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A Comparison of Pharmacologic Interventions in Pregnant Women with Opioid Use Disorder

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Abstract

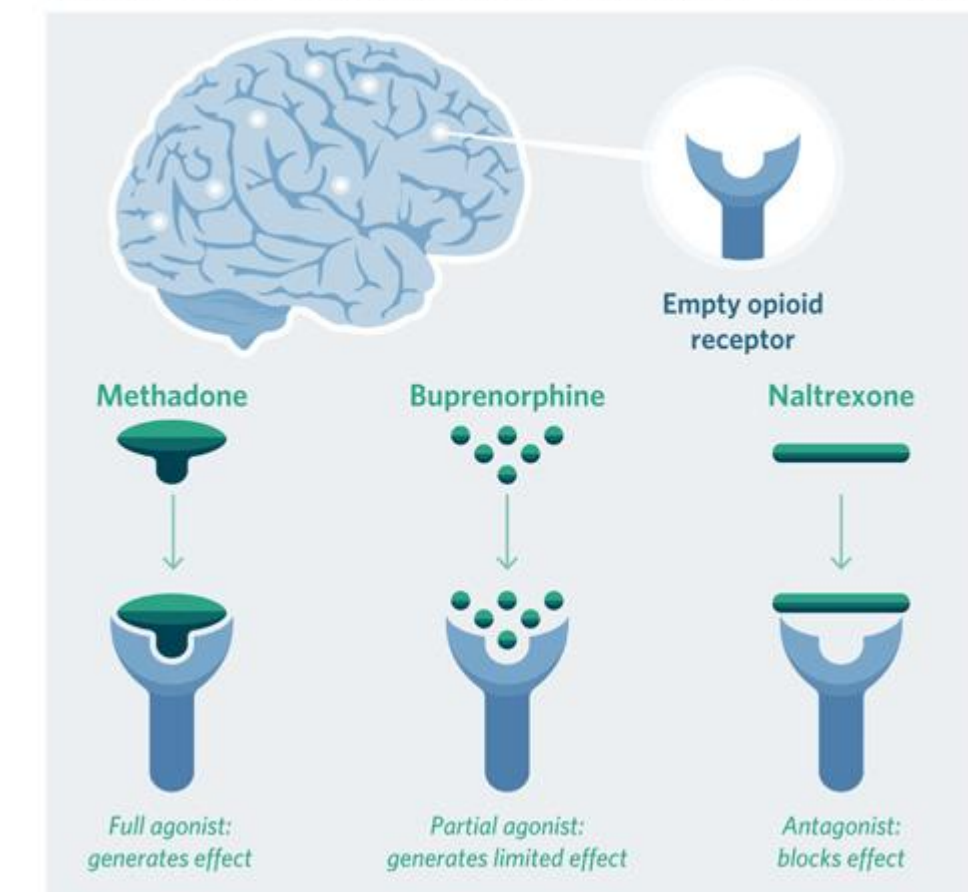
The purpose of this research and systematic literature review is to determine which pharmacotherapeutic agent, methadone or buprenorphine, leads to better outcomes in cases of pregnant mothers with opioid use disorder (OUD). Outcomes considered are maternal compliance, neonatal abstinence syndrome severity, and neonatal length of hospital stay. In the review, PubMed, Clinical Key, Cochrane Database of Systematic Reviews, and DynaMed Plus were searched. Key terms searched were “methadone, buprenorphine, pregnancy”, “opioids, pregnancy”, “neonatal abstinence syndrome” and “medication assisted treatment, pregnancy”. Several studies were excluded, as their study population was not specified to have diagnosed OUD in pregnancy. The drawbacks to many of the studies is the inconsistencies in study conditions, and very small sample sizes. Much of the research presented shows evidence for the use of buprenorphine in the treatment of OUD in pregnancy. Buprenorphine seems to be a better medication assisted treatment (MAT) for the neonate in terms of reduced neonatal abstinence syndrome (NAS) and reduced length of hospital stay postpartum, while methadone still performs better for adherence for the mother. More research still needs to be done in order to demonstrate buprenorphine’s superior efficacy compared to methadone use in pregnant patients with OUD.

Keywords: MAT, methadone, buprenorphine, pregnancy, OUD, opioid, addiction, NAS, neonate

Introduction

Opioid addiction in the United States has become a major public health crisis. The Centers for Disease Control and Prevention (CDC) estimates that 134 people die from opiate overdose each day. Neonates who are heavily exposed to opiates in utero often experience withdrawal upon parturition, a condition called neonatal abstinence syndrome (NAS). NAS increased by 500% in the US between 2000 and 2012. Treatment protocol supports the use of MAT to prevent NAS. Currently, methadone is administered to prevent pregnant women from abusing opiate substances, namely heroin or prescription opiates. However, a growing body of evidence supports other MAT drugs, most notably buprenorphine, for use in pregnant patients.

How OUD Medications Work in the Brain



Note. Adapted from “Children’s Services Practice Notes” (2018) North Carolina Child Welfare Social Workers, 23:2. Retrieved from <http://www.practicenotes.org/v23n2/MAT.htm>

Statement of the Problem

Methadone is the current standard of care for the use of MAT in pregnant women with OUD. Studies are needed to show the safety and efficacy of other treatment options such as buprenorphine for this patient population.

Research Questions

- ❖ In pregnant patients with OUD, how effective is methadone compared to buprenorphine in the reduction of NAS?
- ❖ In pregnant patients with OUD, how effective is methadone compared to buprenorphine in the reduction in length of hospital stay for neonates?
- ❖ In pregnant patients with OUD, how effective is methadone compared to buprenorphine in retention on MAT and prevention of relapse?

Literature Review

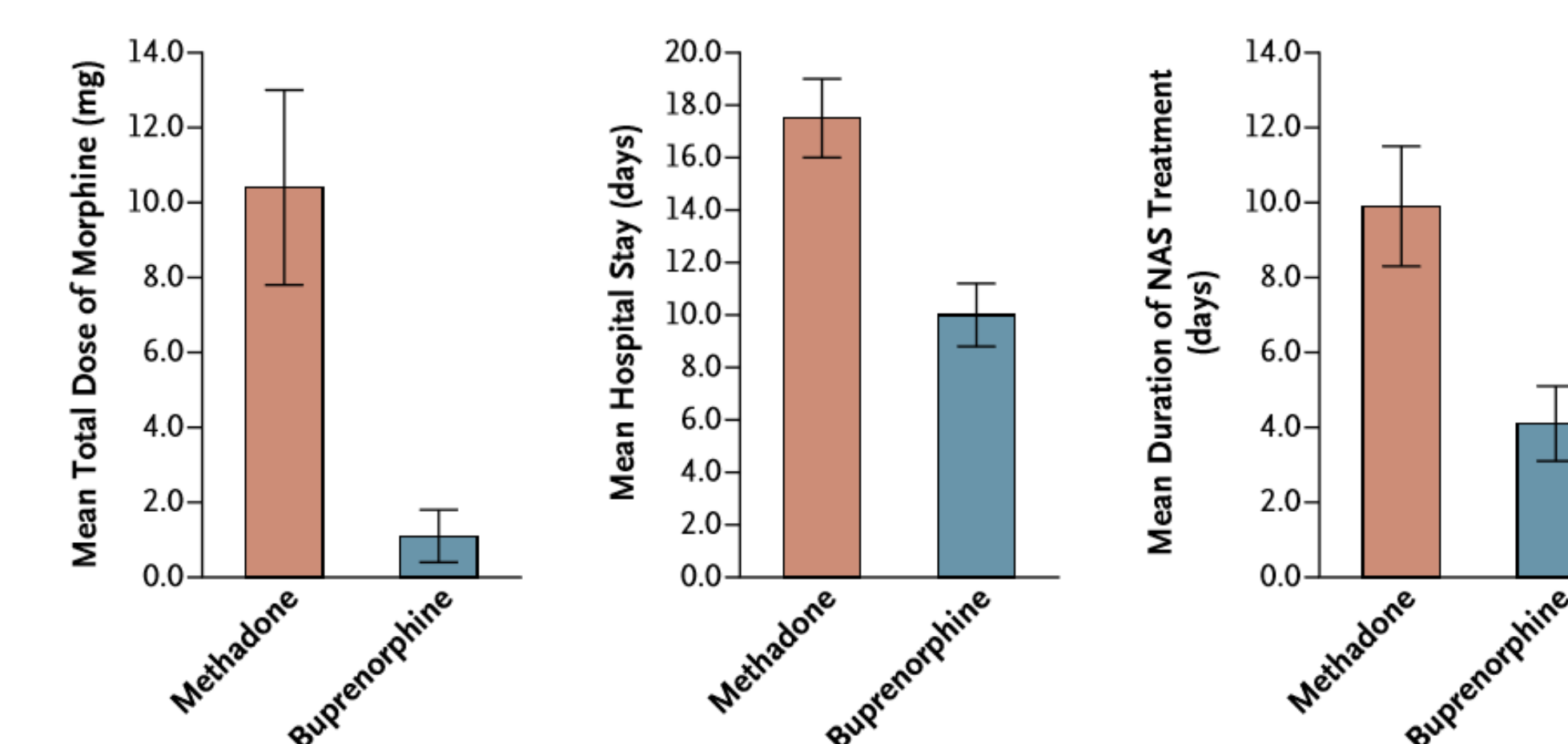
Maintenance treatment provides a steady concentration of opiate in the pregnant woman’s blood and so prevents the adverse effects on the fetus of repeated withdrawals (Minozzi et al., 2013). In conjunction with psychosocial and cognitive behavioral therapy, **MAT is endorsed over medically assisted withdrawal or abstinence for pregnant women with OUD by the Substance Abuse and Mental Health Services Administration and the American College of Obstetricians and Gynecologists Committee** (Tran, Griffin, Stone, Vest, & Todd, 2017).

- Fowler et al., (2013) found that buprenorphine led to better outcomes for neonates but had dropout rates of 56.4% compared to methadone. Also, buprenorphine led to a cost savings of over \$12.4 million healthcare dollars.
- Jansson et al., (2017) found that of mothers treated with buprenorphine, had a high dropout rate, and total length of hospitalization of neonates was 14.7 days on average.
- A Cochrane review found that mothers on methadone therapy are less likely to drop out of the study (RR 0.64, 95% CI 0.41 to 1.01, n=223) compared to those on buprenorphine. There was no significant difference in the number of newborns treated for NAS, but evidence is considered very low (RR 1.22, 95% CI 0.89 to 1.67, three studies, n=166) (Minozzi et al., 2013).
- The MOTHER study by Jones et al., (2010) showed discontinuation of treatment occurred in 18% of women in methadone treatment and 33% of women in buprenorphine treatment (p=0.02). The number of neonates requiring NAS treatment was not significantly different between groups (p=0.26). Neonates from the buprenorphine group needed 89% less morphine than those exposed to methadone (p<0.0091) and spent 43% less time in the hospital (p<0.0091).
- Pregnant women addicted to intravenous heroin were studied in a five-year randomized prospective comparative study by Binder and Vavřínková (2008). The degree of NAS severity was 9.2 in the buprenorphine group, 11 in the heroin group, and 17.8 in the methadone group (buprenorphine to methadone p<0.00001, heroin to methadone p<0.00001).

Discussion

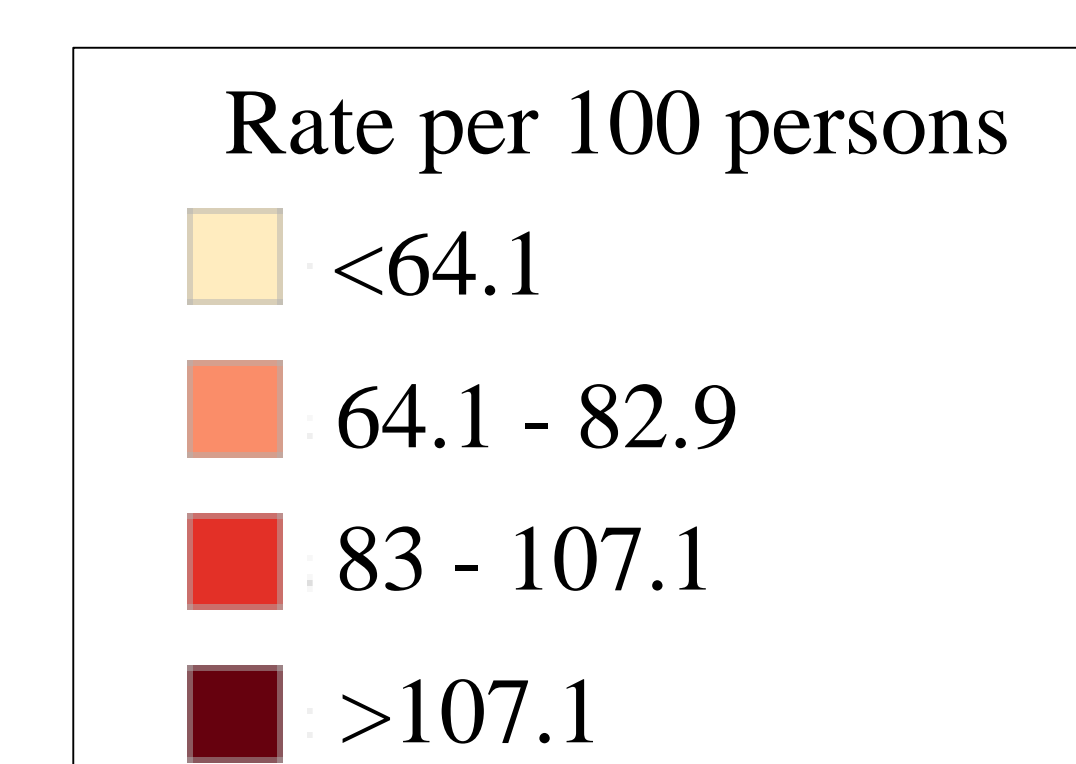
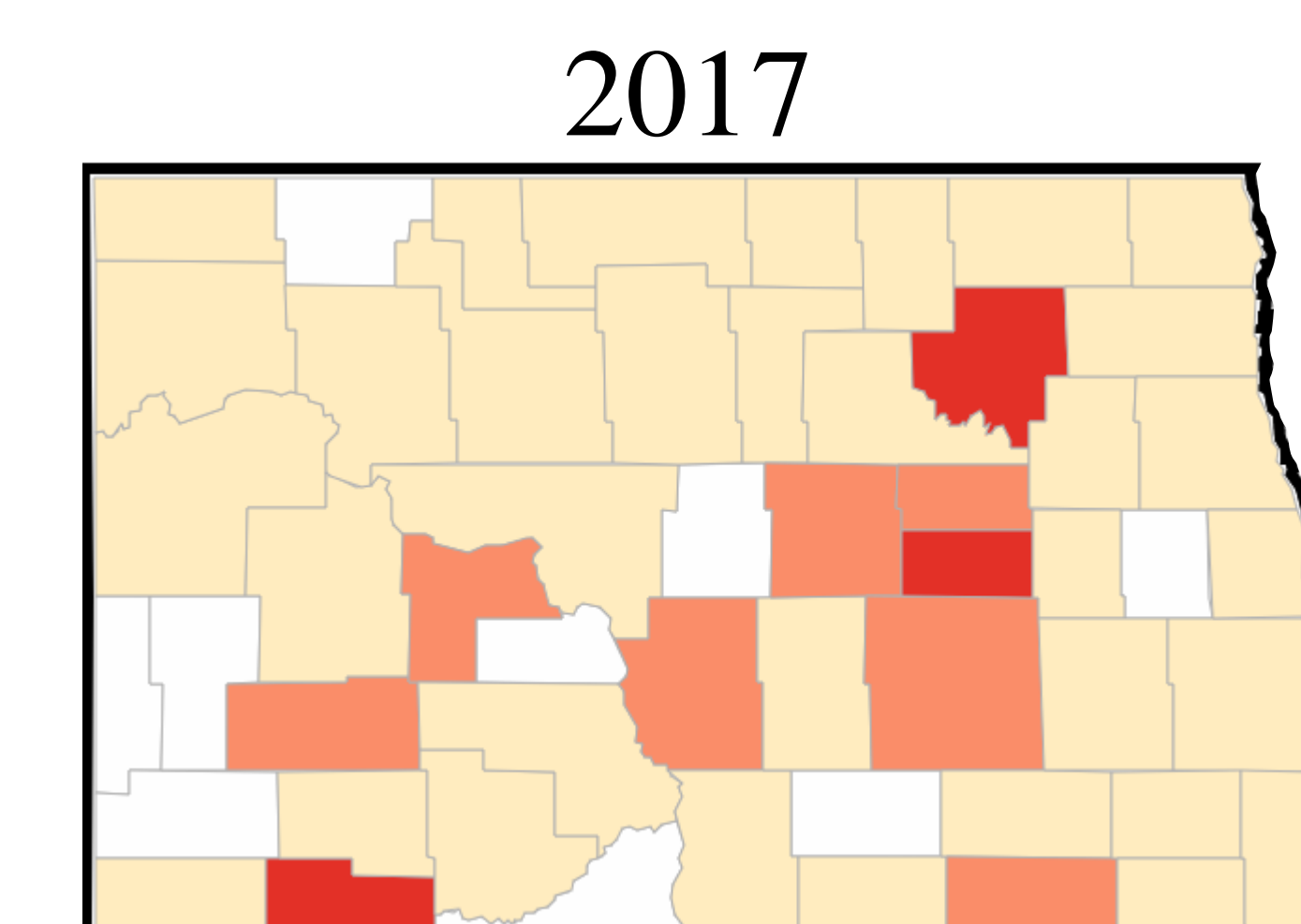
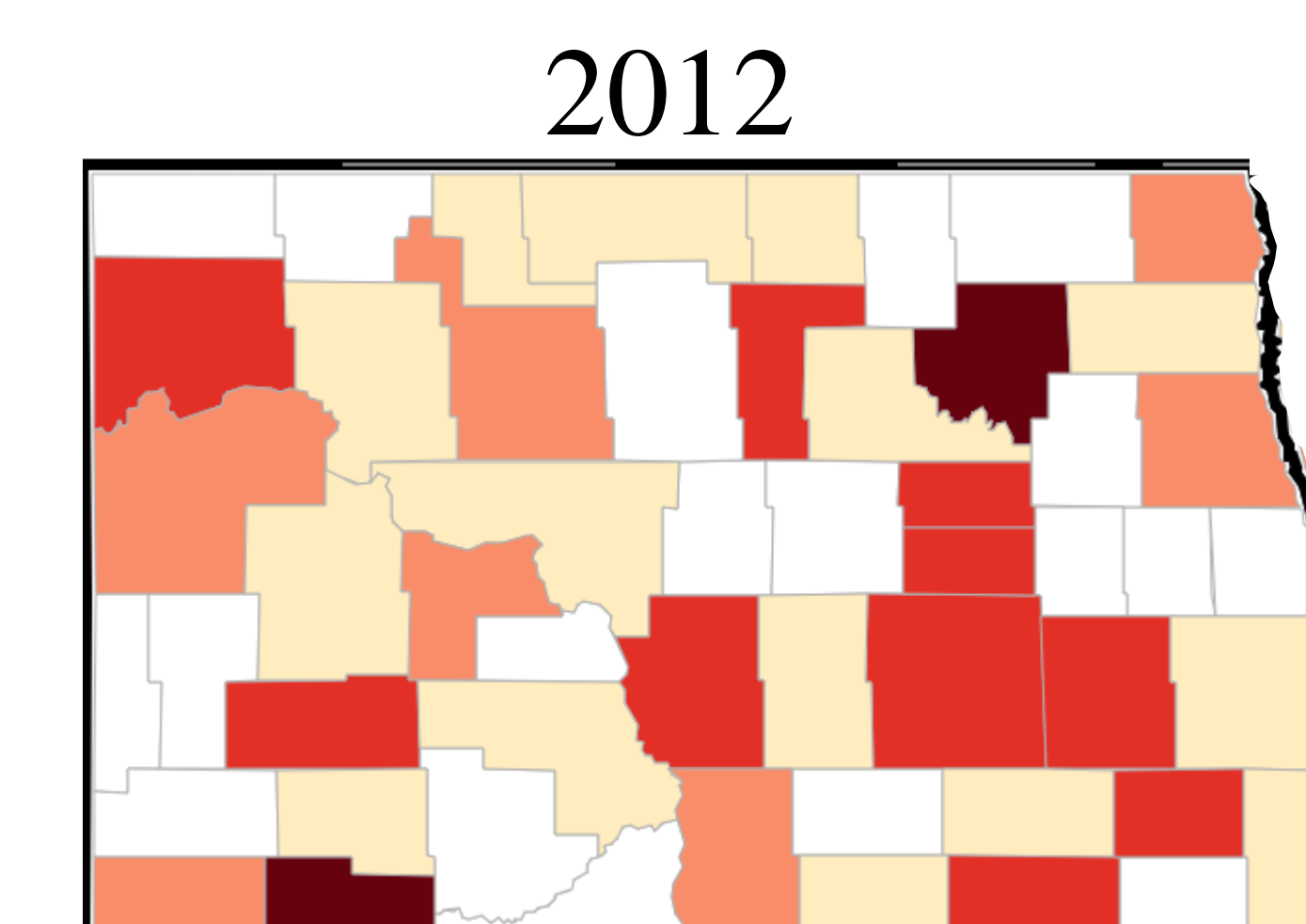
Although buprenorphine is not the standard of care for pregnant women with OUD, it should be considered as an alternative to methadone maintenance therapy. NAS is reduced with buprenorphine compared to methadone treatment, though more women sustain MAT with methadone. Because NAS is less severe with buprenorphine MAT compared to methadone MAT, length of stay (LOS) is less with buprenorphine exposed neonates and thus is a more effective way to spend the very limited healthcare dollars that exist for these patients. In addition, MAT drug choice should be individual. Finally, if one MAT drug is failed, another should be initiated.

Methadone Versus Buprenorphine



Note. Adapted from “Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure” by H.E. Jones, et al., 2010. The New England Journal of Medicine, 363:24 p 2327. Copyright © 2010 Massachusetts Medical Society

ND Opioid Prescribing Rate Maps



Note. Adapted from U.S. Opioid Prescribing Rate Maps. (2018). Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention. U.S. Department of Health and Human Services. Retrieved from: <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html>

Applicability to Clinical Practice

North Dakota experiences opioid addiction across the state but faces challenges for patients to get the care they need due to a lack of specialists and a vastness of rural geography. Since stigma still exists with MAT, providers should be given the tools to screen, refer, and care for pregnant mothers with OUD. Withdrawal during pregnancy should be discouraged, and personal judgements withheld.

- **Project ECHO** or “Extension for Community Healthcare Outcomes” is a hub and spoke model used to train rural providers with resources and information through video conferencing. Project ECHO is focused on the opioid epidemic in North Dakota and provides video sessions weekly from experts and specialists in academic or health care centers to primary care teams in rural parts of the state.
- **Champion Prescriber** initiative expands access to MAT in North Dakota. These providers provide MAT treatment and overdose prevention education, collaborate with providers in project ECHO, and provide training on the use of Naloxone.
- **The First Steps to Healthy Babies** service provided by Sanford in Bemidji, MN aims to help women have safe and healthy pregnancies and encourages sobriety with support services. They have seen a significant increase in the number of mothers who undergo MAT during pregnancy and are able to return home with their infant.

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