Eur Addict Res 2012;18:322

DOI: [10.1159/000341994](https://doi.org/10.1159/000341994)

The Complex Factors Determining Neonatal Abstinence Syndrome and Its Management

Robert G. Newman^a, Susan G. Gevertz^b

^aBaron Edmond de Rothschild Chemical Dependency Institute, Beth Israel Medical Center, New York, N.Y., and ^bWestchester County Health Care Corporation, Valhalla, N.Y., USA

Baewert et al. [1] have provided a dramatic illustration of the influence of unknown site-specific factors in determining clinical observations associated with the use of buprenorphine and methadone in the treatment of opioid-dependent women. They analyzed, by site location, maternal and neonatal outcomes as reported by the investigators of Maternal Opioid Treatment: Human Experimental Research (MOTHER) [2]. Some of the major limitations in the ability to extrapolate the research findings of that study to clinical practice have been noted elsewhere [3], but they are underscored by the disparities noted by Baewert et al. in the three settings in which MOTHER was carried out: urban and rural America, and Central Europe (Vienna).

For example, following randomization to one of the two medications, the overall dropout rate prior to delivery varied from 10% among those participating in Vienna to 37% of the urban American sample (one of the urban US facilities enrolled 32 women in the study, of whom 53% dropped out before giving birth). As for neonatal management, there were major differences among the three location study groups for both the methadone- and the buprenorphine-exposed babies, but they were particularly striking for the former. Thus, to babies whose mothers received methadone the total morphine dose administered to control neonatal abstinence syndrome (NAS) averaged 4.93 mg in rural American sites, 5.04 mg in Vienna, and 34.17 mg in urban US sites; the number of days of medication averaged 4.92, 9.26 and 17.91, respec-

tively. Length of neonatal hospital stay was 12.95 days in rural US locations, 16.16 days in Vienna, and 22.37 days in urban American sites. For each of these neonatal outcomes, the highly variant data for methadone-exposed babies were lumped together and compared to a composite of the reported findings for the newborns whose mothers had received buprenorphine, and the differences were stated to be 'significant'. (No statistically significant differences were cited by the authors of the MOTHER study for any of the other primary or secondary outcomes of neonates or mothers.)

The widely disparate experiences reported for the three site categories render highly tentative any conclusions one might draw from the MOTHER study regarding comparative effect or effectiveness of the two medications, and provide clinicians little guidance in recommending to their patients one or the other treatment option. The analysis of Baewert and colleagues underscores the complexity of NAS in the offspring of women receiving opioid maintenance treatment during pregnancy. Further, it raises critically important questions that must be addressed by additional research before evidence-based, clinically-relevant conclusions can be drawn. For now, it seems clear that there are powerful non-pharmacological factors that influence both the diagnosis and management of NAS.

References

- 1 Baewert A, Jagsch R, Winklbaier B, Kaiser G, Thau K, Unger A, Aschauer C, Weninger M, Metz V: Influence of site differences between urban and rural American and Central European opioid-dependent pregnant women and neonatal outcome characteristics. *Eur Addict Res* 2012;18:130–139.
- 2 Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM, O'Grady KE, Selby P, Martin PR, Fischer G: Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med* 2010;363:2320–2331.
- 3 Newman RG, Gevertz SG: Efficacy versus effectiveness of buprenorphine and methadone maintenance in pregnancy. *J Addict Dis* 2011;30:318–322.