

# Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

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## Background

Methadone, a full mu-opioid agonist, is the recommended treatment for opioid dependence during pregnancy. However, prenatal exposure to methadone is associated with a neonatal abstinence syndrome (NAS) characterized by central nervous system hyperirritability and autonomic nervous system dysfunction, which often requires medication and extended hospitalization. Buprenorphine, a partial mu-opioid agonist, is an alternative treatment for opioid dependence but has not been extensively studied in pregnancy.

## Methods

We conducted a double-blind, double-dummy, flexible-dosing, randomized, controlled study in which buprenorphine and methadone were compared for use in the comprehensive care of 175 pregnant women with opioid dependency at eight international sites. Primary outcomes were the number of neonates requiring treatment for NAS, the peak NAS score, the total amount of morphine needed to treat NAS, the length of the hospital stay for neonates, and neonatal head circumference.

## Results

Treatment was discontinued by 16 of the 89 women in the methadone group (18%) and 28 of the 86 women in the buprenorphine group (33%). A comparison of the 131 neonates whose mothers were followed to the end of pregnancy according to treatment group (with 58 exposed to buprenorphine and 73 exposed to methadone) showed that the former group required significantly less morphine (mean dose, 1.1 mg vs. 10.4 mg;  $P < 0.0091$ ), had a significantly shorter hospital stay (10.0 days vs. 17.5 days,  $P < 0.0091$ ), and had a significantly shorter duration of treatment for the neonatal abstinence syndrome (4.1 days vs. 9.9 days,  $P < 0.003125$ ) ( $P$  values calculated in accordance with prespecified thresholds for significance). There were no significant differences between groups in other primary or secondary outcomes or in the rates of maternal or neonatal adverse events.

## Conclusions

These results are consistent with the use of buprenorphine as an acceptable treatment for opioid dependence in pregnant women. (Funded by the National Institute on Drug Abuse; ClinicalTrials.gov number, [NCT00271219](#).)

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[Disclosure forms](#) provided by the authors are available with the full text of this article at [NEJM.org](#).

## Source Information

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