**Supplemental Table 1.** Interview items for vaccines, BD-STEPS, 2014-2019

|  |  |
| --- | --- |
| **Question Number** | **Question Text** |
| T154 | “During B1P3, did you get any vaccines?” |
| T156 | “Which vaccines did you get?”  PROBE: READ LIST IF NECESSARY  **Vaccines**  Chickenpox Vaccine  Flu Vaccine  Hepatitis A Vaccine  Hepatitis B Vaccine  HPV Vaccine (Human Papillomavirus)  Measles, Mumps, Rubella Vaccine  Meningococcal Vaccine  Pneumococcal Vaccine, Polyvalent  Shingles Vaccine  OTHER, SPECIFY |
| T157 | “When did you get the [NAME OF VACCINE]?” |

Abbreviations: B1P3, the month before pregnancy through the third pregnancy month; BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS.

**Supplemental Table 2.** Distributions of control participant characteristics and exposures by influenza vaccine exposure status for primary analysis, BD-STEPS, 2014-2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Spina Bifida | | Birth Defects Other Than Spina Bifida | |
|  | Control Group, Unexposedb  (n=1,273) | Control Group, Exposedb  (n=60) | Control Group, Unexposedb  (n=1,168) | Control Group, Exposedb  (n=192) |
| Characteristic or Exposure | **N (%) a** | **N (%) a** | **N (%) a** | **N (%) a** |
| Pregnancy plurality |  |  |  |  |
| 1 | 1,223 (96.1) | 56 (93.3) | 1,124 (96.2) | 184 (95.8) |
| 2+ | 50 (3.9) | 4 (6.7) | 44 (3.8) | 8 (4.2) |
| Missing | 0 | 0 | 0 | 0 |
| Age at delivery (years) |  |  |  |  |
| <20 | 41 (3.2) | 0 (0.0) | 40 (3.4) | 2 (1.0) |
| 20-34 | 953 (74.9) | 41 (68.3) | 877 (75.1) | 137 (71.4) |
| ≥35 | 279 (21.9) | 19 (31.7) | 251 (21.5) | 53 (27.6) |
| Missing | 0 | 0 | 0 | 0 |
| Race/ethnicity |  |  |  |  |
| Non-Hispanic White | 670 (52.7) | 38 (63.3) | 618 (53.0) | 109 (56.8) |
| Non-Hispanic Black | 163 (12.8) | 8 (13.3) | 154 (13.2) | 20 (10.4) |
| Hispanic | 323 (25.4) | 12 (20.0) | 293 (25.1) | 46 (24.0) |
| Other | 116 (9.1) | 2 (3.3) | 102 (8.7) | 17 (8.9) |
| Missing | 1 | 0 | 1 | 0 |
| Educational attainment at delivery (years) |  |  |  |  |
| ≤11 | 130 (10.6) | 3 (5.1) | 119 (10.6) | 16 (8.5) |
| 12 | 211 (17.2) | 6 (10.2) | 199 (17.7) | 24 (12.7) |
| ≥13 | 885 (72.2) | 50 (84.7) | 804 (71.7) | 149 (78.8) |
| Missing | 47 | 1 | 46 | 3 |
| Gravidity |  |  |  |  |
| 0 | 344 (27.0) | 20 (33.3) | 304 (26.0) | 70 (36.5) |
| 1 | 386 (30.3) | 17 (28.3) | 358 (30.7) | 50 (26.0) |
| ≥2 | 542 (42.6) | 23 (38.3) | 505 (43.3) | 72 (37.5) |
| Missing | 1 | 0 | 1 | 0 |
| Pre-pregnancy body-mass index (kg/m2) |  |  |  |  |
| <18.5 | 29 (2.4) | 0 (0.0) | 27 (2.5) | 3 (1.6) |
| 18.5-24.9 | 557 (47.0) | 30 (50.8) | 502 (46.3) | 96 (52.2) |
| 25.0-29.9 | 333 (28.1) | 14 (23.7) | 310 (28.6) | 41 (22.3) |
| ≥30.0 | 266 (22.4) | 15 (25.4) | 245 (22.6) | 44 (23.9) |
| Missing | 88 | 1 | 84 | 8 |
| Preexisting hypertension |  |  |  |  |
| Yes | 41 (3.3) | 4 (6.8) | 38 (3.3) | 8 (4.2) |
| No | 1,216 (96.7) | 55 (93.2) | 1,114 (96.7) | 183 (95.8) |
| Missing | 16 | 1 | 16 | 1 |
| Asthmac |  |  |  |  |
| Yes | 176 (13.8) | 12 (20.0) | 164 (14.1) | 26 (13.5) |
| No | 1,096 (86.2) | 48 (80.0) | 1,003 (85.9) | 166 (86.5) |
| Missing | 1 | 0 | 1 | 0 |
| Feverb |  |  |  |  |
| Yes | 29 (2.3) | 2 (3.3) | 62 (5.4) | 13 (6.8) |
| No | 1,228 (97.7) | 58 (96.7) | 1,094 (94.6) | 179 (93.2) |
| Missing | 16 | 0 | 12 | 0 |
| Multivitamin, prenatal vitamin, or folic acid supplement used |  |  |  |  |
| Yes | 957 (76.8) | 49 (81.7) | 872 (76.3) | 152 (80.0) |
| No | 289 (23.2) | 11 (18.3) | 271 (23.7) | 38 (20.0) |
| Missing | 27 | 0 | 25 | 2 |
| Cigarette smokingb |  |  |  |  |
| Yes | 117 (9.5) | 8 (13.6) | 113 (10.0) | 18 (9.5) |
| No | 1,113 (90.5) | 51 (86.4) | 1,012 (90.0) | 172 (90.5) |
| Missing | 43 | 1 | 43 | 2 |
| Alcohol useb |  |  |  |  |
| Yes | 587 (48.0) | 40 (69.0) | 539 (48.1) | 113 (59.5) |
| No | 637 (52.0) | 18 (31.0) | 582 (51.9) | 77 (40.5) |
| Missing | 49 | 2 | 47 | 2 |
| BD-STEPS study center |  |  |  |  |
| Arkansas | 168 (13.2) | 6 (10.0) | 157 (13.4) | 22 (11.5) |
| California | 122 (9.6) | 7 (11.7) | 115 (9.8) | 16 (8.3) |
| Georgia | 187 (14.7) | 7 (11.7) | 174 (14.9) | 23 (12.0) |
| Iowa | 152 (11.9) | 4 (6.7) | 137 (11.7) | 27 (14.1) |
| Massachusetts | 190 (14.9) | 14 (23.3) | 166 (14.2) | 38 (19.8) |
| New York | 280 (22.0) | 13 (21.7) | 262 (22.4) | 35 (18.2) |
| North Carolina | 174 (13.7) | 9 (15.0) | 157 (13.4) | 31 (16.1) |
| Missing | 0 | 0 | 0 | 0 |
| Quarter of estimated date of conception |  |  |  |  |
| January-March | 326 (25.6) | 7 (11.7) | 322 (27.6) | 18 (9.4) |
| April-June | 330 (25.9) | 3 (5.0) | 313 (26.8) | 19 (9.9) |
| July-September | 310 (24.4) | 9 (15.0) | 255 (21.8) | 72 (37.5) |
| October-December | 307 (24.1) | 41 (68.3) | 278 (23.8) | 83 (43.2) |
| Missing | 0 | 0 | 0 | 0 |
| Year of estimated date of conception |  |  |  |  |
| 2013 | 184 (14.5) | 14 (23.3) | 166 (14.2) | 39 (20.3) |
| 2014 | 268 (21.1) | 6 (10.0) | 251 (21.5) | 28 (14.6) |
| 2015 | 30 (2.4) | 4 (6.7) | 27 (2.3) | 7 (3.6) |
| 2016 | 232 (18.2) | 7 (11.7) | 209 (17.9) | 35 (18.2) |
| 2017 | 262 (20.6) | 14 (23.3) | 238 (20.4) | 46 (24.0) |
| 2018 | 220 (17.3) | 10 (16.7) | 202 (17.3) | 30 (15.6) |
| 2019 | 77 (6.0) | 5 (8.3) | 75 (6.4) | 7 (3.6) |
| Missing | 0 | 0 | 0 | 0 |

Abbreviation: BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS.

a Due to rounding, proportions may not total to 100.

b During the one month before pregnancy through the first pregnancy month for spina bifida; during the one month before pregnancy through the third pregnancy month for birth defects other than spina bifida.

c Diagnosed before or during the first trimester.

d During the one month before pregnancy through the first pregnancy month.

**Supplemental Table 3.** Secondary analyses of associations of influenza vaccine exposure and selected birth defects among isolated case children, BD-STEPS, 2014-2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Unexposed** | **Exposeda** | **Secondary Analysis:**  **Isolated Case Children** | |
|  | **N** | **N (%)** | **cOR (95%CI)** | **aORb (95%CI)** |
| **Control group for spina bifida** | 1273 | 60 (4.5) |  |  |
| **Spina bifida** | 174 | 8 (4.4) | 1.0 (0.5-2.1) | 1.0 (0.5-2.2)c |
|  |  |  |  |  |
| **Control group for birth defects other than spina bifida** | 1168 | 192 (14.1) |  |  |
| **Ear** |  |  |  |  |
| Anotia/microtia | 88 | 10 (10.2) | 0.7 (0.4-1.4) | 0.7 (0.3-1.4) |
| **Heart** |  |  |  |  |
| Coarctation of the aorta | 132 | 21 (13.7) | 1.0 (0.6-1.6) | 0.9 (0.5-1.5) |
| Dextro-transposition of the great arteries | 92 | 15 (14.0) | 1.0 (0.6-1.7) | 1.1 (0.6-2.0) |
| Hypoplastic left heart syndrome | 85 | 15 (15.0) | 1.1 (0.6-1.9) | 1.0 (0.5-1.9) |
| Tetralogy of Fallot | 135 | 24 (15.1) | 1.1 (0.7-1.7) | 1.1 (0.6-1.8) |
| Total anomalous pulmonary venous return | 45 | 7 (13.5) | 0.9 (0.4-2.1) | 1.1 (0.4-2.7) |
| **Orofacial Clefts** |  |  |  |  |
| Cleft lip ± palate | 384 | 41 (9.6) | 0.6 (0.5-0.9) | 0.6 (0.4-0.9) |
| Cleft palate alone | 178 | 33 (15.6) | 1.1 (0.8-1.7) | 1.1 (0.7-1.7) |
| **Gastrointestinal** |  |  |  |  |
| Esophageal atresia | 71 | 10 (12.3) | 0.9 (0.4-1.7) | 0.9 (0.4-1.8) |
| **Limb reduction** |  |  |  |  |
| Transverse limb deficiency | 48 | 8 (14.3) | 1.0 (0.5-2.2) | 0.9 (0.4-2.1) |
| **Musculoskeletal** |  |  |  |  |
| Diaphragmatic hernia | 108 | 26 (19.4) | 1.5 (0.9-2.3) | 1.0 (0.6-1.7) |
| Gastroschisis | 191 | 12 (5.9) | 0.5 (0.3-0.7) | 0.3 (0.2-0.7) |

Abbreviations: aOR, adjusted odds ratio; BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS; cOR, crude odds ratio; CI, confidence interval.

a Exposure during the one month before pregnancy through the first pregnancy month for spina bifida; exposure during the one month before pregnancy through the third pregnancy month for birth defects other than spina bifida.

b Adjusted for propensity score calculated from the predicted probability of influenza vaccination during the critical exposure period among control participants, which was estimated from a logistic regression model that included pregnancy plurality and participant age at delivery; race/ethnicity; educational attainment at delivery; gravidity; pre-pregnancy body-mass index (BMI); preexisting hypertension; asthma diagnosed before or during the first trimester; fever during the critical exposure period; multivitamin, prenatal vitamin, or folic acid supplement use during the one month before pregnancy through the first pregnancy month; cigarette smoking during the critical exposure period; alcohol use during the critical exposure period; BD-STEPS study center; and quarter and year of estimated date of conception.

c Participant age at delivery and pre-pregnancy BMI were not used in calculating the propensity score for analysis of spina bifida due to lack of control participants with age <20 or BMI <18.5 who were exposed during the critical exposure period.

**Supplemental Table 4.** Secondary analyses of associations of influenza vaccine exposure and selected birth defects among case children without a family history of a same-site birth defect, BD-STEPS, 2014-2019

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Unexposed Control Children** | **Exposed Control Children a** | **Unexposed Case Children** | **Exposed Case Children a** | **Secondary Analysis:**  **No Family History of**  **Same-Site Birth Defect** | |
|  | **N** | **N (%)** | **N** | **N (%)** | **cOR (95%CI)** | **aORb (95%CI)** |
| **Spina bifida** | 1191 | 55 (4.4) | 169 | 7 (4.0) | 0.9 (0.4-2.0) | 1.0 (0.4-2.2)c |
| **Ear** |  |  |  |  |  |  |
| Anotia/microtia | 1097 | 178 (14.0) | 96 | 12 (11.1) | 0.8 (0.4-1.4) | 0.9 (0.4-1.8) |
| **Heart** |  |  |  |  |  |  |
| Coarctation of the aorta | 1081 | 177 (14.1) | 138 | 22 (13.8) | 1.0 (0.6-1.6) | 0.9 (0.5-1.5) |
| Dextro-transposition of the great arteries | 1081 | 177 (14.1) | 91 | 18 (16.5) | 1.2 (0.7-2.1) | 1.3 (0.7-2.3) |
| Hypoplastic left heart syndrome | 1081 | 177 (14.1) | 85 | 16 (15.8) | 1.1 (0.7-2.0) | 1.2 (0.6-2.1) |
| Tetralogy of Fallot | 1081 | 177 (14.1) | 147 | 26 (15.0) | 1.1 (0.7-1.7) | 1.1 (0.7-1.7) |
| Total anomalous pulmonary venous return | 1081 | 177 (14.1) | 45 | 7 (13.5) | 1.0 (0.4-2.1) | 1.1 (0.4-2.9) |
| **Orofacial Clefts** |  |  |  |  |  |  |
| Cleft lip ± palate | 1095 | 178 (14.0) | 369 | 39 (9.6) | 0.7 (0.5-0.9) | 0.6 (0.4-1.0) |
| Cleft palate alone | 1095 | 178 (14.0) | 181 | 34 (15.8) | 1.2 (0.8-1.7) | 1.1 (0.7-1.8) |
| **Gastrointestinal** |  |  |  |  |  |  |
| Esophageal atresia | 1096 | 178 (14.0) | 107 | 12 (10.0) | 0.7 (0.4-1.3) | 0.8 (0.4-1.5) |
| **Limb reduction** |  |  |  |  |  |  |
| Transverse limb deficiency | 1096 | 178 (14.0) | 53 | 7 (11.7) | 0.8 (0.4-1.8) | 0.7 (0.3-1.7) |
| **Musculoskeletal** |  |  |  |  |  |  |
| Diaphragmatic hernia | 1097 | 178 (14.0) | 115 | 22 (16.1) | 1.2 (0.7-1.9) | 0.9 (0.5-1.5) |
| Gastroschisis | 1094 | 178 (14.0) | 194 | 14 (6.7) | 0.4 (0.3-0.8) | 0.4 (0.2-0.8) |

Abbreviations: aOR, adjusted odds ratio; BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS; cOR, crude odds ratio; CI, confidence interval.

a Exposure during the one month before pregnancy through the first pregnancy month for spina bifida; exposure during the one month before pregnancy through the third pregnancy month for birth defects other than spina bifida.

b Adjusted for propensity score calculated from the predicted probability of influenza vaccination during the critical exposure period among control participants, which was estimated from a logistic regression model that included pregnancy plurality and participant age at delivery; race/ethnicity; educational attainment at delivery; gravidity; pre-pregnancy body-mass index (BMI); preexisting hypertension; asthma diagnosed before or during the first trimester; fever during the critical exposure period; multivitamin, prenatal vitamin, or folic acid supplement use during the one month before pregnancy through the first pregnancy month; cigarette smoking during the critical exposure period; alcohol use during the critical exposure period; BD-STEPS study center; and quarter and year of estimated date of conception.

c Participant age at delivery, race/ethnicity, and pre-pregnancy BMI were not used in calculating the propensity score for analysis of spina bifida due to lack of control participants with age <20, “Other” race/ethnicity, or BMI <18.5 who were exposed during the critical exposure period .

**Supplemental Table 5.** Secondary analyses of associations of influenza vaccine exposure and selected birth defects among singleton births, BD-STEPS, 2014-2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Unexposed** | **Exposeda** | **Secondary Analysis:**  **Singleton Births** | |
|  | **N** | **N (%)** | **cOR (95%CI)** | **aORb (95%CI)** |
| **Control group for spina bifida** | 1223 | 56 (4.4) |  |  |
| **Spina bifida** | 177 | 8 (4.3) | 1.0 (0.5-2.1) | 1.0 (0.5-2.3)c |
|  |  |  |  |  |
| **Control group for birth defects other than spina bifida** | 1124 | 184 (14.1) |  |  |
| **Ear** |  |  |  |  |
| Anotia/microtia | 103 | 11 (9.6) | 0.7 (0.3-1.2) | 0.7 (0.4-1.5) |
| **Heart** |  |  |  |  |
| Coarctation of the aorta | 147 | 22 (13.0) | 0.9 (0.6-1.5) | 0.8 (0.5-1.3) |
| Dextro-transposition of the great arteries | 98 | 16 (14.0) | 1.0 (0.6-1.7) | 1.1 (0.6-2.0) |
| Hypoplastic left heart syndrome | 91 | 15 (14.2) | 1.0 (0.6-1.8) | 0.9 (0.5-1.7) |
| Tetralogy of Fallot | 156 | 26 (14.3) | 1.0 (0.7-1.6) | 1.0 (0.6-1.7) |
| Total anomalous pulmonary venous return | 48 | 6 (11.1) | 0.8 (0.3-1.8) | 0.8 (0.3-2.2) |
| **Orofacial Clefts** |  |  |  |  |
| Cleft lip ± palate | 407 | 43 (9.6) | 0.6 (0.5-0.9) | 0.7 (0.4-1.0) |
| Cleft palate alone | 193 | 41 (17.5) | 1.3 (0.9-1.9) | 1.3 (0.9-2.0) |
| **Gastrointestinal** |  |  |  |  |
| Esophageal atresia | 104 | 10 (8.8) | 0.6 (0.3-1.1) | 0.6 (0.3-1.2) |
| **Limb reduction** |  |  |  |  |
| Transverse limb deficiency | 57 | 7 (10.9) | 0.8 (0.3-1.7) | 0.6 (0.3-1.5) |
| **Musculoskeletal** |  |  |  |  |
| Diaphragmatic hernia | 121 | 24 (16.6) | 1.2 (0.8-1.9) | 0.9 (0.5-1.5) |
| Gastroschisis | 196 | 15 (7.1) | 0.5 (0.3-0.8) | 0.4 (0.2-0.8) |

Abbreviations: aOR, adjusted odds ratio; BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS; cOR, crude odds ratio; CI, confidence interval.

a Exposure during the one month before pregnancy through the first pregnancy month for spina bifida; exposure during the one month before pregnancy through the third pregnancy month for birth defects other than spina bifida.

b Adjusted for propensity score calculated from the predicted probability of influenza vaccination during the critical exposure period among control participants, which was estimated from a logistic regression model that included pregnancy plurality and participant age at delivery; race/ethnicity; educational attainment at delivery; gravidity; pre-pregnancy body-mass index (BMI); preexisting hypertension; asthma diagnosed before or during the first trimester; fever during the critical exposure period; multivitamin, prenatal vitamin, or folic acid supplement use during the one month before pregnancy through the first pregnancy month; cigarette smoking during the critical exposure period; alcohol use during the critical exposure period; BD-STEPS study center; and quarter and year of estimated date of conception.

c Participant age at delivery and pre-pregnancy BMI were not used in calculating the propensity score for analysis of spina bifida due to lack of control participants with age <20 or BMI <18.5 who were exposed during the critical exposure period.

**Supplemental Table 6.** Secondary analyses of associations of influenza vaccine exposure and selected birth defects where T1 occurred during influenza season, BD-STEPS, 2014-2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Unexposed** | **Exposedb** | **Secondary Analysis:**  **T1 During Influenza Seasona** | |
|  | **N** | **N (%)** | **cOR (95%CI)** | **aORc (95%CI)** |
| **Control group for spina bifida** | 1053 | 58 (5.2) |  |  |
| **Spina bifida** | 144 | 8 (5.3) | 1.0 (0.5-2.2) | 1.0 (0.4-2.1)d |
|  |  |  |  |  |
| **Control group for birth defects other than spina bifida** | 950 | 186 (16.4) |  |  |
| **Ear** |  |  |  |  |
| Anotia/microtia | 94 | 11 (10.5) | 0.6 (0.3-1.1) | 0.7 (0.4-1.4) |
| **Heart** |  |  |  |  |
| Coarctation of the aorta | 122 | 24 (16.4) | 1.0 (0.6-1.6) | 0.9 (0.5-1.5) |
| Dextro-transposition of the great arteries | 77 | 16 (17.2) | 1.1 (0.6-1.9) | 1.1 (0.6-1.9) |
| Hypoplastic left heart syndrome | 83 | 16 (16.2) | 1.0 (0.6-1.7) | 1.0 (0.5-1.8) |
| Tetralogy of Fallot | 132 | 27 (17.0) | 1.0 (0.7-1.6) | 1.0 (0.6-1.7) |
| Total anomalous pulmonary venous return | 41 | 7 (14.6) | 0.9 (0.4-2.0) | 1.2 (0.5-2.8) |
| **Orofacial Clefts** |  |  |  |  |
| Cleft lip ± palate | 342 | 42 (10.9) | 0.6 (0.4-0.9) | 0.6 (0.4-0.9) |
| Cleft palate alone | 170 | 40 (19.0) | 1.2 (0.8-1.8) | 1.3 (0.8-1.9) |
| **Gastrointestinal** |  |  |  |  |
| Esophageal atresia | 99 | 12 (10.8) | 0.6 (0.3-1.2) | 0.6 (0.3-1.2) |
| **Limb reduction** |  |  |  |  |
| Transverse limb deficiency | 45 | 8 (15.1) | 0.9 (0.4-2.0) | 0.8 (0.4-1.9) |
| **Musculoskeletal** |  |  |  |  |
| Diaphragmatic hernia | 104 | 27 (20.6) | 1.3 (0.8-2.1) | 1.0 (0.6-1.7) |
| Gastroschisis | 164 | 15 (8.3) | 0.5 (0.3-0.8) | 0.5 (0.3-0.8) |

Abbreviations: aOR, adjusted odds ratio; BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS; cOR, crude odds ratio; CI, confidence interval; T1, first trimester.

a Influenza season was approximated as approximated as September 1-March 31. Participants were included in this secondary analysis if any part of T1 occurred during this time period.

b Exposure during the one month before pregnancy through the first pregnancy month for spina bifida; exposure during the one month before pregnancy through the third pregnancy month for birth defects other than spina bifida.

c Adjusted for propensity score calculated from the predicted probability of influenza vaccination during the critical exposure period among control participants, which was estimated from a logistic regression model that included pregnancy plurality and participant age at delivery; race/ethnicity; educational attainment at delivery; gravidity; pre-pregnancy body-mass index (BMI); preexisting hypertension; asthma diagnosed before or during the first trimester; fever during the critical exposure period; multivitamin, prenatal vitamin, or folic acid supplement use during the one month before pregnancy through the first pregnancy month; cigarette smoking during the critical exposure period; alcohol use during the critical exposure period; BD-STEPS study center; and quarter and year of estimated date of conception.

d Participant age at delivery and pre-pregnancy BMI were not used in calculating the propensity score for analysis of spina bifida due to lack of control participants with age <20 or BMI <18.5 who were exposed during the critical exposure period.

**Supplemental Table 7.** Probabilistic bias analysis to evaluate non-differential influenza vaccine exposurea misclassificationb for associations with selected birth defects, BD-STEPS, 2014-2019

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Primary Analysis** | **Secondary Analysis:**  **Standard Adjustment Using Limited Covariates** | **Secondary Analysis:**  **Expanded Analytical Samplec** |
|  | **aORd (95%CI)** | **aORe (95%CI)** | **aORd (95%CI)** |
| **Spina bifida** | 0.9 (0.2-2.6)f | 1.0 (0.3-2.9) | NA |
| **Ear** |  |  |  |
| Anotia/microtia | 0.6 (0.3-1.3) | 0.6 (0.3-1.3) | 0.8 (0.4-1.5) |
| **Heart** |  |  |  |
| Coarctation of the aorta | 0.9 (0.5-1.6) | 1.0 (0.6-1.7) | 1.0 (0.6-1.6) |
| Dextro-transposition of the great arteries | 1.2 (0.7-2.3) | 1.1 (0.6-2.1) | 1.1 (0.6-2.0) |
| Hypoplastic left heart syndrome | 1.0 (0.5-2.0) | 1.1 (0.5-2.0) | 1.0 (0.6-1.9) |
| Tetralogy of Fallot | 1.1 (0.6-1.8) | 1.1 (0.6-1.8) | 1.0 (0.6-1.5) |
| Total anomalous pulmonary venous return | 1.2 (0.4-3.2) | 1.4 (0.6-3.5) | 1.0 (0.4-2.5) |
| **Orofacial Clefts** |  |  |  |
| Cleft lip ± palate | 0.6 (0.3-0.9) | 0.6 (0.4-0.9) | 0.6 (0.4-0.8) |
| Cleft palate alone | 1.3 (0.8-2.1) | 1.3 (0.8-2.0) | 1.2 (0.8-1.9) |
| **Gastrointestinal** |  |  |  |
| Esophageal atresia | 0.6 (0.3-1.2) | 0.6 (0.3-1.2) | 0.6 (0.3-1.1) |
| **Limb reduction** |  |  |  |
| Transverse limb deficiency | 0.8 (0.3-2.0) | 0.9 (0.4-2.2) | 0.7 (0.3-1.7) |
| **Musculoskeletal** |  |  |  |
| Diaphragmatic hernia | 1.0 (0.6-1.8) | 1.2 (0.7-2.1) | 1.0 (0.6-1.7) |
| Gastroschisis | 0.3 (0.1-0.7) | 0.4 (0.2-0.8) | 0.4 (0.2-0.7) |

Abbreviations: aOR, adjusted odds ratio; BD-STEPS, Birth Defects Study To Evaluate Pregnancy exposureS; cOR, crude odds ratio; CI, confidence interval; NA, not applicable.

a Exposure during the one month before pregnancy through the first pregnancy month for spina bifida; exposure during the one month before pregnancy through the third pregnancy month (B1P3) for birth defects other than spina bifida.

b Triangular distributions were used for sensitivity (mode=0.952, minimum=0.910, maximum=0.978) and specificity (mode=0.982, minimum=0.955, maximum=0.995).

c Included participants who were defined as exposed in the primary analysis and previously excluded participants who provided an affirmative response to receiving a vaccine during B1P3 (Question T154) that was an influenza vaccine (Question T156).

d Adjusted for propensity score calculated from the predicted probability of influenza vaccination during the critical exposure period among control participants, which was estimated from a logistic regression model that included pregnancy plurality and participant age at delivery; race/ethnicity; educational attainment at delivery; gravidity; pre-pregnancy body-mass index (BMI); pre-existing hypertension; asthma diagnosed before or during the first trimester; fever during the critical exposure period; multivitamin, prenatal vitamin, or folic acid supplement use during the one month before pregnancy through the first pregnancy month; cigarette smoking during the critical exposure period; alcohol use during the critical exposure period; BD-STEPS study center; and quarter and year of estimated date of conception.

e Adjusted for participant age at delivery, race/ethnicity, pre-pregnancy BMI, cigarette smoking during the critical exposure period, BD-STEPS study center, and quarter and year of estimated date of conception.

f Participant age at delivery and pre-pregnancy BMI were not used in calculating the propensity score for analysis of spina bifida due to lack of control participants with age <20 or BMI <18.5 who were exposed during the critical exposure period.