (0.89,1.16) |
| * CL with CP | 9505 (87.00) | 1420 (13.00) | 1402 (86.70) | 215 (13.30) | 1.03 (0.88,1.20) | 1.07 (0.92,1.26) |
| * CL without CP | 9505 (87.00) | 1420 (13.00) | 854 (87.32) | 124 (12.68) | 0.97 (0.80,1.18) | 0.94 (0.77,1.15) |
| **Cetirizine** |  |  |  |  |  |  |
| Craniosynostosis | 10897 (98.55) | 160 (1.45) | 1364 (97.78) | 31 (2.22) | 1.55 (1.05,2.28) | 1.17 (0.79,1.75) |
| Diaphragmatic hernia | 10897 (98.55) | 160 (1.45) | 626 (99.05) | 6 (0.95) | 0.65 (0.29,1.48) | 0.65 (0.29,1.48) |
| Esophageal atresia | 10897 (98.55) | 160 (1.45) | 300 (97.72) | 7 (2.28) | 1.59 (0.74,3.42) | 1.49 (0.69,3.23) |
| Gastroschisis | 10897 (98.55) | 160 (1.45) | 1185 (98.91) | 13 (1.09) | 0.75 (0.42,1.32) | 1.13 (0.61,2.09) |
| Hypospadias | 5535 (98.63) | 77 (1.37) | 2163 (97.96) | 45 (2.04) | 1.50 (1.03,2.17) | 1.28 (0.87,1.88) |
| Limb deficiencies | 10897 (98.55) | 160 (1.45) | 863 (98.74) | 11 (1.26) | 0.87 (0.47,1.61) | 0.91 (0.49,1.70) |
| * Longitudinal limb deficiency | 10897 (98.55) | 160 (1.45) | 254 (97.69) | 6 (2.31) | 1.61 (0.71,3.67) | 1.72 (0.75,3.97) |
| Neural tube defects | 10897 (98.55) | 160 (1.45) | 1726 (98.52) | 26 (1.48) | 1.03 (0.68,1.56) | 1.06 (0.70,1.62) |
| * Anencephaly and craniorachischisis | 10897 (98.55) | 160 (1.45) | 522 (98.49) | 8 (1.51) | 1.04 (0.51,2.14) | 1.01 (0.49,2.08) |
| * Spina bifida | 10897 (98.55) | 160 (1.45) | 1047 (98.59) | 15 (1.41) | 0.98 (0.57,1.66) | 1.03 (0.60,1.76) |
| Oral Clefts | 10766 (98.54) | 159 (1.46) | 3771 (98.59) | 54 (1.41) | 0.97 (0.71,1.32) | 0.99 (0.72,1.35) |
| * Cleft palate (CP) | 10766 (98.54) | 159 (1.46) | 1209 (98.29) | 21 (1.71) | 1.18 (0.74,1.86) | 1.16 (0.73,1.85) |
| * Cleft Lip (CL)w/wo CP | 10766 (98.54) | 159 (1.46) | 2562 (98.73) | 33 (1.27) | 0.87 (0.60,1.27) | 0.91 (0.62,1.33) |
| * CL with CP | 10766 (98.54) | 159 (1.46) | 1594 (98.58) | 23 (1.42) | 0.98 (0.63,1.52) | 1.07 (0.68,1.67) |
| * CL without CP | 10766 (98.54) | 159 (1.46) | 968 (98.98) | 10 (1.02) | 0.70 (0.37,1.33) | 0.67 (0.35,1.29) |
| **Dimenhydrinate** |  |  |  |  |  |  |
| Oral Clefts | 10906 (99.83) | 19 (0.17) | 3815 (99.74) | 10 (0.26) | 1.50 (0.70,3.24) | 1.47 (0.68,3.19) |
| * CL w/wo CP | 10906 (99.83) | 19 (0.17) | 2589 (99.77) | 6 (0.23) | 1.33 (0.53,3.33) | 1.30 (0.51,3.29) |
| **Diphenhydramine** |  |  |  |  |  |  |
| ABS-LBW | 10814 (97.80) | 243 (2.20) | 249 (97.27) | 7 (2.73) | 1.25 (0.58,2.68) | 1.19 (0.55,2.59) |
| Anorectal atresia/stenosis | 10814 (97.80) | 243 (2.20) | 435 (98.19) | 8 (1.81) | 0.82 (0.40,1.67) | 0.83 (0.40,1.69) |
| Anotia/microtia | 10814 (97.80) | 243 (2.20) | 446 (97.81) | 10 (2.19) | 1.00 (0.53,1.89) | 1.36 (0.71,2.61) |
| Craniosynostosis | 10814 (97.80) | 243 (2.20) | 1351 (96.85) | 44 (3.15) | 1.45 (1.05,2.01) | 1.34 (0.96,1.87) |
| Diaphragmatic hernia | 10814 (97.80) | 243 (2.20) | 611 (96.68) | 21 (3.32) | 1.53 (0.97,2.41) | 1.52 (0.96,2.40) |
| Duodenal atresia/stenosis | 10814 (97.80) | 243 (2.20) | 138 (95.83) | 6 (4.17) | 1.94 (0.85,4.43) | 2.05 (0.89,4.74) |
| Esophageal atresia | 10814 (97.80) | 243 (2.20) | 301 (98.05) | 6 (1.95) | 0.89 (0.39,2.01) | 0.82 (0.36,1.86) |
| Gastroschisis | 10814 (97.80) | 243 (2.20) | 1164 (97.16) | 34 (2.84) | 1.30 (0.90,1.87) | 1.43 (0.96,2.13) |
| Hypospadias | 5491 (97.84) | 121 (2.16) | 2157 (97.69) | 51 (2.31) | 1.07 (0.77,1.50) | 0.98 (0.70,1.39) |
| Intestinal atresia/stenosis | 10814 (97.80) | 243 (2.20) | 374 (97.65) | 9 (2.35) | 1.07 (0.55,2.10) | 1.23 (0.62,2.43) |
| Limb deficiencies | 10814 (97.80) | 243 (2.20) | 851 (97.37) | 23 (2.63) | 1.20 (0.78,1.86) | 1.23 (0.79,1.90) |
| * Longitudinal limb deficiency | 10814 (97.80) | 243 (2.20) | 252 (96.92) | 8 (3.08) | 1.41 (0.69,2.89) | 1.31 (0.64,2.69) |
| * Transverse limb deficiency | 10814 (97.80) | 243 (2.20) | 562 (97.57) | 14 (2.43) | 1.11 (0.64,1.91) | 1.20 (0.69,2.08) |
| Neural tube defects | 10814 (97.80) | 243 (2.20) | 1702 (97.15) | 50 (2.85) | 1.31 (0.96,1.78) | 1.33 (0.97,1.82) |
| * Anencephaly and craniorachischisis | **10814 (97.80)** | **243 (2.20)** | **510 (96.23)** | **20 (3.77)** | **1.75 (1.10,2.78)** | **1.73 (1.08,2.78)** |
| * Spina bifida | 10814 (97.80) | 243 (2.20) | 1036 (97.55) | 26 (2.45) | 1.12 (0.74,1.68) | 1.16 (0.76,1.75) |
| Oral Clefts | 10685 (97.80) | 240 (2.20) | 3737 (97.70) | 88 (2.30) | 1.05 (0.82,1.34) | 1.04 (0.81,1.34) |
| * Cleft palate (CP) | 10685 (97.80) | 240 (2.20) | 1208 (98.21) | 22 (1.79) | 0.81 (0.52,1.26) | 0.78 (0.50,1.22) |
| * Cleft Lip (CL)w/wo CP | 10685 (97.80) | 240 (2.20) | 2529 (97.46) | 66 (2.54) | 1.16 (0.88,1.53) | 1.18 (0.89,1.55) |
| * CL with CP | 10685 (97.80) | 240 (2.20) | 1575 (97.40) | 42 (2.60) | 1.19 (0.85,1.65) | 1.23 (0.88,1.72) |
| * CL without CP | 10685 (97.80) | 240 (2.20) | 954 (97.55) | 24 (2.45) | 1.12 (0.73,1.71) | 1.07 (0.70,1.65) |
| **Doxylamine** |  |  |  |  |  |  |
| ABS-LBW | **10870 (98.31)** | **187 (1.69)** | **247 (96.48)** | **9 (3.52)** | **2.12 (1.07,4.19)** | **2.09 (1.04,4.21)** |
| * Limb anomalies only | **10870 (98.31)** | **187 (1.69)** | **162 (95.86)** | **7 (4.14)** | **2.51 (1.16,5.43)** | **2.75 (1.24,6.09)** |
| Anotia/microtia | 10870 (98.31) | 187 (1.69) | 448 (98.25) | 8 (1.75) | 1.04 (0.51,2.12) | 1.21 (0.58,2.51) |
| Craniosynostosis | 10870 (98.31) | 187 (1.69) | 1367 (97.99) | 28 (2.01) | 1.19 (0.80,1.78) | 0.85 (0.56,1.28) |
| Diaphragmatic hernia | 10870 (98.31) | 187 (1.69) | 618 (97.78) | 14 (2.22) | 1.32 (0.76,2.28) | 1.27 (0.73,2.21) |
| Gastroschisis | 10870 (98.31) | 187 (1.69) | 1178 (98.33) | 20 (1.67) | 0.99 (0.62,1.57) | 1.06 (0.64,1.74) |
| Hypospadias | 5523 (98.41) | 89 (1.59) | 2170 (98.28) | 38 (1.72) | 1.09 (0.74,1.59) | 1.03 (0.69,1.53) |
| Intestinal atresia/stenosis | 10870 (98.31) | 187 (1.69) | 374 (97.65) | 9 (2.35) | 1.40 (0.71,2.75) | 1.64 (0.82,3.27) |
| Limb deficiencies | 10870 (98.31) | 187 (1.69) | 857 (98.05) | 17 (1.95) | 1.15 (0.70,1.90) | 1.09 (0.66,1.82) |
| * Transverse limb deficiency | 10870 (98.31) | 187 (1.69) | 565 (98.09) | 11 (1.91) | 1.13 (0.61,2.09) | 1.08 (0.58,2.01) |
| Neural tube defects | 10870 (98.31) | 187 (1.69) | 1716 (97.95) | 36 (2.05) | 1.22 (0.85,1.75) | 1.21 (0.84,1.75) |
| * Anencephaly and craniorachischisis | 10870 (98.31) | 187 (1.69) | 518 (97.74) | 12 (2.26) | 1.35 (0.75,2.43) | 1.32 (0.72,2.40) |
| * Spina bifida | 10870 (98.31) | 187 (1.69) | 1043 (98.21) | 19 (1.79) | 1.06 (0.66,1.71) | 1.04 (0.64,1.68) |
| Omphalocele | 10870 (98.31) | 187 (1.69) | 242 (97.19) | 7 (2.81) | 1.68 (0.78,3.61) | 1.71 (0.78,3.71) |
| Oral Clefts | 10745 (98.35) | 180 (1.65) | 3764 (98.41) | 61 (1.59) | 0.97 (0.72,1.30) | 0.92 (0.68,1.23) |
| * Cleft palate (CP) | 10745 (98.35) | 180 (1.65) | 1206 (98.05) | 24 (1.95) | 1.19 (0.77,1.83) | 1.19 (0.77,1.84) |
| * Cleft Lip (CL)w/wo CP | 10745 (98.35) | 180 (1.65) | 2558 (98.57) | 37 (1.43) | 0.86 (0.60,1.23) | 0.80 (0.56,1.14) |
| * CL with CP | 10745 (98.35) | 180 (1.65) | 1593 (98.52) | 24 (1.48) | 0.90 (0.59,1.38) | 0.87 (0.57,1.35) |
| * CL without CP | 10745 (98.35) | 180 (1.65) | 965 (98.67) | 13 (1.33) | 0.80 (0.46,1.42) | 0.69 (0.39,1.22) |
| **Fexofenadine** |  |  |  |  |  |  |
| Craniosynostosis | 10964 (99.16) | 93 (0.84) | 1376 (98.64) | 19 (1.36) | 1.63 (0.99,2.67) | 1.40 (0.84,2.32) |
| Gastroschisis | 10964 (99.16) | 93 (0.84) | 1192 (99.50) | 6 (0.50) | 0.59 (0.26,1.36) | 0.72 (0.30,1.71) |
| Hypospadias | 5569 (99.23) | 43 (0.77) | 2175 (98.51) | 33 (1.49) | 1.97 (1.25,3.10) | 1.54 (0.96,2.46) |
| Neural tube defects | 10964 (99.16) | 93 (0.84) | 1730 (98.74) | 22 (1.26) | 1.50 (0.94,2.39) | 1.55 (0.96,2.48) |
| * Anencephaly and craniorachischisis | 10964 (99.16) | 93 (0.84) | 524 (98.87) | 6 (1.13) | 1.35 (0.59,3.10) | 1.32 (0.57,3.05) |
| * Spina bifida | 10964 (99.16) | 93 (0.84) | 1048 (98.68) | 14 (1.32) | 1.57 (0.89,2.77) | 1.63 (0.92,2.89) |
| Oral Clefts | 10833 (99.16) | 92 (0.84) | 3791 (99.11) | 34 (0.89) | 1.06 (0.71,1.57) | 1.05 (0.70,1.56) |
| * Cleft palate (CP) | 10833 (99.16) | 92 (0.84) | 1218 (99.02) | 12 (0.98) | 1.16 (0.63,2.12) | 1.13 (0.62,2.08) |
| * Cleft Lip (CL)w/wo CP | 10833 (99.16) | 92 (0.84) | 2573 (99.15) | 22 (0.85) | 1.01 (0.63,1.61) | 1.01 (0.63,1.61) |
| * CL with CP | 10833 (99.16) | 92 (0.84) | 1600 (98.95) | 17 (1.05) | 1.25 (0.74,2.10) | 1.29 (0.76,2.19) |
| **Hydroxyzine** |  |  |  |  |  |  |
| Oral Clefts | 10918 (99.94) | 7 (0.06) | 3819 (99.84) | 6 (0.16) | 2.45 (0.82,7.30) | 2.06 (0.69,6.21) |
| * CL w/wo CP | **10918 (99.94)** | **7 (0.06)** | **2589 (99.77)** | **6 (0.23)** | **3.61 (1.21,10.76)** | **3.11 (1.03,9.36)** |
| **Loratadine** |  |  |  |  |  |  |
| ABS-LBW | 10775 (97.45) | 282 (2.55) | 249 (97.27) | 7 (2.73) | 1.07 (0.50,2.30) | 1.17 (0.54,2.52) |
| Anorectal atresia/stenosis | 10775 (97.45) | 282 (2.55) | 432 (97.52) | 11 (2.48) | 0.97 (0.53,1.79) | 1.03 (0.56,1.91) |
| Anotia/microtia | 10775 (97.45) | 282 (2.55) | 448 (98.25) | 8 (1.75) | 0.68 (0.34,1.39) | 0.82 (0.40,1.68) |
| Bilateral renal agenesis or hypoplasia | **10775 (97.45)** | **282 (2.55)** | **119 (94.44)** | **7 (5.56)** | **2.25 (1.04,4.86)** | **2.37 (1.08,5.21)** |
| Craniosynostosis | 10775 (97.45) | 282 (2.55) | 1361 (97.56) | 34 (2.44) | 0.96 (0.67,1.37) | 0.88 (0.61,1.27) |
| Dandy Walker Malformation | **10775 (97.45)** | **282 (2.55)** | **101 (94.39)** | **6 (5.61)** | **2.27 (0.99,5.22)** | **2.42 (1.04,5.65)** |
| Diaphragmatic hernia | 10775 (97.45) | 282 (2.55) | 614 (97.15) | 18 (2.85) | 1.12 (0.69,1.82) | 1.10 (0.68,1.79) |
| Duodenal atresia/stenosis | 10775 (97.45) | 282 (2.55) | 137 (95.14) | 7 (4.86) | 1.95 (0.91,4.21) | 1.96 (0.90,4.26) |
| Esophageal atresia | 10775 (97.45) | 282 (2.55) | 298 (97.07) | 9 (2.93) | 1.15 (0.59,2.26) | 1.02 (0.52,2.01) |
| Gastroschisis | 10775 (97.45) | 282 (2.55) | 1168 (97.50) | 30 (2.50) | 0.98 (0.67,1.44) | 1.31 (0.87,1.97) |
| Hypospadias | 5466 (97.40) | 146 (2.60) | 2121 (96.06) | 87 (3.94) | 1.54 (1.17,2.01) | 1.33 (1.00,1.76) |
| Intestinal atresia/stenosis | 10775 (97.45) | 282 (2.55) | 372 (97.13) | 11 (2.87) | 1.13 (0.61,2.08) | 1.29 (0.70,2.39) |
| Limb deficiencies | 10775 (97.45) | 282 (2.55) | 850 (97.25) | 24 (2.75) | 1.08 (0.71,1.65) | 1.10 (0.72,1.68) |
| * Longitudinal limb deficiency | 10775 (97.45) | 282 (2.55) | 254 (97.69) | 6 (2.31) | 0.90 (0.40,2.05) | 0.93 (0.41,2.11) |
| * Transverse limb deficiency | 10775 (97.45) | 282 (2.55) | 557 (96.70) | 19 (3.30) | 1.30 (0.81,2.09) | 1.32 (0.82,2.13) |
| Neural tube defects | 10775 (97.45) | 282 (2.55) | 1699 (96.97) | 53 (3.03) | 1.19 (0.88,1.61) | 1.24 (0.92,1.68) |
| * Anencephaly and craniorachischisis | 10775 (97.45) | 282 (2.55) | 511 (96.42) | 19 (3.58) | 1.42 (0.89,2.28) | 1.48 (0.92,2.40) |
| * Spina bifida | 10775 (97.45) | 282 (2.55) | 1033 (97.27) | 29 (2.73) | 1.07 (0.73,1.58) | 1.10 (0.75,1.63) |
| Omphalocele | 10775 (97.45) | 282 (2.55) | 243 (97.59) | 6 (2.41) | 0.94 (0.42,2.14) | 0.87 (0.38,1.99) |
| Oral Clefts | 10644 (97.43) | 281 (2.57) | 3720 (97.25) | 105 (2.75) | 1.07 (0.85,1.34) | 1.07 (0.85,1.34) |
| * Cleft palate (CP) | 10644 (97.43) | 281 (2.57) | 1197 (97.32) | 33 (2.68) | 1.05 (0.73,1.51) | 0.99 (0.69,1.44) |
| * Cleft Lip (CL)w/wo CP | 10644 (97.43) | 281 (2.57) | 2523 (97.23) | 72 (2.77) | 1.08 (0.83,1.41) | 1.11 (0.85,1.45) |
| * CL with CP | 10644 (97.43) | 281 (2.57) | 1575 (97.40) | 42 (2.60) | 1.01 (0.73,1.40) | 1.08 (0.77,1.50) |
| * CL without CP | 10644 (97.43) | 281 (2.57) | 948 (96.93) | 30 (3.07) | 1.20 (0.82,1.76) | 1.17 (0.80,1.72) |
| **Meclizine** |  |  |  |  |  |  |
| Oral Clefts | 10918 (99.94) | 7 (0.06) | 3818 (99.82) | 7 (0.18) | 2.86 (1.00,8.15) | 2.77 (0.96,7.98) |
| **Pheniramine** |  |  |  |  |  |  |
| Craniosynostosis | 10871 (98.32) | 186 (1.68) | 1371 (98.28) | 24 (1.72) | 1.02 (0.67,1.57) | 1.05 (0.68,1.62) |
| Diaphragmatic hernia | 10871 (98.32) | 186 (1.68) | 624 (98.73) | 8 (1.27) | 0.75 (0.37,1.53) | 0.79 (0.38,1.61) |
| Gastroschisis | 10871 (98.32) | 186 (1.68) | 1181 (98.58) | 17 (1.42) | 0.84 (0.51,1.39) | 1.03 (0.61,1.74) |
| Hypospadias | 5527 (98.49) | 85 (1.51) | 2173 (98.41) | 35 (1.59) | 1.05 (0.70,1.56) | 1.03 (0.68,1.56) |
| Limb deficiencies | 10871 (98.32) | 186 (1.68) | 859 (98.28) | 15 (1.72) | 1.02 (0.60,1.74) | 1.08 (0.63,1.84) |
| * Transverse limb deficiency | 10871 (98.32) | 186 (1.68) | 567 (98.44) | 9 (1.56) | 0.93 (0.47,1.82) | 1.01 (0.52,2.00) |
| Neural tube defects | 10871 (98.32) | 186 (1.68) | 1723 (98.34) | 29 (1.66) | 0.98 (0.66,1.46) | 1.06 (0.71,1.58) |
| * Anencephaly and craniorachischisis | 10871 (98.32) | 186 (1.68) | 521 (98.30) | 9 (1.70) | 1.01 (0.51,1.98) | 1.08 (0.55,2.13) |
| * Spina bifida | 10871 (98.32) | 186 (1.68) | 1043 (98.21) | 19 (1.79) | 1.06 (0.66,1.71) | 1.15 (0.71,1.86) |
| Oral Clefts | 10740 (98.31) | 185 (1.69) | 3755 (98.17) | 70 (1.83) | 1.08 (0.82,1.43) | 1.17 (0.88,1.55) |
| * Cleft palate (CP) | 10740 (98.31) | 185 (1.69) | 1207 (98.13) | 23 (1.87) | 1.11 (0.71,1.71) | 1.17 (0.75,1.82) |
| * Cleft Lip (CL) w/wo CP | 10740 (98.31) | 185 (1.69) | 2548 (98.19) | 47 (1.81) | 1.07 (0.78,1.48) | 1.17 (0.84,1.62) |
| * CL with CP | 10740 (98.31) | 185 (1.69) | 1586 (98.08) | 31 (1.92) | 1.13 (0.77,1.67) | 1.25 (0.85,1.85) |
| * CL without CP | 10740 (98.31) | 185 (1.69) | 962 (98.36) | 16 (1.64) | 0.97 (0.58,1.62) | 1.04 (0.62,1.75) |
| **Promethazine** |  |  |  |  |  |  |
| ABS-LBW | 10652 (96.34) | 405 (3.66) | 247 (96.48) | 9 (3.52) | 0.96 (0.49,1.88) | 1.05 (0.53,2.09) |
| * Limb anomalies only | 10652 (96.34) | 405 (3.66) | 162 (95.86) | 7 (4.14) | 1.14 (0.53,2.44) | 1.32 (0.60,2.90) |
| Anorectal atresia/stenosis | 10652 (96.34) | 405 (3.66) | 432 (97.52) | 11 (2.48) | 0.67 (0.37,1.23) | 0.67 (0.36,1.24) |
| Anotia/microtia | 10652 (96.34) | 405 (3.66) | 446 (97.81) | 10 (2.19) | 0.59 (0.31,1.11) | 0.94 (0.49,1.80) |
| Craniosynostosis | **10652 (96.34)** | **405 (3.66)** | **1317 (94.41)** | **78 (5.59)** | **1.56 (1.21,2.00)** | **1.37 (1.06,1.77)** |
| Diaphragmatic hernia | 10652 (96.34) | 405 (3.66) | 607 (96.04) | 25 (3.96) | 1.08 (0.72,1.64) | 1.08 (0.71,1.65) |
| Duodenal atresia/stenosis | 10652 (96.34) | 405 (3.66) | 135 (93.75) | 9 (6.25) | 1.75 (0.89,3.47) | 2.00 (0.99,4.06) |
| Esophageal atresia | 10652 (96.34) | 405 (3.66) | 294 (95.77) | 13 (4.23) | 1.16 (0.66,2.04) | 1.28 (0.72,2.29) |
| Gastroschisis | 10652 (96.34) | 405 (3.66) | 1149 (95.91) | 49 (4.09) | 1.12 (0.83,1.52) | 1.09 (0.78,1.51) |
| Hypospadias | 5418 (96.54) | 194 (3.46) | 2129 (96.42) | 79 (3.58) | 1.04 (0.79,1.35) | 1.03 (0.78,1.36) |
| Intestinal atresia/stenosis | 10652 (96.34) | 405 (3.66) | 370 (96.61) | 13 (3.39) | 0.92 (0.53,1.62) | 1.09 (0.61,1.94) |
| Limb deficiencies | 10652 (96.34) | 405 (3.66) | 847 (96.91) | 27 (3.09) | 0.84 (0.56,1.25) | 0.88 (0.59,1.32) |
| * Longitudinal limb deficiency | 10652 (96.34) | 405 (3.66) | 249 (95.77) | 11 (4.23) | 1.16 (0.63,2.14) | 1.06 (0.57,1.98) |
| * Transverse limb deficiency | 10652 (96.34) | 405 (3.66) | 560 (97.22) | 16 (2.78) | 0.75 (0.45,1.25) | 0.86 (0.52,1.45) |
| Neural tube defects | 10652 (96.34) | 405 (3.66) | 1687 (96.29) | 65 (3.71) | 1.01 (0.78,1.32) | 0.98 (0.75,1.29) |
| * Anencephaly and craniorachischisis | 10652 (96.34) | 405 (3.66) | 513 (96.79) | 17 (3.21) | 0.87 (0.53,1.43) | 0.76 (0.46,1.26) |
| * Spina bifida | 10652 (96.34) | 405 (3.66) | 1016 (95.67) | 46 (4.33) | 1.19 (0.87,1.63) | 1.22 (0.89,1.68) |
| Omphalocele | 10652 (96.34) | 405 (3.66) | 241 (96.79) | 8 (3.21) | 0.87 (0.43,1.78) | 0.91 (0.44,1.87) |
| Oral Clefts | 10521 (96.30) | 404 (3.70) | 3700 (96.73) | 125 (3.27) | 0.88 (0.72,1.08) | 0.88 (0.71,1.08) |
| * Cleft palate (CP) | 10521 (96.30) | 404 (3.70) | 1193 (96.99) | 37 (3.01) | 0.81 (0.57,1.14) | 0.80 (0.56,1.13) |
| * Cleft Lip (CL) w/wo CP | 10521 (96.30) | 404 (3.70) | 2507 (96.61) | 88 (3.39) | 0.91 (0.72,1.16) | 0.92 (0.72,1.17) |
| * CL with CP | 10521 (96.30) | 404 (3.70) | 1565 (96.78) | 52 (3.22) | 0.87 (0.65,1.16) | 0.87 (0.64,1.18) |
| * CL without CP | 10521 (96.30) | 404 (3.70) | 942 (96.32) | 36 (3.68) | 1.00 (0.70,1.41) | 0.98 (0.69,1.40) |
| ABS-LBW = Amniotic band syndrome and limb body wall complex. Note: inconsistencies in the number of controls due to 1) hypospadias - males only, 2) no controls for clefts from Utah in 2003. Logistic regression models adjusted for: maternal age, maternal race, maternal education, parity, folic acid use, prenatal care (time of entry), smoking and alcohol status, and study site (see Table 2 for categorizations). | | | | | | |

**Supplemental Table 6:** Number of days exposed to antihistamines during one-month prior pregnancy through first trimester, among significant positive associations presented in Tables 3 and 4. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine** |  | **Days Controls Exposed** | | | | |  | **Days Cases Exposed** | | | | | **Crude ERR (95% CI)** |
| **N\*** | **Mean** | **Percentiles** | | |  | **N\*** | **Mean** | **Percentiles** | | |
|  |  | **25th** | **50th** | **75th** |  |  |  | **25th** | **50th** | **75th** |
|  | **Cardiac Defects** |  |  |  |  |  |  |  |  |  |  |  |  |
| Cetirizine | Truncus Arteriosus | 160 | 63.0 | 23 | 57 | 121 |  | 6 | 61.0 | 30 | 47 | 121 | 0.97 (0.87,1.08) |
|  | Tetralogy of Fallot | 160 | 63.0 | 23 | 57 | 121 |  | 26 | 58.3 | 5 | 42 | 121 | **0.93 (0.88,0.98)** |
| Diphenhydramine | Tricuspid atresia | 243 | 43.9 | 3 | 29 | 82 |  | 8 | 47.3 | 3 | 4 | 121 | 1.08 (0.97,1.19) |
| Doxylamine | HLHS | 187 | 30.9 | 3 | 18 | 55 |  | 21 | 32.2 | 2 | 34 | 51 | 1.04 (0.97,1.13) |
| Hydroxyzine | Conotruncal defect | 7 | 59.9 | 2 | 56 | 121 |  | 6 | 7.8 | 3 | 8 | 14 | **0.13 (0.10,0.18)** |
| Loratadine | Truncus Arteriosus | 282 | 55.4 | 14 | 47 | 94 |  | 8 | 71.8 | 20 | 85 | 121 | **1.29 (1.19,1.41)** |
|  | **Non-Cardiac Defects** |  |  |  |  |  |  |  |  |  |  |  |  |
| Any antihistamine | Craniosynostosis | 1435 | 44.7 | 7 | 32 | 72 |  | 254 | 50.0 | 10 | 36 | 84 | **1.12 (1.10,1.14)** |
|  | Duodenal atresia/stenosis | 1435 | 44.7 | 7 | 32 | 72 |  | 40 | 47.0 | 8 | 34 | 73 | 1.05 (1.00,1.10) |
|  | Neural tube defects | 1435 | 44.7 | 7 | 32 | 72 |  | 301 | 41.6 | 4 | 31 | 62 | **0.93 (0.91,0.95)** |
|  | Anencephaly and craniorachischisis | 1435 | 44.7 | 7 | 32 | 72 |  | 97 | 40.0 | 5 | 31 | 61 | **0.90 (0.87,0.93)** |
|  | Spina bifida | 1435 | 44.7 | 7 | 32 | 72 |  | 179 | 41.9 | 5 | 31 | 61 | **0.94 (0.92,0.96)** |
| Diphenhydramine | Craniosynostosis | 243 | 43.9 | 3 | 29 | 82 |  | 51 | 52.3 | 5 | 48 | 94 | **1.19 (1.14,1.24)** |
|  | Anencephaly and craniorachischisis | 243 | 43.9 | 3 | 29 | 82 |  | 22 | 37.6 | 1 | 25 | 49 | **0.86 (0.80,0.92)** |
| Doxylamine | ABS-LBWC: Limb anomalies only | 187 | 30.9 | 3 | 18 | 55 |  | 7 | 22.7 | 3 | 14 | 42 | **0.74 (0.63,0.86)** |
|  | Omphalocele | 187 | 30.9 | 3 | 18 | 55 |  | 14 | 26.9 | 3 | 7 | 51 | **0.88 (0.79,0.97)** |
| Fexofenadine | Bilateral renal agenesis/hypoplasia | 93 | 56.6 | 29 | 50 | 78 |  | 6 | 62.8 | 32 | 36 | 121 | 1.11 (1.0,1.23) |
| Loratadine | Bilateral renal agenesis/hypoplasia | 282 | 55.4 | 14 | 47 | 94 |  | 10 | 66.4 | 33 | 58 | 121 | **1.20 (1.11,1.29)** |
|  | Duodenal atresia/stenosis | 282 | 55.4 | 14 | 47 | 94 |  | 12 | 35.3 | 17 | 35 | 51 | **0.64 (0.58,0.70)** |
| Pheniramine | Choanal atresia | 186 | 24.9 | 2 | 5 | 31 |  | 6 | 22.8 | 4 | 7 | 56 | 0.92 (0.77,1.09) |
| Promethazine | Craniosynostosis | 405 | 34.1 | 7 | 30 | 55 |  | 85 | 36.1 | 7 | 30 | 59 | **1.06 (1.02,1.10)** |
| \*N = number of pregnancies exposed  ERR = Exposure rate ratio.  ABS-LBWC = Amniotic band syndrome and limb body wall complex  HLHS = Hypoplastic left heart syndrome, VSD = ventricular septal defect. | | | | | | | | | | | | | |

**Supplemental Table 7:** Sensitivity analyses: Birth defects adversely associated with exposure to antihistamines during month four through month six of pregnancy (trimester two), among those not exposed to the antihistamine of interest during one-month prior to pregnancy through first trimester. Results presented have more than 5 exposed cases. National Birth Defects Prevention Study, 1997-2011.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antihistamine**  Birth defect | **Controls** | | **Cases** | | **Odds Ratios (95% CI)** | |
| **Not Exposed** | **Exposed** | **Not Exposed** | **Exposed** | **Crude** | **Adjusted** |
| **Diphenhydramine** |  |  |  |  |  |  |
| ASD secundum (NOS) | 10713 (99.07) | 101 (0.93) | 2816 (98.53) | 42 (1.47) | 1.58 (1.10,2.27) | 1.47 (1.01,2.13) |
| Anotia/Microtia | 10713 (99.07) | 101 (0.93) | 633 (98.14) | 12 (1.86) | 2.01 (1.10,3.68) | 2.61 (1.40,4.86) |
| Cleft Palate | 10585 (99.06) | 100 (0.94) | 1475 (98.01) | 30 (1.99) | 2.15 (1.43,3.25) | 2.06 (1.36,3.12) |
| **Fexofenadine** |  |  |  |  |  |  |
| Hypospadias | 5565 (99.93) | 4 (0.07) | 2421 (99.75) | 6 (0.25) | 3.44 (0.97,12.18) | 4.19 (1.10,16.00) |
| **Promethazine** |  |  |  |  |  |  |
| ASD secundum | 10588 (99.40) | 64 (0.60) | 2189 (98.43) | 35 (1.57) | 2.65 (1.75,4.00) | 2.13 (1.39,3.26) |
| PVS | 10157 (99.42) | 59 (0.58) | 1396 (98.73) | 18 (1.27) | 2.22 (1.31,3.77) | 1.76 (1.02,3.02) |
| RVOTO | 10588 (99.40) | 64 (0.60) | 1898 (98.85) | 22 (1.15) | 1.92 (1.18,3.12) | 1.63 (1.00,2.68) |
| Septal Defects | 10588 (99.40) | 64 (0.60) | 4301 (98.87) | 49 (1.13) | 1.89 (1.30,2.74) | 1.69 (1.15,2.47) |
| Anorectal atresia (NC) | 10588 (99.40) | 64 (0.60) | 812 (98.78) | 10 (1.22) | 2.04 (1.04,3.98) | 2.06 (1.05,4.06) |
| Omphalocele | 10588 (99.40) | 64 (0.60) | 402 (98.29) | 7 (1.71) | 2.88 (1.31,6.33) | 2.61 (1.17,5.83) |
| ASD = Atrial septal defect, NC = Non-complex, NOS = Not Otherwise Stated, PVS = Pulmonary valve stenosis, RVOTO = Right ventricular outflow tract obstruction, VSD = Ventricular septal defects. Note: Inconsistencies in the number of controls due to no controls for PVS from CA prior to 2002.  Logistic regression models adjusted for: maternal age, maternal race, maternal education, parity, folic acid use, prenatal care (time of entry), smoking and alcohol status, and study site (see Table 2 for categorizations). | | | | | | |

A close up of a map

Description automatically generated

**Supplement Figure 1:** Daily distribution of cases and controls exposed to antihistamines during one month prior to pregnancy through first trimester (among the 20 positive findings reported in Tables 3 and 4). National Birth Defects Prevention Study, 1997-2011.