

# Comparing Buprenorphine and Methadone to Morphine in the Treatment of Neonatal Abstinence Syndrome

## Background

### What is neonatal abstinence syndrome (NAS)?

- NAS is a compilation of conditions affecting the gastrointestinal, autonomic and central nervous systems after a baby is exposed to certain drugs, classically opioids, in utero.

### How is NAS treated?

- Nonpharmacologic and pharmacologic interventions are utilized to treat NAS.
- Currently, morphine is the most widely used first-line pharmacologic agent for symptoms of withdrawal.
- No standards of practice have been established.

## Introduction

### Rational of importance

- Incidence has increased four-fold in a decade.
- Financial burden from longer hospital stays.

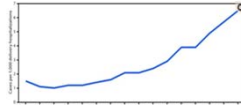


Figure 1: Incidence of NAS per 1,000 births, 1999-2014

- Currently no organized state reporting, leading to lack of framework for policy and clinical intervention.

### PICO Question

In opioid-dependent newborn babies with NAS, is treatment with buprenorphine or methadone superior to morphine?

## Methods

### Search Strategies

- Databases used: Google Scholar, PubMed, Embase, and JSTOR. Search terms included neonatal abstinence syndrome, morphine, methadone, buprenorphine.
- No studies on the antenatal prevention of NAS were included.
- Priority given to systematic reviews and meta-analyses

## Result overview

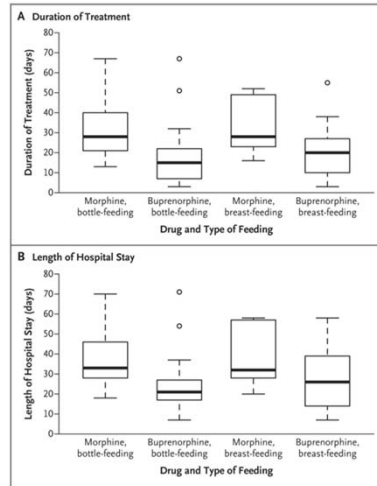


Figure 2: Duration of treatment (Panel A) and length of hospital stay (Panel B) using box-and-whisker plots represent medians (horizontal lines) and interquartile ranges (top and bottom of the boxes).

## Comparison of Treatments

### Morphine to buprenorphine

- Median length of treatment (LOT) was significantly shorter with buprenorphine than with morphine (15 days vs. 28 days), as was the median length of hospital stay (LOS) (21 days vs. 33 days) ( $P < 0.001$  for both comparisons).

### Morphine to methadone

- Mixed results from various studies, but overall favor morphine treatment over methadone due to less side effects and shorter LOS and LOT.

### Buprenorphine to methadone

- Buprenorphine shortens LOS (4.4 days) and length of treatment (4.6 days).

## Overall

- Significantly more research exists on use of morphine to treat NAS compared to buprenorphine, methadone, and alternative treatment options.
- Though limited data is available, buprenorphine may be the new treatment of choice.

## Analysis/Discussion

### Barriers

- There are many tools used to evaluate NAS, and different studies used different tools. This makes comparing results difficult.
- Demographics were not consistent across studies.
- History of mothers' opioid use is not always clear or considered.
- Range of sample sizes, from 26 to 7667

### Supplemental Research

- Various treatment options for opioid-dependent pregnant women can affect overall LOS and LOT for the infant with NAS, and may even help prevent NAS.

## Conclusions/Further Study

- This analysis was conducted based on primarily level 1 evidence.
- Positive and consistent results show treatment of NAS with buprenorphine is superior to morphine in term of reducing LOS and LOT.
- Data is still limited and replication studies must occur before practice guidelines are established or changed.
- To improve NAS research in the future, a national standardized system for NAS monitoring should be developed.

## Acknowledgements

### References

- Figure 1: National prevalence of opioid use disorder per 1,000 delivery hospitalizations: — National Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP), United States, 1999–2014
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- Figure 2: Kraft, W. K., Adeniyi-Jones, S. C., Chervoneva, I., Greenspan, J. S., Abatemarco, D., Kaitenbach, K., & Ehrlich, M. E. (2017). Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome. *New England Journal of Medicine*, 376(24), 2341–2348. doi: 10.1056/nejmoa1614835