**Appendix S3.** Characteristics of mothers of infants with no major birth defects and case infants with selected birth defects. Data from the National Birth Defects Prevention Study, 1997–2005

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Controls(*n* = 6,556) |  | Anencephaly(*n* = 329) |  | Perimembranous VSD(*n* = 1,363) |  | Cleft lip ± cleft palate(*n* = 1,735) |  | Esophageal atresia(*n* = 419) |
| No. | (%) |  | No. | (%) | OR [95% CI] |  | No. | (%) | OR [95% CI] |  | No. | (%) | OR [95% CI] |  | No. | (%) | OR [95% CI] |
| Reported cannabis use in periconceptional period |
|  No | 6,305 | (96) |  | 311 | (95) | 1.0 [Reference] |  | 1,311 | (96) | 1.0 [Reference] |  | 1,653 | (95) | 1.0 [Reference] |  | 402 | (96) | 1.0 [Reference] |
|  Yes | 251 | (4) |  | 18 | (5) | 1.5 [0.9, 2.4] |  | 52 | (4) | 1.0 [0.7, 1.4] |  | 82 | (5) | 1.2 [1.0, 1.6] |  | 17 | (4) | 1.1 [0.6, 1.8] |
| Maternal age at delivery |
|  <25 years | 2,169 | (33) |  | 101 | (31) | 0.9 [0.7, 1.1] |  | 435 | (32) | 1.0 [0.9, 1.2] |  | 657 | (38) | 1.3 [1.1, 1.4] |  | 116 | (28) | 0.8 [0.7, 1.1] |
|  25–34 years | 3,461 | (53) |  | 184 | (56) | 1.0 [Reference] |  | 678 | (50) | 1.0 [Reference] |  | 836 | (48) | 1.0 [Reference] |  | 220 | (53) | 1.0 [Reference] |
|  ≥35 years | 926 | (14) |  | 44 | (13) | 0.9 [0.6, 1.3] |  | 250 | (18) | 1.4 [1.2, 1.6] |  | 242 | (14) | 1.1 [0.9, 1.3] |  | 83 | (20) | 1.4 [1.1, 1.8] |
| Race or ethnicity |
|  NH white | 3,923 | (60) |  | 164 | (50) | 1.0 [Reference] |  | 780 | (57) | 1.0 [Reference] |  | 1,074 | (62) | 1.0 [Reference] |  | 298 | (71) | 1.0 [Reference] |
|  NH black | 749 | (11) |  | 25 | (8) | 0.8 [0.5, 1.2] |  | 186 | (14) | 1.2 [1.0, 1.5] |  | 99 | (6) | 0.5 [0.4, 0.6] |  | 14 | (3) | 0.2 [0.1, 0.4] |
|  Hispanic | 1,456 | (22) |  | 112 | (34) | 1.8 [1.4, 2.4] |  | 294 | (22) | 1.0 [0.9, 1.2] |  | 447 | (26) | 1.1 [1.0, 1.2] |  | 79 | (19) | 0.7 [0.6, 0.9] |
|  Other | 400 | (6) |  | 26 | (8) | 1.6 [1.0, 2.4] |  | 96 | (7) | 1.2 [1.0, 1.5] |  | 110 | (6) | 1.0 [0.8, 1.2] |  | 28 | (7) | 0.9 [0.6, 1.4] |
| Level of education |
|  ≤12 years | 2,697 | (41) |  | 165 | (50) | 1.4 [1.2, 1.8] |  | 585 | (43) | 1.1 [1.0, 1.2] |  | 838 | (48) | 1.3 [1.2, 1.5] |  | 148 | (35) | 0.8 [0.6, 1.0] |
|  >12 years | 3,852 | (59) |  | 164 | (50) | 1.0 [Reference] |  | 778 | (57) | 1.0 [Reference] |  | 896 | (52) | 1.0 [Reference] |  | 271 | (65) | 1.0 [Reference] |
| Cigarette smoking in periconceptional period |
|  No | 5,358 | (82) |  | 290 | (88) | 1.0 [Reference] |  | 1,100 | (81) | 1.0 [Reference] |  | 1,310 | (76) | 1.0 [Reference] |  | 346 | (83) | 1.0 [Reference] |
|  Yes | 1,197 | (18) |  | 39 | (12) | 0.6 [0.4, 0.8] |  | 262 | (19) | 1.1 [0.9, 1.2] |  | 425 | (24) | 1.4 [1.3, 1.6] |  | 73 | (17) | 0.9 [0.7, 1.2] |
| Binge drinking in periconceptional period |
|  No | 5,740 | (88) |  | 292 | (89) | 1.0 [Reference] |  | 1,201 | (88) | 1.0 [Reference] |  | 1,507 | (87) | 1.0 [Reference] |  | 371 | (89) | 1.0 [Reference] |
|  Yes | 762 | (12) |  | 31 | (9) | 0.8 [0.5, 1.2] |  | 152 | (11) | 1.0 [0.8, 1.1] |  | 215 | (12) | 1.1 [0.9, 1.2] |  | 44 | (11) | 0.9 [0.6, 1.2] |
| Prepregnancy BMI |
|  <30 | 5,284 | (81) |  | 250 | (76) | 1.0 [Reference] |  | 1,079 | (79) | 1.0 [Reference] |  | 1,371 | (79) | 1.0 [Reference] |  | 334 | (80) | 1.0 [Reference] |
|  ≥30 | 762 | (12) |  | 57 | (17) | 1.2 [0.9, 1.6] |  | 232 | (17) | 1.1 [1.0, 1.3] |  | 284 | (16) | 1.1 [0.9, 1.3] |  | 65 | (16) | 1.0 [0.8, 1.3] |
| Periconceptional folic acid use |
|  No | 3,196 | (49) |  | 157 | (48) | 1.0 [Reference] |  | 675 | (50) | 1.0 [Reference] |  | 909 | (52) | 1.0 [Reference] |  | 178 | (42) | 1.0 [Reference] |
|  Yes | 3,360 | (51) |  | 172 | (52) | 1.0 [0.8, 1.3] |  | 688 | (50 | 1.0 [0.9, 1.1] |  | 826 | (48) | 0.9 [0.8, 1.0] |  | 241 | (58) | 1.3 [1.1, 1.6] |

 CI, confidence interval; OR, odds ratio; VSD, ventricular septal defect.

**Appendix S3.** (Continued)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Controls(*n* = 6,556) |  | Hypospadias(*n* = 1,291) |  | Diaphragmatic hernia(*n* = 498) |  | Gastroschisis(*n* = 688) |
| No. | (%) |  | No. | (%) | OR [95% CI] |  | No. | (%) | OR [95% CI] |  | No. | (%) | OR [95% CI] |
| Reported cannabis use in periconceptional period |
|  No | 6,305 | (96) |  | 1,259 | (98) | 1.0 [Reference] |  | 473 | (95) | 1.0 [Reference] |  | 606 | (88) | 1.0 [Reference] |
|  Yes | 251 | (4) |  | 32 | (2) | 0.6 [0.4, 0.9] |  | 25 | (5) | 1.3 [0.9, 2.0] |  | 82 | (12) | 3.4 [2.6, 4.4] |
| Maternal age at delivery |
|  <25 years | 2,169 | (33) |  | 292 | (23) | 0.6 [0.5, 0.7] |  | 154 | (31) | 0.9 [0.8, 1.1] |  | 542 | (79) | 6.4 [5.2, 7.7] |
|  25–34 years | 3,461 | (53) |  | 726 | (56) | 1.0 [Reference] |  | 266 | (53) | 1.0 [Reference] |  | 136 | (20) | 1.0 [Reference] |
|  ≥35 years | 926 | (14) |  | 273 | (21) | 1.4 [1.2, 1.7] |  | 78 | (16) | 1.1 [0.8, 1.4] |  | 10 | (1) | 0.3 [0.1, 0.5] |
| Race or ethnicity |
|  NH white | 3,923 | (60) |  | 923 | (71) | 1.0 [Reference] |  | 312 | (63) | 1.0 [Reference] |  | 366 | (53) | 1.0 [Reference] |
|  NH black | 749 | (11) |  | 165 | (13) | 0.9 [0.8, 1.2] |  | 38 | (8) | 0.6 [0.5, 0.9] |  | 54 | (8) | 0.8 [0.6, 1.0] |
|  Hispanic | 1,456 | (22) |  | 110 | (9) | 0.3 [0.3, 0.4] |  | 112 | (22) | 1.0 [0.8, 1.2] |  | 212 | (31) | 1.6 [1.3, 1.9] |
|  Other | 400 | (6) |  | 86 | (7) | 0.8 [0.6, 1.1] |  | 33 | (7) | 1.0 [0.7, 1.5] |  | 55 | (8) | 1.5 [1.1, 2.0] |
| Level of education |
|  ≤12 years | 2,697 | (41) |  | 352 | (27) | 0.5 [0.5, 0.6] |  | 201 | (40) | 1.0 [0.8, 1.2] |  | 474 | (69) | 3.2 [2.7, 3.8] |
|  >12 years | 3,852 | (59) |  | 939 | (73) | 1.0 [Reference] |  | 296 | (59) | 1.0 [Reference] |  | 211 | (31) | 1.0 [Reference] |
| Cigarette smoking in periconceptional period |
|  No | 5,358 | (82) |  | 1,073 | (83) | 1.0 [Reference] |  | 396 | (80) | 1.0 [Reference] |  | 442 | (64) | 1.0 [Reference] |
|  Yes | 1,197 | (18) |  | 218 | (17) | 0.9 [0.7, 1.0] |  | 102 | (20) | 1.2 [0.9, 1.4] |  | 246 | (36) | 2.5 [2.1, 2.9] |
| Binge drinking in periconceptional period |
|  No | 5,740 | (88) |  | 1,135 | (88) | 1.0 [Reference] |  | 435 | (87) | 1.0 [Reference] |  | 538 | (78) | 1.0 [Reference] |
|  Yes | 762 | (12) |  | 140 | (11) | 0.9 [0.7, 1.1] |  | 61 | (12) | 1.1 [0.8, 1.4] |  | 141 | (20) | 2.0 [1.6, 2.4] |
| Prepregnancy BMI |
|  <30 | 5,284 | (81) |  | 1,054 | (82) | 1.0 [Reference] |  | 387 | (78) | 1.0 [Reference] |  | 643 | (93) | 1.0 [Reference] |
|  ≥30 | 762 | (12) |  | 211 | (16) | 1.1 [0.9, 1.3] |  | 91 | (18) | 1.2 [1.0, 1.6] |  | 30 | (4) | 0.2 [0.2, 0.4] |
| Periconceptional folic acid use |
|  No | 3,196 | (49) |  | 487 | (38) | 1.0 [Reference] |  | 245 | (49) | 1.0 [Reference] |  | 433 | (63) | 1.0 [Reference] |
|  Yes | 3,360 | (51) |  | 804 | (62) | 1.7 [1.4, 1.9] |  | 253 | (51) | 1.0 [0.8, 1.2] |  | 255 | (37) | 0.6 [0.5, 0.7] |

 CI, confidence interval; OR, odds ratio.