# Naltrexone Use and Positive Outcomes in Treating Opioid Use Disorder in Pregnancy

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## BACKGROUND

- Opioid agonist drugs buprenorphine and methadone are the mainstay of medication assisted treatment (MAT) for opioid use disorder (OUD) during pregnancy.
- Research has suggested that treatment with opioid antagonist naltrexone may result in superior maternal and fetal outcomes, related to lack of abuse and tolerance development in mothers, and significantly reduced rates of neonatal abstinence syndrome (NAS).
- Despite this, naltrexone remains understudied and under prescribed as an alternative MAT for pregnant women with OUD, due to fear of withdrawal and higher rates of relapse and overdose.

## OBJECTIVE

**This study aimed to evaluate obstetric and neonatal outcomes following naltrexone administration during pregnancy in comparison with other MATs, buprenorphine and methadone.**

## METHODS

- A retrospective cohort study was performed on chart data for all deliveries between 2017 and 2023 at the University of Vermont Medical Center to mothers with OUD treated with naltrexone at any point during pregnancy compared to those treated with either buprenorphine or methadone.
- We collected and assessed maternal and fetal outcomes across these medication groups, including birth growth parameters, APGAR scores, gestational age, delivery complications, congenital abnormalities, NICU admission incidence, NAS incidence and related outcomes.

## RESULTS

**Table 1. Maternal demographic characteristics.***

| Demographic variable | Naltrexone (n=17) | Buprenorphine (n=710) | Methadone (n=169) | MD/OR (Ntx vs. Bup) | MD/OR (Ntx vs. Mth) |
|---|---|---|---|---|---|
| **Maternal age** | 31.9 (5.2) | 29.2 (5.5) | 30.6 (5.7) | **-2.7 (-5.3 to -0.05), P=0.045** | -1.3 (-4.1 to 1.5), P=0.37 |
| **Maternal race** | | | | | |
| **White** | 17 (100%) | 669 (94%) | 152 (90%) | 2.2 (0.13 36.7), P=0.59 | 4.0 (0.23-69.7), P=0.33 |
| **Black** | 0 | 20 (3%) | 7 (4%) | | |
| **Other** | 0 | 21 (3%) | 10 (6%) | | |
| **Other substance exposures** | | | | | |
| **Alcohol** | 7 (41%) | 170 (24%) | 55 (33%) | 2.2 (0.83-5.9), P=0.11 | 1.5 (0.52-4.0), P=0.47 |
| **Nicotine** | 10 (59%) | 267 (38%) | 61 (36%) | 2.4 (0.89-6.3), P=0.08 | 2.5 (0.92-6.0), P=0.07 |
| **Other** | 8 (47%) | 116 (16%) | 42 (25%) | **4.6 (1.7-12.0), P=0.002** | 2.7 (0.97-7.4), P=0.06 |
| **Co-occurring psychiatric disorders** | | | | | |
| **Anxiety** | 15 (88%) | 222 (31%) | 53 (31%) | **16.5 (3.7-72.7), P=0.0002** | **16.4 (3.6-74.4), P=0.0003** |
| **Depression** | 12 (71%) | 280 (39%) | 85 (50%) | **3.7 (1.3-10.6), P=0.015** | 2.4 (0.8-7.0), P=0.12 |
| **PTSD** | 3 (18%) | 54 (8%) | 34 (20%) | 2.6 (0.73-9.3), P=0.14 | 0.9 (0.23-3.1), P=0.81 |
| **Other** | 6 (35%) | 324 (46%) | 69 (41%) | 0.64 (0.24-1.8), P=0.40 | 0.8 (0.28-2.2), P=0.66 |
| **History of relevant communicable disease(s)** | 7 (41%) | 196 (28%) | 61 (36%) | 1.8 (0.69-4.9), P=0.22 | 1.2 (0.45-3.4), P=0.68 |
| **Received prenatal care** | 15 (88%) | 667 (94%) | 145 (86%) | 0.48 (0.11-2.2), P=0.34 | 1.2 (0.27-5.8), P=0.78 |
| **Delivery type** | | | | | |
| **Vaginal** | 10 (59%) | 454 (64%) | 104 (62%) | 0.80 (0.30-2.1), P=0.66 | 0.9 (0.32-2.5), P=0.82 |
| **Cesarian** | 7 (41%) | 256 (36%) | 65 (38%) | 1.2 (0.47-3.3), P=0.66 | 1.1 (0.40-3.1), P=0.82 |

**Table 2. Maternal/fetal outcomes.***

| Maternal/fetal Variable | Naltrexone (n=17) | Buprenorphine (n=710) | Methadone (n=169) | MD/OR (Ntx vs. Bup) | MD/OR (Ntx vs. Mth) |
|---|---|---|---|---|---|
| **Gestational age (weeks)** | 39.2 (1.3) | 38.6 (1.6) | 37.8 (2.1) | -0.6 (-1.4 to 0.17), P= 0.13 | **-1.4 (-2.4 to -0.37), P= 0.01** |
| **Birth weight (grams)** | 3130 (335) | 2983 (551) | 2923 (625) | -147 (-411 to 116), P= 0.27 | -207 (-511 to 97), P= 0.18 |
| **Head circumference (cm)** | 33.8 (1.2) | 33.6 (1.8) | 33.3 (1.7) | -0.2 (-1.1 to 0.7), P=0.65 | -0.5 (-1.3 to 0.3), P=0.24 |
| **APGAR Scores** | | | | | |
| **1 min** | 8.4(0.7) | 8.0 (1.2) | 7.6 (1.7) | -0.4 (-1.0 to 0.2), P= 0.17 | -0.8 (-1.6 to 0.02), P= 0.06 |
| **5 mins** | 8.7 (0.4) | 8.7 (0.8) | 8.4 (1.3) | NA | -0.3 (-0.9 to 0.3), P=0.34 |
| **NICU Admissions** | 0 (0%) | 26 (4%) | 10 (6%) | NA | NA |
| **Length of stay (days)** | 4.2 (5.4) | 6.4 (5.7) | 9.2 (9.9) | 2.2 (-0.5-4.9), P=0.12 | **5.0 (0.18 to 9.8), P=0.04** |
| **NAS outcomes** | | | | | |
| **NAS diagnosis** | 1 (6%) | 371 (52%) | 125 (74%) | **0.06 (0.01-0.43), P<0.001** | **0.02 (0.003-0.17), P<0.001** |
| **Pharmacologic tx** | 0 (0%) | 55 (8%) | 53 (31%) | NA | NA |
| **Congenital Anomalies** | 0 (0%) | 17 (2%) | 11 (7%) | NA | NA |

*Statistics reported to 95% CI. Statistics reported in means unless otherwise indicated.

## DISCUSSION

- We find that among naltrexone-maintained mothers with OUD, there was a higher likelihood of history of other substance exposure, co-occurring anxiety and depression, and older maternal age than among buprenorphine or methadone mothers.
- The naltrexone group also showed significant reduction in NAS diagnoses than either buprenorphine or methadone. Compared to methadone, particularly, naltrexone showed better efficacy across many parameters such as LOS or need for pharmacologic treatment of neonatal withdrawal.
- Our study suggests that maintenance of pregnant women with OUD on naltrexone may have as adequate of fetal outcomes as MAT with buprenorphine or methadone. We identify preliminary evidence that naltrexone could therefore be a potential option for OUD treatment for mother/infant dyads, especially when addressing NAS and NAS-related outcomes.
- Our study may be limited by the small sample size of naltrexone exposed pregnancies and retrospective design of our study. Outcomes may also have been driven by confounding polysubstance use during pregnancy. More research will be required to better understand long-term safety and efficacy of naltrexone administration in pregnancy.

## REFERENCES

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