| Author, Year and Quality | Outcome | Subgroup or Specific Drug Exposure | Exposure Group | n | Results | Between Group Difference |
| --- | --- | --- | --- | --- | --- | --- |
| **Maternal outcomes** |
| Palmsten, 2013a151Good | Pre-eclampsia, n (%) | SSRI | Exposed | 19000 | 1033 (5) | OR 1.03 (95% CI, 0.95 to 1.12), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| SSRI (by dose) | High (>midpoint of usual dose range) | 2726 | 171 (6.3) | High (> midpoint of usual dose range) vs. Nonexposed: RR 1.10 (95% CI, 0.95 to 1.28), p=NR‡‡Medium (≤ midpoint of usual dose range) vs. Nonexposed: RR 1.00 (95% CI, 0.91 to 1.09), p=NR‡‡Low (< lowest usual dose) vs. Nonexposed: RR 0.95 (95% CI, 0.84 to 1.08), p=NR‡‡ |
| Medium (≤midpoint of usual dose range) | 11361 | 614 (5.4) |
| Low (<lowest usual dose) | 4913 | 248 (5.1) |
| Nonexposed | 59219 | 3215 (5.4) |
| SSRI (by duration) | Long (>90 days) | 4586 | 267 (5.8) | Long (> 90 days) vs. Nonexposed: RR 1.05 (95% CI, 0.93 to 1.19), p=NR‡‡Medium (31-90 days) vs. Nonexposed: RR 0.98 (95% CI, 0.89 to 1.09), p=NR‡‡Short (≤ 30 days) vs. Nonexposed: RR 0.99 (95% CI, 0.89 to 1.10), p=NR‡‡ |
| Medium (31-90 days) | 7782 | 416 (5.4) |
| Short (≤30 days) | 6632 | 350 (5.3) |
| Nonexposed | 59219 | 3215 (5.4) |
| Buproprion | Exposed | 2622 | 153 (6) | RR 1.06 (95% CI, 0.91 to 1.25), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Buproprion (by dose) | High or Medium (≥midpoint of usual dose range) | 424 | 24 (5.7) | High or Medium (≥ midpoint of usual dose range) vs. Nonexposed: RR 1.01 (95% CI, 0.68 to 1.50), p=NR‡‡Low (< lowest usual dose) vs. Nonexposed: RR 1.07 (95% CI, 0.90 to 1.28), p=NR‡‡ |
| Low (<lowest usual dose) | 2198 | 129 (5.9) |
| Nonexposed | 59219 | 3215 (5.4) |
| Buproprion (by duration) | Long (>90 days) | 423 | 26 (6.2) | Long (> 90 days) vs. Nonexposed: RR 1.05 (95% CI, 0.72 to 1.52), p=NR‡‡Medium (31-90 days) vs. Nonexposed: RR 1.01 (95% CI, 0.78 to 1.31), p=NR‡‡Short (≤ 30 days) vs. Nonexposed: RR 1.12 (95% CI, 0.89 to 1.40), p=NR‡‡ |
| Medium (31-90 days) | 987 | 56 (5.7) |
| Short (≤30 days) | 1212 | 71 (5.9) |
| Nonexposed | 59219 | 3215 (5.4) |
| Citalopram | Exposed | 1680 | 91 (5) | RR 1.01 (95% CI, 0.82 to 1.23), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Duloxetine | Exposed | NR | NR (7) | RR 0.89 (95% CI, 0.43 to 1.83), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Escitalopram | Exposed | 1936 | 125 (6) | RR 1.14 (95% CI, 0.96 to 1.36), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Fluoxetine | Exposed | 5650 | 299 (5) | RR 0.97 (95% CI, 0.87 to 1.09), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Mirtazapine | Exposed | 253 | 14 (6) | RR 0.81 (95% CI, 0.50 to 1.34), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Paroxetine | Exposed | 3517 | 183 (5) | RR 0.99 (95% CI, 0.86 to 1.15), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Sertraline | Exposed | 7143 | 398 (6) | RR 1.03 (95% CI, 0.93 to 1.14), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| SNRI | Exposed | 1216 | 107 (9) | OR 1.52 (95% CI, 1.17 to 1.98), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| SNRI (by dose) | High (>midpoint of usual dose range) | NR | NR (11.9) | High (> midpoint of usual dose range) vs. Nonexposed: RR 1.98 (95% CI, 1.08 to 3.64), p=NR‡‡Medium (≤ midpoint of usual dose range) vs. Nonexposed: RR 1.63 (95% CI, 1.32 to 2.00), p=NR‡‡Low (< lowest usual dose) vs. Nonexposed: RR 1.01 (95% CI, 0.63 to 1.64), p=NR‡‡ |
| Low (<lowest usual dose) | 239 | 15 (6.3) |
| Medium (≤midpoint of usual dose range) | 910 | 84 (9.2) |
| Nonexposed | 59219 | 3215 (5.4) |
| SNRI (by duration) | Long (> 90 days) | 507 | 48 (9.5) | Long (> 90 days) vs. Nonexposed: RR 1.64 (95% CI, 1.25 to 2.16), p=NR‡‡Medium (31-90 days) vs. Nonexposed: RR 1.75 (95% CI, 1.31 to 2.34), p=NR‡‡Short (≤ 30 days) vs. Nonexposed: RR 1.01 (95% CI, 0.64 to 1.57), p=NR‡‡ |
| Medium (31-90 days) | 407 | 41 (10.1) |
| Short (≤ 30 days) | 302 | 18 (6.0) |
| Nonexposed | 59219 | 3215 (5.4) |
| Trazadone | Exposed | 339 | 14 (4) | RR 0.63 (95% CI, 0.38 to 1.05), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Venlafaxine | Exposed | 1113 | 100 (9) | RR 1.57 (95% CI, 1.29 to 1.91), p=NR‡‡ |
| Nonexposed | 59219 | 3215 (5) |
| Palmsten, 2013b150Good | Postpartum hemorrhage, n (%) | All anti-depressants | Current exposure | 16029 | 620 (3.9) | Current exposure vs. Nonexposed: RR 1.44 (95% CI, 1.32 to 1.58), p=NR§§Recent exposure vs. Nonexposed: RR 1.21 (95% CI, 1.06 to 1.38), p=NR§§Past exposure vs. Nonexposed: RR 0.98 (95% CI, 0.88 to 1.10), p=NS§§ |
| Recent exposure | 7577 | 247 (3.3) |
| Past exposure | 13350 | 357 (2.7) |
| Nonexposed | 69044 | 1896 (2.8) |
| SSRI + venlafaxine | Depressed - Current exposure | 8917 | 357 (4.0) | Depressed - Current exposure vs. Depressed - No exposure: RR 1.46 (95% CI, 1.29 to 1.65), p=NR§§Depressed - Recent exposure vs. Depressed - No exposure: RR 1.28 (95% CI, 1.08 to 1.52), p=NR§§Depressed - Past exposure vs. Depressed - No exposure: RR 0.92 (95% CI, 0.79 to 1.08), p=NR§§Exposed vs. Nonexposed: OR 1.52 (95% CI, 1.35 to 1.71), p=NR§§ |
| Depressed - Recent exposure | 4344 | 153 (3.5) |
| Depressed - Past exposure | 7432 | 190 (2.6) |
| Depressed - No exposure | 36457 | 1008 (2.8) |
| Exposed | 10203 | 415 (4.1) |
| Nonexposed | 53348 | 1479 (2.8) |
| SSRI + venlafaxine (by dose) | High dose | 1597 | 66 (4.1) | High dose vs. Nonexposed: RR 1.55 (95% CI, 1.21 to 1.97), p=NR§§Medium dose vs. Nonexposed: RR 1.51 (95% CI, 1.34 to 1.70), p=NR§§Low dose vs. Nonexposed: RR 1.29 (95% CI, 1.07 to 1.55), p=NR§§ |
| Low dose | 3236 | 113 (3.5) |
| Medium dose | 7877 | 324 (4.1) |
| Nonexposed | 69044 | 1896 (2.8) |
| SSRI + venlafaxine monotherapy | Current exposure | 12710 | 503 (4.0) | Current exposure vs. Nonexposed: RR 1.47 (95% CI, 1.33 to 1.62), p=NR§§Recent exposure vs. Nonexposed: RR 1.19 (95% CI, 1.03 to 1.38), p=NR§§Past exposure vs. Nonexposed: RR 0.93 (95% CI, 0.82 to 1.06), p=NR§§ |
| Recent exposure | 6096 | 196 (3.2) |
| Past exposure | 10416 | 264 (2.5) |
| Nonexposed | 69044 | 1896 (2.8) |
| SSRI | Current exposure | 11516 | 440 (3.8) | Current exposure vs. Nonexposed: RR 1.42 (95% CI, 1.27 to 1.57), p=NR§§Recent exposure vs. Nonexposed: RR 1.21 (95% CI, 1.04 to 1.40), p=NR§§Past exposure vs. Nonexposed: RR 0.93 (95% CI, 0.81 to 1.06), p=NR§§ |
| Recent exposure | 5706 | 186 (3.3) |
| Past exposure | 9675 | 244 (2.5) |
| Nonexposed | 69044 | 1896 (2.8) |
| Buproprion | Current exposure | 1162 | 42 (3.6) | Current exposure vs. Nonexposed: RR 1.32 (95% CI, 0.98 to 1.79), p=NR§§Recent exposure vs. Nonexposed: RR 1.17 (95% CI, 0.77 to 1.79), p=NR§§Past exposure vs. Nonexposed: RR 1.32 (95% CI, 1.02 to 1.69), p=NR§§ |
| Recent exposure | 660 | 21 (3.2) |
| Past exposure | 1712 | 61 (3.6) |
| Nonexposed | 69044 | 1896 (2.8) |
| Buproprion monotherapy | Current exposure | 1114 | 40 (3.6) | Current exposure vs. Nonexposed: RR 1.32 (95% CI, 0.97 to 1.80), p=NR§§Recent exposure vs. Nonexposed: RR 1.20 (95% CI, 0.79 to 1.83), p=NR§§Past exposure vs. Nonexposed: RR 1.33 (95% CI, 1.03 to 1.71), p=NR§§ |
| Recent exposure | 649 | 21 (3.2) |
| Past exposure | 1666 | 60 (3.6) |
| Nonexposed | 69044 | 1896 (2.8) |
| Citalopram | Current exposure | 891 | 36 (4.0) | Current exposure vs. Nonexposed: RR 1.48 (95% CI, 1.07 to 2.04), p=NR§§Recent exposure vs. Nonexposed: RR 0.70 (95% CI, 0.37 to 1.34), p=NR§§Past exposure vs. Nonexposed: RR 0.76 (95% CI, 0.47 to 1.23), p=NR§§ |
| Recent exposure | 462 | NR |
| Past exposure | 830 | 17 (2.1) |
| Nonexposed | 69044 | 1896 (2.8) |
| Escitalopram | Current exposure | 1022 | 43 (4.2) | Current exposure vs. Nonexposed: RR 1.56 (95% CI, 1.16 to 2.09), p=NR§§Recent exposure vs. Nonexposed: RR 1.01 (95% CI, 0.61 to 1.70), p=NR§§Past exposure vs. Nonexposed: RR 0.96 (95% CI, 0.64 to 1.42), p=NR§§ |
| Recent exposure | 520 | 14 (2.7) |
| Past exposure | 940 | 24 (2.6) |
| Nonexposed | 69044 | 1896 (2.8) |
| Fluoxetine | Current exposure | 3322 | 137 (4.1) | Current exposure vs. Nonexposed: RR 1.51 (95% CI, 1.27 to 1.79), p=NR§§Recent exposure vs. Nonexposed: RR 1.14 (95% CI, 0.86 to 1.50), p=NR§§Past exposure vs. Nonexposed: RR 0.93 (95% CI, 0.75 to 1.17), p=NR§§ |
| Recent exposure | 1628 | 50 (3.1) |
| Past exposure | 3075 | 78 (2.5) |
| Nonexposed | 69044 | 1896 (2.8) |
| Mirtazapine | Current exposure | 129 | NR | Current exposure vs. Nonexposed: RR 0.87 (95% CI, 0.29 to 2.66), p=NR§§Recent exposure vs. Nonexposed: RR NR (95% CI, NR to NR), p=NR§§Past exposure vs. Nonexposed: RR 1.07 (95% CI, 0.40 to 2.82), p=NR§§ |
| Recent exposure | 57 | 0 (0) |
| Past exposure | 135 | NR |
| Nonexposed | 69044 | 1896 (2.8) |
| Atypical anti-depressants | Depressed - Current exposure | 1012 | 42 (4.2) | Depressed - Current exposure vs. Depressed - No exposure: RR 1.52 (95% CI, 1.12 to 2.06), p=NR§§Depressed - Recent exposure vs. Depressed - No exposure: RR 1.08 (95% CI, 0.68 to 1.70), p=NR§§Depressed - Past exposure vs. Depressed - No exposure: RR 1.26 (95% CI, 0.95 to 1.67), p=NR§§Exposed vs. Nonexposed: OR 1.39 (95% CI, 1.03 to 1.89), p=NR§§ |
| Depressed - Recent exposure | 616 | 18 (2.9) |
| Depressed - Past exposure | 1460 | 51 (3.5) |
| Depressed - No exposure | 36457 | 1008 (2.8) |
| Exposed | 1162 | 45 (3.9) |
| Nonexposed | 52192 | 1475 (2.8) |
| Paroxetine | Current exposure | 2055 | 77 (3.8) | Current exposure vs. Nonexposed: RR 1.36 (95% CI, 1.09 to 1.71), p=NR§§Recent exposure vs. Nonexposed: RR 1.52 (95% CI, 1.12 to 2.07), p=NR§§Past exposure vs. Nonexposed: RR 1.13 (95% CI, 0.85 to 1.49), p=NR§§ |
| Recent exposure | 962 | 40 (4.2) |
| Past exposure | 1617 | 49 (3.0) |
| Nonexposed | 69044 | 1896 (2.8) |
| Sertraline | Current exposure | 4526 | 162 (3.6) | Current exposure vs. Nonexposed: RR 1.31 (95% CI, 1.12 to 1.54), p=NR§§Recent exposure vs. Nonexposed: RR 1.27 (95% CI, 1.01 to 1.59), p=NR§§Past exposure vs. Nonexposed: RR 0.82 (95% CI, 0.66 to 1.01), p=NR§§ |
| Recent exposure | 2266 | 78 (3.4) |
| Past exposure | 3812 | 85 (2.2) |
| Nonexposed | 69044 | 1896 (2.8) |
| SNRI monotherapy | Current exposure | 702 | 35 (5.0) | Current exposure vs. Nonexposed: RR 1.90 (95% CI, 1.37 to 2.63), p=NR§§ Recent exposure vs. Nonexposed: RR 1.21 (95% CI, 0.58 to 2.54), p=NR§§ Past exposure vs. Nonexposed: RR 1.05 (95% CI, 0.60 to 1.83), p=NR§§ |
| Recent exposure | 217 | NR |
| Past exposure | 423 | 12 (2.8) |
| Nonexposed | 69044 | 1896 (2.8) |
| Trazadone | Current exposure | 139 | NR | Current exposure vs. Nonexposed: RR 1.85 (95% CI, 0.90 to 3.80), p=NR§§Recent exposure vs. Nonexposed: RR 2.01 (95% CI, 0.77 to 5.24), p=NR§§Past exposure vs. Nonexposed: RR 0.61 (95% CI, 0.23 to 1.67), p=NR§§ |
| Recent exposure | 73 | NR |
| Past exposure | 226 | NR |
| Nonexposed | 69044 | 1896 (2.8) |
| Venlafaxine | Current exposure | 763 | 46 (6.0) | Current exposure vs. Nonexposed: RR 2.24 (95% CI, 1.69 to 2.97), p=NR§§Recent exposure vs. Nonexposed: RR 1.10 (95% CI, 0.53 to 2.30), p=NR§§Past exposure vs. Nonexposed: RR 0.98 (95% CI, 0.56 to 1.70), p=NR§§ |
| Recent exposure | 237 | NR |
| Past exposure | 458 | 12 (2.6) |
| Nonexposed | 69044 | 1896 (2.8) |
| Lupattelli, 2014146Fair | Postpartum hemorrhage, n (%) | SSRIs/SNRIs | Exposed (week 30 to birth) | 122 | 18 (14.6) | Exposed (week 30 to birth) vs. Nonexposed (week 30 to birth): OR 0.97 (95% CI, 0.57 to 1.65), p=NR†† |
| Nonexposed (week 30 to birth) | 55862 | 8009 (14.3) |
| Vaginal bleeding, any type during early pregnancy, n (%) | SSRIs/SNRIs | Depressed- nonexposed | 1282 | 293 (22.9) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.22 (95% CI, 1.06 to 1.39), p=NR††Exposed (first trimester) vs. Nonexposed (first trimester): OR 0.91 (95% CI, 0.72 to 1.16), p=NS†† |
| Exposed (1st trimester) | 427 | 90 (21.1) |
| Nonexposed (1st trimester) | 55533 | 11066 (19.9) |
| Not depressed- nonexposed | 55411 | 11037 (19.9) |
| Vaginal bleeding, any type during mid-pregnancy, n (%) | SSRIs/SNRIs | Depressed- nonexposed | 1282 | 158 (12.3) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.28 (95% CI, 1.07 to 1.55), p=NR††Exposed (second trimester) vs. Nonexposed (second trimester): OR 0.81 (95% CI, 0.5 to 1.31), p=NS†† |
| Exposed (2nd trimester) | 222 | 22 (9.9) |
| Nonexposed (2nd trimester) | 55750 | 5212 (9.3) |
| Not depressed- nonexposed | 55411 | 5176 (9.3) |
| Andersen, 2014132Good | Miscarriage, n (%) | SSRIs | Exposed | 22884 | 2883 (12.6) | Exposed vs. Nonexposed: HR 1.27 (95% CI, 1.22 to 1.33), p=NR¶Exposed vs. Previous exposure: p=0.47¶Exposed (low dose) vs. Exposed (high dose): HR 1.00 (95% CI, 0.91 to 1.09), p=NS¶Previous exposure vs. Nonexposed: HR 1.24 (95% CI, 1.18 to 1.30), p=NR¶ |
| Exposed (high dose) | NR | NR |
| Exposed (low dose) | NR | NR |
| Previous exposure | 14016 | 1936 (13.8) |
| Nonexposed | 1256956 | 139210 (11.1) |
| Citalopram | Exposed | 9927 | NR | Exposed vs. Nonexposed: HR 1.29 (95% CI, 1.21 to 1.37), p=NR¶Exposed vs. Previous exposure: p=0.94¶Exposed (low dose) vs. Exposed (high dose): HR 1.08 (95% CI, 0.94 to 1.23), p=NS¶Previous exposure vs. Nonexposed: HR 1.26 (95% CI, 1.17 to 1.35), p=NR¶ |
| Exposed (high dose) | NR | NR |
| Exposed (low dose) | NR | NR |
| Previous exposure | 6857 | NR |
| Nonexposed | 1256956 | NR |
| Escitalopram | Exposed | 2377 | NR | Exposed vs. Previous exposure: p=0.13¶Exposed vs. Nonexposed: HR 1.25 (95% CI, 1.09 to 1.42), p=NR¶Exposed (low dose) vs. Exposed (high dose): HR 0.99 (95% CI, 0.76 to 1.31), p=NR¶Previous exposure vs. Nonexposed: HR 1.33 (95% CI, 1.17 to 1.51), p=NR¶ |
| Exposed (high dose) | NR | NR |
| Exposed (low dose) | NR | NR |
| Previous exposure | 1839 | NR |
| Nonexposed | 1256956 | NR |
| Fluoxetine | Exposed | 4111 | NR | Exposed vs. Nonexposed: HR 1.10 (95% CI, 1.01 to 1.21), p=NR¶Exposed vs. Previous exposure: p=0.69¶Exposed (low dose) vs. Exposed (high dose): HR 0.83 (95% CI, 0.68 to 1.02), p=NS¶Previous exposure vs. Nonexposed: HR 1.17 (95% CI, 1.03 to 1.33), p=NR¶ |
| Exposed (high dose) | NR | NR |
| Exposed (low dose) | NR | NR |
| Previous exposure | 1738 | NR |
| Nonexposed | 1256956 | NR |
| Paroxetine | Exposed | 2739 | NR | Exposed vs. Nonexposed: HR 1.27 (95% CI, 1.14 to 1.42), p=NR¶Exposed vs. Previous exposure: p=0.59¶Exposed (low dose) vs. Exposed (high dose): HR 1.03 (95% CI, 0.8 to 1.32), p=NS¶Previous exposure vs. Nonexposed: HR 1.20 (95% CI, 1.05 to 1.37), p=NR¶ |
| Exposed (high dose) | NR | NR |
| Exposed (low dose) | NR | NR |
| Previous exposure | 1469 | NR |
| Nonexposed | 1256956 | NR |
| Sertraline | Exposed | 4453 | NR | Exposed vs. Nonexposed: HR 1.45 (95% CI, 1.33 to 1.58), p=NR¶Exposed vs. Previous exposure: p=0.13¶Exposed (low dose) vs. Exposed (high dose): HR 0.95 (95% CI, 0.79 to 1.14), p=NS¶Previous exposure vs. Nonexposed: HR 1.20 (95% CI, 1.08 to 1.34), p=NR¶ |
| Exposed (high dose) | NR | NR |
| Exposed (low dose) | NR | NR |
| Previous exposure | 2755 | NR |
| Nonexposed | 1256956 | NR |
| Kjaersgaard, 2013144Good | Spontaneous abortion, n (%) | Any anti-depressant | Depressed- exposed | 1674 | 210 (12.5) | Depressed- exposed vs. Depressed- nonexposed: RR 1.00 (95% CI, 0.80 to 1.24), p=NR\*\*Not depressed- exposed vs. Not depressed- nonexposed: RR 1.17 (95% CI, 1.13 to 1.22), p=NR\*\*Exposed vs. Nonexposed: RR 1.14 (95% CI, 1.10 to 1.18), p=NR\*\* |
| Depressed- nonexposed | 820 | 105 (12.8) |
| Exposed | 15463 | 2637 (17.1) |
| Nonexposed | 819246 | 110482 (13.5) |
| Not depressed- exposed | 13789 | 2427 (17.6) |
| Not depressed- nonexposed | 818426 | 110377 (13.5) |
| Citalopram | Depressed- exposed | NR | NR | RR 1.11 (95% CI, 0.79 to 1.55), p=NS |
| Depressed- nonexposed | NR | NR |
| Duloxetine | Depressed- exposed | NR | NR | RR 3.12 (95% CI, 1.55 to 6.31), p=NR |
| Depressed - nonexposed | NR | NR |
| Escitalopram | Depressed- exposed | NR | NR | RR 0.94 (95% CI, 0.49 to 1.94), p=NS |
| Depressed- nonexposed | NR | NR |
| Fluoxetine | Depressed- exposed | NR | NR | RR 0.63 (95% CI, 0.38 to 1.06), p=NS |
| Depressed - nonexposed | NR | NR |
| Mirtazapine | Depressed- exposed | NR | NR | RR 2.23 (95% CI, 1.34 to 3.7), p=NR |
| Depressed - nonexposed | NR | NR |
| Paroxetine | Depressed- exposed | NR | NR | RR 0.70 (95% CI, 0.29 to 1.65), p=NS |
| Depressed - nonexposed | NR | NR |
| Sertraline | Depressed- exposed | NR | NR | RR 0.84 (95% CI, 0.55 to 1.27), p=NS |
| Depressed - nonexposed | NR | NR |
| SSRI | Depressed- exposed | NR | NR | RR 0.8 (95% CI, 0.62 to 1.03), p=NS |
| Depressed - nonexposed | NR | NR |
| Venlafaxine | Depressed- exposed | NR | NR | RR 1.8 (95% CI, 1.19 to 2.72), p=NR |
| Depressed – nonexposed | NR | NR |
| **Infant Outcomes** |
| Hayes, 2012137Good | Gestational age, mean (SD) | Any anti-depressant | Depressed- ≥3 prescriptions | 6196 | 269.7 (16.2) | *Pre-term labor:*Depressed- ≥ 3 prescriptions vs. Depressed- no prescription: OR 1.04 (95% CI, 0.98 to 1.11), p=NR║║ Depressed – 1-2 prescription vs. Depressed- no prescription: OR 2.55 (95% CI, 2.40 to 2.71)║║ |
| Depressed- 1-2 prescriptions | 10700 | 270.6 (16.3) |
| Depressed- no prescription | 16907 | 270.5 (16.5) |
| Not depressed- nonexposed | 195079 | 270.8 (17.7) |
| Second trimester exposure | Depressed - 1 prescription | NR | NR | Depressed- ≥ 3 prescriptions vs. Women with no prescriptions during indicated trimester: Mean Difference -6.6 (95% CI, -4.6 to -8.6), p<0.0001†Depressed - 2 prescriptions vs. Women with no prescriptions during indicated trimester: Mean Difference -5.8 (95% CI, -3.9 to -7.8), p<0.0001†Depressed - 1 prescription vs. Women with no prescriptions during indicated trimester: Mean Difference -2.6 (95% CI, -1.3 to -3.9), p<0.0001† |
| Depressed - 2 prescriptions | NR | NR |
| Depressed- ≥3 prescriptions | NR | NR |
| Women with no prescriptions during indicated trimester | NR | NR |
| Third trimester exposure | All women with no prescriptions | NR | NR | Depressed- ≥ 3 prescriptions vs. Women with no prescriptions during indicated trimester: Mean Difference 6.4 (95% CI, 5.5 to 7.3), p=NR†Depressed - 2 prescriptions vs. Women with no prescriptions during indicated trimester: Mean Difference 1.8 (95% CI, 0.9 to 2.7), p=NR†Depressed - 1 prescription vs. Women with no prescriptions during indicated trimester: Mean Difference 0.9 (95% CI, 0.3 to 1.6), p=NR† |
| Depressed - 1 prescription | NR | NR |
| Depressed - 2 prescriptions | NR | NR |
| Depressed- ≥3 prescriptions | NR | NR |
| Women with no prescriptions during indicated trimester | NR | NR |
| Hayes, 2012137Good | Preterm birth, born 32-37 weeks, n (%) | Any anti-depressant | Depressed- ≥3 prescriptions | 6196 | 787 (12.7) | *Gestational age 32-36 weeks (calculated):*Depressed- ≥ 3 prescriptions vs. Depressed- no prescription: OR 1.12 (95% CI, 1.03 to 1.23), p=NR║║ Depressed – 1-2 prescription vs. Depressed- no prescription: OR 1.91 (95% CI, 1.77 to 2.07)║║*Gestational age < 32 weeks (calculated):*Depressed- ≥ 3 prescriptions vs. Depressed- no prescription: OR 0.95 (95% CI, 0.77 to 1.17), p=NR║║ Depressed – 1-2 prescription vs. Depressed- no prescription: OR 1.54 (95% CI, 1.29 to 1.85)║║ |
| Depressed- 1-2 prescriptions | 10700 | 1231 (11.5) |
| Depressed- no prescription | 16907 | 1939 (11.5) |
| Not depressed- nonexposed | 195079 | 21524 (11.1) |
| Jensen, 2013a143Good | Small for gestational age, number | Any anti-depressant | Depressed- exposed | 166 | NR | Depressed- exposed (pre- and during pregnancy) vs. Not depressed- nonexposed: HR 1.42 (95% CI, 1.2 to 1.68), p=NR§Depressed- nonexposed vs. Not depressed- nonexposed: HR 1.04 (95% CI, 0.92 to 1.20), p=NS§Depressed- nonexposed (pre- or during pregnancy) vs. Not depressed- nonexposed: HR 0.91 (95% CI, 0.72 to 1.16), p=NS§Exposed- SSRI vs. Not depressed- nonexposed: HR 1.22 (95% CI, 1.13 to 1.32), p=NR§Exposed vs. Not depressed- nonexposed: HR 1.19 (95% CI, 1.11 to 1.28), p=NR§Depressed- exposed vs. Not depressed- nonexposed: HR 1.44 (95% CI, 0.89 to 2.31), p=NS§ |
| Depressed- exposed (pre- and during pregnancy) | 1134 | NR |
| Depressed- nonexposed | 1926 | NR |
| Depressed- nonexposed (pre- or during pregnancy) | 740 | NR |
| Exposed | 8511 | NR |
| Exposed- SSRI | NR | NR |
| Not depressed- nonexposed | 638116 | NR |
| First trimester exposure | Exposed | NR | NR | HR 1.07 (95% CI, 0.98 to 1.16), p=NR§ |
| Not depressed- nonexposed | NR | NR |
| Second trimester exposure | Exposed | NR | NR | HR 1.15 (95% CI, 0.97 to 1.35), p=NR§ |
| Not depressed- nonexposed | NR | NR |
| Third trimester exposure | Exposed | NR | NR | HR 1.18 (95% CI, 1.00 to 1.40), p=NR§ |
| Not depressed- nonexposed | NR | NR |
| Hayes, 2012137Good | Neonatal convulsions, n (%) | Any anti-depressant | Depressed- ≥ 3 prescriptions | 6196 | 41 (0.66) | Depressed- ≥ 3 prescriptions vs. Depressed- no prescription: OR 2.39 (95% CI, 1.57 to 3.64), p=NR║║ Depressed – 1-2 prescription vs. Depressed- no prescription: OR 1.04 (95% CI, 0.66 to 1.64)║║ |
| Depressed- 1-2 prescriptions | 10700 | 31 (0.29) |
| Depressed- no prescription | 16901 | 47 (0.28) |
| Not depressed- nonexposed | 195079 | 429 (0.22) |
| Second trimester exposure | Depressed - 1 prescription | NR | NR | Depressed- ≥ 3 prescriptions vs. Women with no prescriptions during indicated trimester: OR 1.12 (95% CI, 0.50 to 2.44), p=NR†Depressed - 2 prescriptions vs. Women with no prescriptions during indicated trimester: OR 1.59 (95% CI, 0.79 to 3.24), p=NR†Depressed - 1 prescription vs. Women with no prescriptions during indicated trimester: OR 0.85 (95% CI, 0.47 to 1.76), p=NR† |
| Depressed - 2 prescriptions | NR | NR |
| Depressed- ≥3 prescriptions | NR | NR |
| Women with no prescriptions during indicated trimester | NR | NR |
| Third trimester exposure | Depressed - 1 prescription | NR | NR | Depressed- ≥ 3 prescriptions vs. Women with no prescriptions during indicated trimester: OR 4.9 (95% CI, 2.6 to 9.5), p=NR†Depressed - 2 prescriptions vs. Women with no prescriptions during indicated trimester: OR 2.8 (95% CI, 1.4 to 5.5), p=NR†Depressed - 1 prescription vs. Women with no prescriptions during indicated trimester: OR 1.4 (95% CI, 0.7 to 2.8), p=NR† |
| Depressed - 2 prescriptions | NR | NR |
| Depressed- ≥3 prescriptions | NR | NR |
| Women with no prescriptions during indicated trimester | NR | NR |
| Hayes, 2012137Good | Respiratory distress, n (%) | Any anti-depressant | Depressed- ≥3 prescriptions | 6196 | 333 (5.4) | Depressed- ≥ 3 prescriptions vs. Depressed- no prescription: OR 1.18 (95% CI, 1.04 to 1.35), p=NR║║ Depressed – 1-2 prescription vs. Depressed- no prescription: OR 1.06 (95% CI, 0.94 to 1.18)║║ |
| Depressed- 1-2 prescriptions | 10700 | 516 (4.8) |
| Depressed- no prescription | 16907 | 774 (4.6) |
| Not depressed- nonexposed | 195079 | 8358 (4.3) |
| Second trimester exposure | Depressed - 1 prescription | NR | NR | Depressed- ≥ 3 prescriptions vs. Women with no prescriptions during indicated trimester: OR 1.6 (95% CI, 1.2 to 2.0), p=NR†Depressed - 2 prescriptions vs. Women with no prescriptions during indicated trimester: OR 1.4 (95% CI, 1.1 to 1.8), p=NR†Depressed - 1 prescription vs. Women with no prescriptions during indicated trimester: OR 1.1 (95% CI, 0.9 to 1.3), p=NR† |
| Depressed - 2 prescriptions | NR | NR |
| Depressed- ≥ 3 prescriptions | NR | NR |
| Women with no prescriptions during indicated trimester | NR | NR |
| Third trimester exposure | Depressed - 1 prescription | NR | NR | Depressed- ≥ 3 prescriptions vs. Women with no prescriptions during indicated trimester: OR 0.6 (95% CI, 0.5 to 0.8), p=NR†Depressed - 2 prescriptions vs. Women with no prescriptions during indicated trimester: OR 0.8 (95% CI, 0.6 to 1.0), p=NR†Depressed - 1 prescription vs. Women with no prescriptions during indicated trimester: OR 0.9 (95% CI, 0.7 to 1.1), p=NR† |
| Depressed - 2 prescriptions | NR | NR |
| Depressed- ≥3 prescriptions | NR | NR |
| Women with no prescriptions during indicated trimester | NR | NR |
| Polen, 2013152Fair | Anencephaly, n (%) | Venlafaxine | Cases-Exposed | 91 | 4 (4.4) | Cases vs. Controls: OR 6.3 (95% CI, 1.5 to 20.2), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 6.5 (95% CI, 1.5 to 21.7), p=NR |
| Cases-Exposed (2003-2007) | 69 | 4 (5.8) |
| Cases-Nonexposed | 26954 | 407 (1.5) |
| Cases-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Cleft palate (alone), n (%) | Venlafaxine | Cases-Exposed | 91 | 7 (7.7) | Cases vs. Controls: OR 3.3 (95% CI, 1.1 to 8.8), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 3.1 (95% CI, 0.9 to 9.6), p=NR |
| Cases-Exposed (2003-2007) | 69 | 5 (7.2) |
| Cases-Nonexposed | 26954 | 1116 (4.1) |
| Cases-Nonexposed (2003-2007) | 13462 | 517 (3.8) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Gastroschisis, n (%) | Venlafaxine | Cases-Exposed | 91 | 6 (6.7) | Cases vs. Controls: OR 5.7 (95% CI, 1.8 to 15.9), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 3.3 (95% CI, 0.9 to 10.2), p=NR |
| Cases-Exposed (2003-2007) | 69 | 5 (7.2) |
| Cases-Nonexposed | 26954 | 905 (9.9) |
| Cases-Nonexposed (2003-2007) | 13462 | 503 (3.7) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Ban, 2014134Good | Major congenital anomaly -all combined, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | 204 (266) | Depressed- exposed vs. Not depressed- nonexposed: OR 1.01 (95% CI, 0.88 to 1.17), p=NS\*Depressed- exposed vs. Depressed- nonexposed: OR 0.93 (95% CI, 0.78 to 1.11), p=NS\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.07 (95% CI, 0.96 to 1.18), p=NS\* |
| Depressed- nonexposed | 13432 | 380 (283) |
| Not depressed- nonexposed | 325294 | 8731 (268) |
| Citalopram | Depressed- exposed | 1946 | NR (267)  | Depressed- exposed vs. Depressed- nonexposed: OR 0.97 (95% CI, 0.71 to 1.31), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 1.06 (95% CI, 0.80 to 1.40), p=NS\* |
| Depressed- nonexposed | 13432 | 380 (283) |
| Not depressed- nonexposed | 325294 | 8731 (268) |
| Escitalopram | Depressed- exposed | 333 | NR (210) | Depressed- exposed vs. Not depressed- nonexposed: OR 0.85 (95% CI, 0.4 to 1.81), p=NS\*Depressed- exposed vs. Depressed- nonexposed: OR 0.77 (95% CI, 0.36 to 1.66), p=NS\* |
| Depressed- nonexposed | 13432 | 380 (283) |
| Not depressed- nonexposed | 325294 | 8731 (268) |
| Fluoxetine | Depressed- exposed | 3189 | NR (241) | Depressed- exposed vs. Depressed- nonexposed: OR 0.85 (95% CI, 0.66 to 1.09), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 0.91 (95% CI, 0.73 to 1.15), p=NS\* |
| Depressed- nonexposed | 13432 | 380 (283) |
| Not depressed- nonexposed | 325294 | 8731 (268) |
| Paroxetine | Depressed- exposed | 1200 | NR (300) | Depressed- exposed vs. Not depressed- nonexposed: OR 1.08 (95% CI, 0.77 to 1.50), p=NS\*Depressed- exposed vs. Depressed- nonexposed: OR 1.01 (95% CI, 0.71 to 1.44), p=NS\* |
| Depressed- nonexposed | 13432 | 380 (283) |
| Not depressed- nonexposed | 325294 | 8731 (268) |
| Sertraline | Depressed- exposed | 757 | NR (330) | Depressed- exposed vs. Depressed- nonexposed: OR 1.17 (95% CI, 0.78 to 1.77), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 1.27 (95% CI, 0.85 to 1.89), p=NS\* |
| Depressed- nonexposed | 13432 | 380 (283) |
| Not depressed- nonexposed | 325294 | 8731 (268) |
| Specific heart anomalies-atrial septal defect, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | NR (18) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 0.85 (95% CI, 0.48 to 1.51), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 1.68 (95% CI, 0.98 to 2.91), p=NS\* |
| Depressed- nonexposed | 13432 | NR (9) |
| Not depressed- nonexposed | 325294 | NR (10) |
| Specific heart anomalies-other, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | NR (44) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.20 (95% CI, 0.90 to 1.58), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 1.27 (95% CI, 0.90 to 1.80), p=NS\* |
| Depressed- nonexposed | 13432 | NR (40) |
| Not depressed- nonexposed | 325294 | NR (33) |
| Specific heart anomalies- right ventricular outflow tract defect, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | NR (8) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.58 (95% CI, 0.73 to 3.4), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 2.22 (95% CI, 0.98 to 5.03), p=NS\* |
| Depressed- nonexposed | 13432 | NR (5) |
| Not depressed- nonexposed | 325294 | NR (3) |
| Specific heart anomalies-septal defect, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | NR (43) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.09 (95% CI, 0.86 to 1.39), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 0.89 (95% CI, 0.63 to 1.27), p=NS\* |
| Depressed- nonexposed | 13432 | NR (51) |
| Not depressed- nonexposed | 325294 | NR (47) |
| Specific heart anomalies-ventricular septal defect, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | NR (21) | Depressed- exposed vs. Not depressed- nonexposed: OR 1.09 (95% CI, 0.81 to 1.45), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 0.63 (95% CI, 0.38 to 1.03), p=NS\* |
| Depressed- nonexposed | 13432 | NR (36) |
| Not depressed- nonexposed | 325294 | NR (33) |
| Specific heart anomalies- left ventricular outflow tract defect, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | NR (1) | Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.59 (95% CI, 0.36 to 7.16), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 1.5 (95% CI, 0.2 to 11.24), p=NS\* |
| Depressed- nonexposed | 13432 | NR (1) |
| Not depressed- nonexposed | 325294 | NR (1) |
| Cardiac malform-ations, n (per 10,000) | SSRIs alone | Depressed- exposed | 7683 | 68 (89) | Depressed- exposed vs. Depressed- nonexposed: OR 1.04 (95% CI, 0.76 to 1.41), p=NS\*Depressed- exposed vs. Not depressed- nonexposed: OR 1.14 (95% CI, 0.89 to 1.45), p=NS\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.10 (95% CI, 0.91 to 1.33), p=NS\* |
| Depressed- nonexposed | 13432 | 112 (83) |
| Not depressed- nonexposed | 325294 | 2444 (75) |
| Citalopram | Depressed- exposed | 1946 | NR (87) | Depressed- exposed vs. Depressed- nonexposed: OR 1.02 (95% CI, 0.61 to 1.70), p=NS\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.13 (95% CI, 0.70 to 1.82), p=NS\* |
| Depressed- nonexposed | 13432 | 112 (83) |
| Not depressed- nonexposed | 325294 | 2444 (75) |
| Escitalopram | Depressed- exposed | 333 | NR (90) | Depressed- exposed vs. Depressed- nonexposed: OR 1.09 (95% CI, 0.34 to 3.50), p=NS\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.15 (95% CI, 0.36 to 3.65), p=NS\* |
| Depressed- nonexposed | 13432 | 112 (83) |
| Not depressed- nonexposed | 325294 | 2444 (75) |
| Fluoxetine | Depressed- exposed | 3189 | NR (66) | Depressed- exposed vs. Depressed- nonexposed: OR 0.79 (95% CI, 0.49 to 1.26), p=NS\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 0.84 (95% CI, 0.55 to 1.30), p=NS\* |
| Depressed- nonexposed | 13432 | 112 (83) |
| Not depressed- nonexposed | 325294 | 2444 (75) |
| Paroxetine | Depressed- exposed | 1200 | NR (142) | Depressed- exposed vs. Depressed- nonexposed: OR 1.67 (95% CI, 1.00 to 2.80), p=0.051\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.78 (95% CI, 1.09 to 2.88), p=0.02\* |
| Depressed- nonexposed | 13432 | 112 (83) |
| Not depressed- nonexposed | 325294 | 2444 (75) |
| Sertraline | Depressed- exposed | 757 | NR (119) | Depressed- exposed vs. Depressed- nonexposed: OR 1.39 (95% CI, 0.70 to 2.74), p=NS\*Depressed- nonexposed vs. Not depressed- nonexposed: OR 1.52 (95% CI, 0.78 to 2.96), p=NS\* |
| Depressed- nonexposed | 13432 | 112 (83) |
| Not depressed- nonexposed | 325294 | 2444 (75) |
| Polen, 2013152Fair | Atrial septal defect, type 2 or not otherwise specified, n (%) | Venlafaxine | Cases-Exposed | 91 | 11 (12.1) | Cases vs. Controls: OR 3.1 (95% CI, 1.3 to 7.4), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 1.7 (95% CI, 0.5 to 4.8), p=NS |
| Cases-Exposed (2003-2007) | 69 | 6 (8.7) |
| Cases-Nonexposed | 26954 | 2170 (8.1) |
| Cases-Nonexposed (2003-2007) | 13462 | 1215 (9.0) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Coarctation of the aorta, n (%) | Venlafaxine | Cases-Exposed | 91 | 6 (6.0) | Cases vs. Controls: OR 4.1 (95% CI, 1.3 to 11.5), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 3.2 (95% CI, 0.7 to 10.5), p=NS |
| Cases-Exposed (2003-2007) | 69 | 4 (5.8) |
| Cases-Nonexposed | 26954 | 762 (2.8) |
| Cases-Nonexposed (2003-2007) | 13462 | 423 (3.1) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Conotruncal heart defects, n (%) | Venlafaxine | Cases-Exposed | 91 | 6 (6.6) | Cases vs. Controls: OR 1.9 (95% CI, 0.6 to 5.3), p=NS║Cases (2003-2007) vs. Controls (2003-2007): OR 1.2 (95% CI, 0.2 to 4.5), p=NS |
| Cases-Exposed (2003-2007) | 69 | 3 (4.3) |
| Cases-Nonexposed | 26954 | 1748 (6.5) |
| Cases-Nonexposed (2003-2007) | 13462 | 823 (6.1) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Hypoplastic left heart syndrome, n (%) | Venlafaxine | Cases-Exposed | 91 | 2 (2.2) | NR |
| Cases-Exposed (2003-2007) | 69 | 2 (2.9) |
| Cases-Nonexposed | 26954 | 423 (1.6) |
| Cases-Nonexposed (2003-2007) | 13462 | 218 (1.6) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Left ventricular outflow tract obstruction defects, n (%) | Venlafaxine | Cases-Exposed | 91 | 9 (9.9) | Cases vs. Controls: OR 3.3 (95% CI, 1.2 to 8.2), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 3.0 (95% CI, 1.0 to 8.3), p=NR |
| Cases-Exposed (2003-2007) | 69 | 7 (10.1) |
| Cases-Nonexposed | 26954 | 1435 (5.3) |
| Cases-Nonexposed (2003-2007) | 13462 | 783 (5.8) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Peri-membranous ventricular septal defect, n (%) | Venlafaxine | Cases-Exposed | 91 | 6 (6.6) | Cases vs. Controls: OR 2.4 (95% CI, 0.8 to 6.7), p=NS║Cases (2003-2007) vs. Controls (2003-2007): OR 2.0 (95% CI, 0.5 to 6.8), p=NS |
| Cases-Exposed (2003-2007) | 69 | 4 (5.8) |
| Cases-Nonexposed | 26954 | 1404 (5.2) |
| Cases-Nonexposed (2003-2007) | 13462 | 655 (4.9) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Pulmonary valve stenosis, n (%) | Venlafaxine | Cases-Exposed | 91 | 5 (5.5) | Cases vs. Nonexposed: OR 2.7 (95% CI, 0.8 to 7.9), p=NS║Cases (2003-2007) vs. Nonexposed (2003-2007): OR 1.9 (95% CI, 0.3 to 6.9), p=NS |
| Cases-Exposed (2003-2007) | 69 | 3 (4.3) |
| Cases-Nonexposed | 26954 | 980 (3.6) |
| Cases-Nonexposed (2003-2007) | 13462 | 540 (4.0) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Right ventricular outflow tract obstruction defects, n (%) | Venlafaxine | Cases-Exposed | 91 | 5 (5.5) | Cases vs. Controls: OR 2.3 (95% CI, 0.6 to 6.6), p=NS║Cases (2003-2007) vs. Controls (2003-2007): OR 1.5 (95% CI, 0.3 to 5.6), p=NS |
| Cases-Exposed (2003-2007) | 69 | 3 (4.3) |
| Cases-Nonexposed | 26954 | 1245 (4.6) |
| Cases-Nonexposed (2003-2007) | 13462 | 666 (4.9) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Septal heart defects, n (%) | Venlafaxine | Cases-Exposed | 91 | 18 (19.8) | Cases vs. Controls: OR 3.0 (95% CI, 1.4 to 6.4), p=NR║Cases (2003-2007) vs. Controls (2003-2007): OR 2.1 (95% CI, 0.8 to 5.1), p=NS |
| Cases-Exposed (2003-2007) | 69 | 11 (15.9) |
| Cases-Nonexposed | 26954 | 3603 (13.4) |
| Cases-Nonexposed (2003-2007) | 13462 | 1784 (13.3) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Ventricular septal defect-atrial septal defect association, n (%) | Venlafaxine | Cases-Exposed | 91 | 3 (3.3) | Cases vs. Controls: OR 3.1 (95% CI, 0.6 to 11.3), p=NS║ |
| Cases-Exposed (2003-2007) | 69 | 1 (1.4) |
| Cases-Nonexposed | 26954 | 573 (2.1) |
| Cases-Nonexposed (2003-2007) | 13462 | 307 (2.3) |
| Controls-Exposed | 91 | 14 (15.4) |
| Controls-Exposed (2003-2007) | 69 | 4 (5.8) |
| Controls-Nonexposed | 26954 | 7988 (29.6) |
| Controls-Nonexposed (2003-2007) | 13462 | 206 (1.5) |
| Yazdy, 2014158 | Clubfoot, n (%) | SSRI | Cases- Depressed, Exposed >30 days | 622 | 33 (5) | Cases- Depressed, Exposed > 30 days vs. Controls- Depressed, Exposed > 30 days: OR 1.8 (95% CI, 1.1 to 2.8), p=NR\*\*\* |
| Cases- Not Depressed, Nonexposed | 622 | 477 (77) |
| Controls- Depressed, Exposed >30 days | 2002 | 58 (3) |
| Controls- Not Depressed, Nonexposed | 2002 | 1650 (82) |
| Escitalopram | Cases- Depressed, Exposed >30 days | 622 | 9 (1) | Cases- Depressed, Exposed > 30 days vs. Controls- Depressed, Exposed > 30 days: OR 2.9 (95% CI, 1.1 to 7.2), p=NR\*\*\* |
| Cases- Not Depressed, Nonexposed | 622 | 477 (77) |
| Controls- Depressed, Exposed > 30 days | 2002 | 11 (1) |
| Controls- Not Depressed, Nonexposed | 2002 | 1650 (82) |
| Fluoxetine | Cases- Depressed, Exposed > 30 days | 622 | 13 (2) | Cases- Depressed, Exposed > 30 days vs. Controls- Depressed, Exposed > 30 days: OR 1.6 (95% CI, 0.8 to 3.2), p=NR\*\*\* |
| Cases- Not Depressed, Nonexposed | 622 | 477 (77) |
| Controls- Depressed, Exposed > 30 days | 2002 | 26 (1) |
| Controls- Not Depressed, Nonexposed | 2002 | 1650 (82) |
| Louik, 2014159Good | Atrial septal defects, n (%) | SSRI | Cases- exposed | 1135 | 42 (3.7) | Cases vs. Controls: OR 1.3 (95% CI, 0.9 to 1.8), p=NR¶¶ |
| Cases- nonexposed | 1135 | NR |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Atrioventricular canal defects, n (%) | SSRI | Cases- exposed | 514 | 19 (3.7) | Cases vs. Controls: OR 1.3 (95% CI, 0.8 to 2.0), p=NR¶¶ |
| Cases- nonexposed | 514 | NR |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Coarcation of aorta, n (%) | SSRI | Cases- exposed | 471 | 22 (4.7) | Cases vs. Controls: OR 1.8 (95% CI, 1.2 to 2.9), p=NR¶¶ |
| Cases- nonexposed | 471 | 442 (93.8) |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Conotruncal / major arch anomalies, n (%) | SSRI | Cases- exposed | 1418 | 61 (4.3) | Cases vs. Controls: OR 1.6 (95% CI, 1.2 to 2.1), p=NR¶¶ |
| Cases- nonexposed | 1418 | NR |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Left-sided defects, n (%) | SSRI | Cases- exposed | 1220 | 48 (3.9) | Cases vs. Controls: OR 1.4 (95% CI, 1.0 to 1.9), p=NR¶¶ |
| Cases- nonexposed | 1220 | 1159 (95.0) |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Right-sided defects, n (%) | SSRI | Cases- exposed | 1022 | 47 (4.6) | Cases vs. Controls: OR 1.7 (95% CI, 1.2 to 2.3), p=NR¶¶ |
| Cases- nonexposed | 1022 | NR |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Ventricular septal defects, n (%) | SSRI | Cases- exposed | 2704 | 102 (3.8) | Cases vs. Controls: OR 1.3 (95% CI, 1.0 to 1.6), p=NR¶¶ |
| Cases- nonexposed | 2704 | 2571 (95.1) |
| Controls- exposed | 8611 | 290 (3.4) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Ventricular septal defects, n (%) | Buproprion | Cases- exposed | 2704 | 23 (0.9) | Cases vs. Controls: OR 1.6 (95% CI, 1.0 to 2.8), p=NR¶¶ |
| Cases- nonexposed | 2704 | 2571 (95.1) |
| Controls- exposed | 8611 | 39 (0.5) |
| Controls- nonexposed | 8611 | 8241 (95.7) |
| Huybrechts, 2014142Good | Any cardiac malformations, number | Buproprion | Depressed- exposed | 6698 | 57 | OR 0.95 (95% CI, 0.71 to 1.26), p=NS‡ |
| Depressed- nonexposed | 180563 | 1497 |
| Fluoxetine | Depressed- exposed | 8676 | 84 | OR 1.10 (95% CI, 0.87 to 1.40), p=NS‡ |
| Depressed- nonexposed | 180563 | 1497 |
| Paroxetine | Depressed- exposed | 8756 | 71 | OR 0.93 (95% CI, 0.72 to 1.19), p=NS‡ |
| Depressed- nonexposed | 180563 | 1497 |
| Sertraline | Depressed- exposed | 11045 | 106 | OR 1.06 (95% CI, 0.86 to 1.32), p=NS‡ |
| Depressed- nonexposed | 180563 | 1497 |
| SNRI | Depressed- exposed | 5999 | 69 | OR 1.20 (95% CI, 0.91 to 1.56), p=NS‡ |
| Depressed- nonexposed | 180563 | 1497 |
| SSRI | Depressed- exposed | 36783 | 341 | OR 1.08 (95% CI, 0.94 to 1.23), p=NS‡ |
| Depressed- nonexposed | 180563 | 1497 |
| Other cardiac defect, number | Buproprion | Depressed- exposed | 6687 | 37 | OR 1.26 (95% CI, 0.88 to 1.81), p=NS‡ |
| Depressed- nonexposed | 180563 | 743 |
| Fluoxetine | Depressed- exposed | 8655 | 45 | OR 1.22 (95% CI, 0.88 to 1.69), p=NS‡ |
| Depressed- nonexposed | 180563 | 743 |
| Paroxetine | Depressed- exposed | 8751 | 40 | OR 1.08 (95% CI, 0.77 to 1.52), p=NS‡ |
| Depressed- nonexposed | 180563 | 743 |
| Sertraline | Depressed- exposed | 11069 | 57 | OR 1.19 (95% CI, 0.89 to 1.59), p=NS‡ |
| Depressed- nonexposed | 180563 | 743 |
| SNRI | Depressed- exposed | 6001 | 37 | OR 1.36 (95% CI, 0.94 to 1.97), p=NS‡ |
| Depressed- nonexposed | 180563 | 743 |
| SSRI | Depressed- exposed | 36783 | 189 | OR 1.21 (95% CI, 1.00 to 1.45), p=NR‡ |
| Depressed- nonexposed | 180563 | 743 |
| Right ventricular outflow tract obstruction, number | Buproprion | Depressed- exposed | 6696 | <11 | OR 1.07 (95% CI, 0.55 to 2.08), p=NS‡ |
| Depressed- nonexposed | 180563 | 246 |
| Fluoxetine | Depressed- exposed | 8676 | 12 | OR 0.87 (95% CI, 0.47 to 1.63), p=NS‡ |
| Depressed- nonexposed | 180563 | 246 |
| Paroxetine | Depressed- exposed | 8760 | 13 | OR 1.03 (95% CI, 0.57 to 1.85), p=NS‡ |
| Depressed- nonexposed | 180563 | 246 |
| Sertraline | Depressed- exposed | 11064 | 17 | OR 1.08 (95% CI, 0.64 to 1.82), p=NS‡ |
| Depressed- nonexposed | 180563 | 246 |
| SNRI | Depressed- exposed | 36783 | 53 | OR 0.99 (95% CI, 0.70 to 1.38), p=NS‡ |
| Depressed- nonexposed | 180563 | 246 |
| SSRI | Depressed- exposed | 36783 | 53 | OR 0.99 (95% CI, 0.7 to 1.38), p=NS‡ |
| Depressed- nonexposed | 180563 | 246 |
| Ventricular septal defect, number | Buproprion | Depressed- exposed | 6696 | 26 | OR 0.86 (95% CI, 0.57 to 1.31), p=NS‡ |
| Depressed- nonexposed | 180563 | 751 |
| Fluoxetine | Depressed- exposed | 8676 | 41 | OR 1.04 (95% CI, 0.74 to 1.46), p=NS‡ |
| Depressed- nonexposed | 180563 | 751 |
| Paroxetine | Depressed- exposed | 36783 | 155 | OR 0.99 (95% CI, 0.81 to 1.21), p=NS‡ |
| Depressed- nonexposed | 180563 | 751 |
| Sertraline | Depressed- exposed | 11065 | 50 | OR 0.98 (95% CI, 0.72 to 1.34), p=NS‡ |
| Depressed- nonexposed | 180563 | 751 |
| SNRI | Depressed- exposed | 5993 | 34 | OR 1.18 (95% CI, 0.80 to 1.73), p=NS‡ |
| Depressed- nonexposed | 180563 | 751 |
| SSRI | Depressed- exposed | 36783 | 189 | OR 1.21 (95% CI, 1.00 to 1.45), p=NR‡ |
| Depressed- nonexposed | 180563 | 743 |

\*Adjusted by maternal age at end of pregnancy, year of childbirth, Townsend deprivation quintile, maternal smoking history, body mass index before pregnancy, maternal diabetes, hypertension, asthma, and epilepsy in the year pre-conception or during pregnancy.

†Adjusted by maternal age, smoking during pregnancy, maternal race, education, comorbidity, adequacy of prenatal care, maternal parity, infant sex, year of delivery, depression diagnosis before last menstrual period, anxiety disorder, substance abuse, filling prescription before last menstrual period, psych med polytherapy, co-existing psych diagnoses.

‡Adjusted by sociodemographics, multiple gestation, chronic maternal illnesses, use of antidiabetic and antihypertension medications, depression severity, other mental health disorders, sleep disorders, smoking, pain-related diagnoses, premenstrual tension syndrome, chronic fatigue syndrome.

§Adjusted by maternal age, smoking, social status, calendar year, sex of newborn, and use of antiepileptics, antipsychotics and other meds.

║Adjusted by age and race/ethnicity.

¶Adjusted by year of outcome or censoring, maternal age, educational length, income, and number of previous miscarriages.

\*\*Adjusted by maternal age, cohabitation, education, and history of severe mental disorders and drug abuse.

††Adjusted by maternal age, body mass index, parity, educational level, smoking, placenta previa, coagulation defects, abortion history, placental abruption, and depressive symptoms.

‡‡Adjusted by pre-eclampsia risk factor adjustment and number of outpatient depression diagnoses, number of inpatient depression diagnoses, mental disorder complicating pregnancy, pain-related diagnosis, sleep disorder, anticonvulsant dispensing, benzodiazepine dispensing, number of baseline prescription drugs, and number of baseline outpatient visits.

§§Adjusted by delivery year, age, race, multiple pregnancy, diabetes, coagulopathy, number of outpatient mood/anxiety disorder diagnoses, number of inpatient mood/anxiety disorder diagnoses, psychotic disorder, other mental health disorder, pain indication, sleep disorder, anticonvulsant dispensing, benzodiazepine dispensing, aspirin dispensing, heparin dispensing, low molecular weight heparin dispensing, warfarin dispensing, and number of outpatient visits and days in hospital during baseline.

║║Calculated crude OR.

¶¶Adjusted by study center and last menstrual period.

\*\*\*Adjusted by maternal smoking, alcohol use, and BMI.

**Abbreviations:**CI = confidence interval; HR = hazard ratio; NR = not reported; NS = not significant; NSD = no significant difference; OR = odds ratio; RR = relative risk; SNRI = selective norepinephrine reuptake inhibitor; SRI = serotnonin reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.