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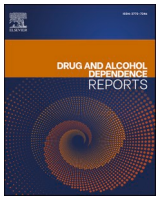

County-level neonatal opioid withdrawal syndrome rates and real-world access to buprenorphine during pregnancy: An audit ("secret shopper") study in Missouri

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HIGHLIGHTS

- This secret shopper study shows that 81 of Missouri's 115 counties have no capacity for buprenorphine prescribing during pregnancy.
- Greater buprenorphine capacity did not correspond to decreased neonatal opioid withdrawal syndrome rates.
- Rurality did not significantly predict elevated rates of neonatal opioid withdrawal syndrome.

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ABSTRACT

Background: Amid rising rates of neonatal opioid withdrawal syndrome (NOWS) worldwide and in many regions of the USA, we conducted an audit study ("secret shopper study") to evaluate the influence of county-level buprenorphine capacity and rurality on county-level NOWS rates.

Methods: In 2019, up to three phone calls were made to buprenorphine prescribers in the state of Missouri (USA). County-level buprenorphine capacity was defined as the number of clinicians (across all specialties) accepting pregnant people divided by the number of births. Multivariable negative binomial regression models estimated associations between buprenorphine capacity, rurality, and county-level NOWS rates, controlling for potential confounders (i.e., poverty, unemployment, and physician shortages) that may correspond to higher rates of NOWS and lower rates of buprenorphine prescribing. Analyses were stratified using tertiles of county-level overdose rates (top, middle, and lowest 1/3 of overdose rates).

Results: Of 115 Missouri counties, 81(70 %) had no buprenorphine capacity, 17(15 %) were low-capacity (<0.5-clinicians/1,000 births), and 17(15 %) were high-capacity (≥0.5/1,000 births). The mean NOWS rate was 6.5/1,000 births. In Missouri counties with both the highest and lowest opioid overdose rates, higher buprenorphine capacity did not correspond to decreases in NOWS rates (incidence rate ratio[IRR]=1.23[95 %-confidence-interval[CI]=0.65–2.32] and IRR=1.57[1.21–2.03] respectively). Rurality did not correspond to greater NOWS burden in both Missouri counties with highest and lowest opioid overdose rates.

Conclusions: The vast majority of counties in Missouri have no capacity for buprenorphine prescribing during pregnancy. Rurality and lower buprenorphine capacity did not significantly predict elevated rates of NOWS.

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1. Introduction

Opioid use disorder (OUD) is a major public health problem globally, evidenced by over 26 million people living with OUD worldwide in 2016 and 100,000 opioid overdose deaths occurring annually (Strang et al., 2020). Over the past two decades, the incidence of OUD in pregnant people has also risen worldwide, particularly in the United States of America (USA) and Canada (Davies et al., 2016). In the USA, rates of OUD during pregnancy have increased from approximately 1/1000 delivery hospitalizations in 2000 to over 6/1000 in 2014 (Haight et al., 2018). From 2017 to 2020, overdose mortality increased 81 % among pregnant and postpartum people in the USA (Bruzelius and Martins, 2022), as a recent comparison of pre- and post-COVID-19 data showed that overdose mortality increased more than 3-fold in pregnant and postpartum people aged 35–45 years in the USA from 2018 to 2021 (Han et al., 2023).

Opioid exposure during pregnancy is associated with adverse maternal and fetal outcomes, including increased rates of neonatal opioid withdrawal syndrome (NOWS), a condition characterized by nervous system irritability, autonomic dysfunction, and gastrointestinal dysfunction, in neonates (Patrick et al., 2012, 2020). While recent years have seen promising advances in diagnostic criteria development, clinical assessment, and non-pharmacologic (i.e., environmental and feeding interventions) and pharmacologic management (i.e., symptom-triggered dosing protocols) of NOWS (Mascarenhas et al., 2024), the prevalence of NOWS has grown in the USA, from 1.5/1000 births in 2004 (Kocherlakota, 2014) to 6.0/1000 births in 2020 (CDC, 2021). A January 2024 analysis of prenatal opioid exposure in the USA notes that while some states have experienced a decline in NOWS rates since 2017 (i.e., Massachusetts, Rhode Island, Connecticut, Vermont, Colorado), other states have seen increases in NOWS, especially in the Appalachian, Southern, Western, and Midwestern regions (Mascarenhas et al., 2024) Furthermore, prenatal opioid exposure is not only a problem in the USA but also worldwide. In England, the incidence of NOWS admissions to National Health Service neonatal units increased nearly 30 % from 2012 to 2017 (Rees et al., 2021). In Canada, national data (excluding Quebec) showed that NOWS hospitalizations have gradually increased from 3.5/1000 live births in 2010 to 6.3/1000 live births in 2020 (Canada.Ca, 2021). Elevated rates of NOWS have also been observed in studies from Western Australia throughout the 2000s and 2010s, remaining stable at 3–4/1000 live births (Kelty et al., 2022).

Treating OUD during pregnancy with medications such as buprenorphine and methadone improves outcomes for mothers and infants compared to non-treatment, thus decreasing the likelihood and/or severity of NOWS (Jones et al., 2010, 2008; Piske et al., 2021). Against the backdrop that approximately 50 % of pregnant people with OUD do not receive medications to treat OUD in the USA (Xu et al., 2023a, 2023b), policymakers and physicians suggested that boosting buprenorphine uptake was a critical component for improving OUD outcomes (Sciences, 2019), particularly in suburban and rural communities thought to be most heavily impacted by OUD during earlier waves of the opioid epidemic (Hansen and Netherland, 2016). Although improvements in all maternal, fetal, and pregnancy outcomes with buprenorphine have been well-documented in clinical studies (ACOG, 2017; Jones et al., 2010), the relationship between real-world buprenorphine access, area-based characteristics, and NOWS rates remains a topic area that requires more research. Amid such uncertainties surrounding the influence of buprenorphine capacity on OUD outcomes, we conducted a "secret shopper" (audit) study, a method allowing us to gain insight into the real-world challenges of accessing buprenorphine that may be difficult to study via other methods (i.e., clinical trials, administrative data analyses) (Rankin et al., 2022).

Our study sought to identify the number of prescribers offering buprenorphine to pregnant patients in the 115 counties of the Midwestern USA state of Missouri, where the rate of OUD diagnosis during pregnancy (2 %) is close to the USA national mean (2.7 % among pregnant people and 2 % among adults overall in the USA),(Roberts et al., 2023) Yet, Missouri has recently seen its rate of NOWS increase from 5.2/1000 births in 2017 to 7/1000 births in 2020.(Mascarenhas et al., 2024). Recent estimates suggesting that 40 % of pregnant and postpartum Missourans with OUD receive no medication to treat OUD (Roberts et al., 2023).

By linking the availability of buprenorphine with county-level data on NOWS, we sought to investigate the relationship between the real-world challenges of accessing buprenorphine and OUD outcomes during pregnancy in Missouri. We were especially interested in the association between rurality and NOWS rates, given that rurality has historically received much attention for co-localizing with overdoses and more severe OUD outcomes (Friedman et al., 2023). Because the association of buprenorphine capacity and NOWS may be confounded by regional differences in OUD severity, our analyses sought to control for confounding variables such as overdose rates, physician shortages, and social determinants of health such as manufacturing, poverty, and unemployment.

2. Methods

This study was exempt from review by the Washington University institutional review board as "secret shopper" analyses are not considered human subjects research (Rankin et al., 2022).

2.1. Study design and analysis

To determine county-level capacity for buprenorphine, we used our previously published retrospective cross-sectional phone audit of opioid treatment programs and buprenorphine clinicians in Missouri (Bedrick et al., 2020). Methods for the present "secret shopper" study have been previously described in detail and are also included in the eMethods (Bedrick et al., 2020). In brief, as part of the Drug Addiction Treatment Act (also known as DATA 2000), the Substance Abuse and Mental Health Services Administration (SAMHSA) maintains practice locations for physicians with buprenorphine waivers who have granted permission to be listed in the buprenorphine treatment practitioner locator, which can be used to study buprenorphine capacity (Jones and McCance-Katz, 2019; Jones et al., 2018). We thus used the SAMHSA locator to identify buprenorphine practitioners in December 2018.Subsequently, between February and April 2019, up to three phone calls were made to each practice to determine if the listed clinicians and treatment programs in the SAMHSA directory were currently accepting new pregnant patients. The practices were grouped by county to determine the total number of practices accepting pregnant patients per county from February to April 2019. County buprenorphine capacity was defined as the total number of clinicians treating pregnant patients divided by the number of county births from all available years (2014 to 2018).

2.2. Predictor variable

The primary predictor variable was buprenorphine capacity, categorized as 1) no capacity, 2) low capacity, or 3) high capacity. A county was defined as having no capacity if there were no clinicians (of any specialty) available to prescribe buprenorphine to pregnant individuals. Past work has shown that the mean number of buprenorphine clinicians per 1000 individuals in the U.S. is fewer than 0.5 full-time equivalents per 1000 births, suggesting less than half-time availability (Pourat et al., 2020). We thus employed a cutoff of $\geq$0.5 clinicians per 1000 births to signify counties with high buprenorphine capacity. Counties with fewer than 0.5 clinicians per 1000 births but more than zero were classified as low capacity.

2.3. Outcome variable

The primary outcome variable was county-level NOWS rates. The

county of NOWS was assigned based on the location of any hospitalization, as opposed to the patient's residence (Patrick et al., 2020; Winkelman et al., 2018). Our data does not differentiate between transfer admissions or readmissions, but past studies have shown that NOWS identified in transfers was <1 % (S. Patrick, S. et al., 2019). In our secondary analysis, we were particularly interested in how the relationship between buprenorphine access and NOWs may be influenced by rurality, given that much attention has historically been focused on increasing rates of OUD in rural areas since the start of the USA's overdose crisis. Using established methods, county rurality was operationalized as a three-level variable based on the degree of urbanization and adjacency to a metropolitan area: urban ("metro," Rural-Urban Commuting Area Codes, RUC 1–3), versus intermediate (metro-adjacent, capturing suburban areas, RUC 4, 6, 8), versus rural ("nonmetro," RUC 5, 7, 9) (S. Patrick, S. et al., 2019).

Covariates in our analyses included county-level socioeconomic characteristics, with such variables selected a priori based on previous studies demonstrating links between opioid overdose or NOWS and poverty (Corr and Hollenbeak, 2017), unemployment (Hollingsworth et al., 2017; S. Patrick, S. et al., 2019), and manufacturing jobs (S. Patrick, S. et al., 2019). To capture how well health care served each county, we utilized Health Provider Shortage Area (HPSA) designations (HRSA, 2020). These designations are based on what proportion of the county and its populations are underserved in primary care or mental health,[30] grouped as binary variables (whole county versus partial/no shortage) (Ku and Druss, 2020).

2.4. Data sources

The Missouri Department of Health provided data for non-fatal and fatal overdoses from 2015 to 2019 (collected from outpatient and inpatient hospitalizations at non-federal hospitals and ambulatory centers), as well as cases of NOWS, which were determined using International Classification of Diseases (ICD-10 codes) from hospitalization or emergency room visits (ICD-10 codes, P96.1 or P04.49) (CSTE, 2019; Goyal et al., 2020; UrbanInstitute, 2018). Overdose data were accessed via the Missouri overdose dashboard, which is based on the Centers for Disease Control and Prevention (CDC)'s Drug Overdose Surveillance and Epidemiology program, capturing electronic health record information in a syndromic surveillance system based on established and publically available ICD-10 codes on the CDC website (CDC, 2020). As overdose codes were available by age and sex, the total number of fatal and nonfatal overdoses in reproductive-age women, defined as aged 15–45 years per CDC guidelines (CDC, 2014), was calculated per county. Population size for reproductive-age women in each county and number of births from 2014 to 2018 were obtained from the Missouri Department of Health and Senior Services (Missouri, 2020). Sociodemographic and economic characteristics of Missouri counties were acquired from the 2018–2019 Health Resources and Services Administration Area Health Resources Files, encompassing data on mental health and primary care shortage areas collected between 2017 and 2019 and data on economic characteristics collected from 2013 to 2017 (HRSA, 2020).

2.5. Statistical analyses

Univariate chi-square tests, Fisher exact tests, and analyses of variance were performed as appropriate. Multivariable negative binomial regression was performed to assess for associations between county demographics, buprenorphine capacity, and NOWS rates. We calculated variance inflation factors to check for multicollinearity, finding no significant collinearity among all covariates using a threshold of less than 2.0. Because the local severity of OUD may confound the relationship between buprenorphine capacity and NOWs, analyses were stratified by county fatal and non-fatal opioid overdose rates in women aged 15–45 years old. County overdose rates were divided into tertiles (with "tertile 1″=lowest 1/3 of overdose rates). P <0.05 was our threshold for significance. SAS version 9.4 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

3. Results

3.1. Descriptive analyses

Overall, we found 454 buprenorphine prescribers or opioid treatment program listings in the State of Missouri, corresponding to 349 unique practices. Of 126 addresses that were not initially reachable, 12 were reachable via an alternative phone number that was provided. In total, we were able to reach 235 practices, of which 128 were accepting new patients and 97 accepting specifically pregnant patients. The most common reason for practices being unreachable was that the phone call went to voicemail for all 3 phone call attempts, but other reasons included disconnected numbers, fax numbers provided in lieu of phone numbers, and wrong numbers (Bedrick et al., 2020).

Next, we first conducted descriptive analyses after linking the addresses of buprenorphine prescribers or opioid treatment programs to their surrounding counties, showing that out of 115 counties in Missouri, 81 (70 %) had no capacity for buprenorphine treatment, 17 (15 %) had low capacity (<0.5 clinicians/1000 births), and 17 (15 %) had high capacity (>0.5 clinicians/1000 births). NOWS rates in Missouri ranged from 5.7 to 16.6 per 1000 births during the study period, with an average of 6.5 per 1000 births (Fig. 1). Twenty-eight counties had NOWS rates in the highest quartile (>8.19 cases per 1000 births) and were clustered in the Southeast region of the state (Fig. 2).

Of the 98 counties with low or no buprenorphine capacity, 32 were rural (32.6 %), 36 were intermediate (36.8 %), and 30 were urban (30.6 %). (Table 1). Of the 17 counties with high buprenorphine capacity, 8 were rural (47.1 %), 5 were intermediate (29.4 %), and 4 were urban (23.5 %). The majority (99 out of 115, 86 %) of all counties were designated as having mental health clinician shortages. Of the 16 counties with adequate mental health clinicians, the majority (88 %) were in counties with no capacity to care for pregnant people with OUD.

In terms of opioid overdose burden, 38 counties fell into the lowest tertile for fatal and nonfatal overdoses (tertile 1, <2.8 cases per 1000 reproductive-age women), and 38 counties fell into the highest tertile category (tertile 3, >4.0 cases per 1000 reproductive-age women). There was no statistically significant difference in rural/urban status based on opioid overdose rates, nor were counties with the highest rates of opioid overdose (tertile 3) more likely to be mental health shortage areas. However, the counties with the highest rates of opioid overdose (tertile 3) did have higher unemployment rates (p = 0.02) than the counties with the lowest or medium rates (tertiles 1 and 2).

3.2. Association between buprenorphine capacity and nows rates: unadjusted and adjusted analyses

In unadjusted analyses, we found that greater county-level capacity for buprenorphine (ρ=0.34, p<0.001) and higher county-level opioid

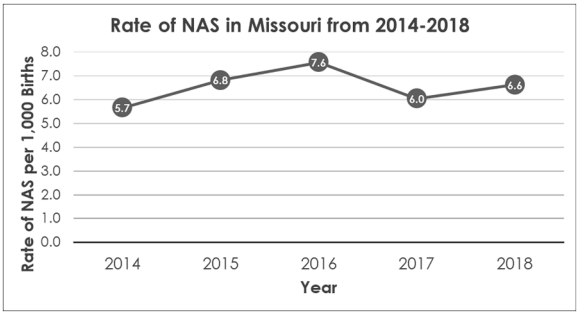

Fig. 1. Rate of NOWS per 1000 births in Missouri from 2014 to 2018.

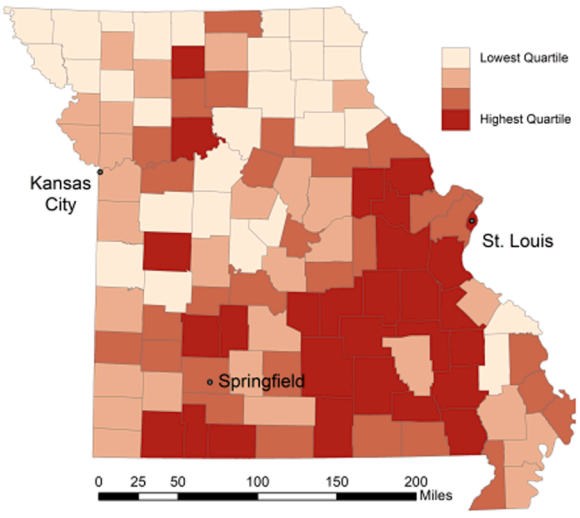

Fig. 2. County-level NOWS per 1000 births in Missouri (2014–2018).

overdose rates in reproductive-aged women (ρ=0.64, $p<0.001$) were associated with higher NOWS rates. We found that counties with no buprenorphine capacity had a NOWS rate of 4.99/1000 births versus 6.99/1000 vs 7.51/1000 for low and high-capacity counties. To investigate these findings further, we conducted adjusted analyses that were stratified by county-level opioid overdose rates and controlled for potential structural confounders such as poverty, employment, and access to health care. Among counties with the lowest rates of opioid overdose (tertile 1), we found that buprenorphine capacity did not correlate with a lower NOWS burden.

Counties with low buprenorphine capacity (<0.5 clinicians/1000 births) had higher NOWS rates than counties with zero buprenorphine capacity (incidence rate ratio [IRR]=2.13, 95 % confidence interval [CI]=1.26–3.59, $p = 0.005$, Table 2). In contrast, counties with high buprenorphine capacity had comparable NOWS rates to counties with zero buprenorphine capacity (IRR=1.23, 95 % CI=0.65–2.32, $p = 0.53$, Table 2). After stratifying by overdose rates, our adjusted analyses showed that buprenorphine capacity did not necessarily translate to a lower NOWS burden within counties with the highest rates of opioid overdose (tertile 3). For instance, counties with low buprenorphine capacity had lower NOWS rates (IRR=0.69 95 % CI=0.51–0.95, $p = 0.02$) than counties with zero buprenorphine capacity. Notably, counties with high buprenorphine capacity had higher NOWS rates than counties with zero buprenorphine capacity (IRR=1.57, 95 % CI=1.21–2.03, $p<0.001$).

3.3. Association between rurality and nows rates: unadjusted and adjusted analyses

In unadjusted analyses, we calculated that rural counties had a NOWS rate of 7.44/1000 births versus 5.90/1000 vs 6.54/1000 for urban and intermediate counties. We subsequently conducted adjusted analyses stratifying by OUD overdose severity (tertile) and potential structural confounders. We found that among counties with lower rates of opioid overdose (tertile 1), rural status was not associated with rates of NOWS. In contrast, in counties with higher rates of overdose (tertile 3), rurality was associated with lower NOWS rate (IRR=0.50, 95 % CI=0.35–0.73, $p<0.001$).

4. Discussion

4.1. Principal findings

The present study shows that Missouri has an overall low capacity for buprenorphine provision during pregnancy, consistent with previous data showing a lack of accessible treatment for pregnant patients with OUD throughout the US (Xu et al., 2023a, 2023b). Our study shows that Missouri counties with greater buprenorphine capacity for pregnant patients had higher rates of NOWS rather than lower rates. Our data also showed that high rates of NOWS are associated with high opioid overdose rates, which is consistent with previous studies (Villapiano et al., 2017). Recognizing that increased buprenorphine capacity may be confounded by a higher need for treatment (due to greater OUD severity), we conducted analyses stratifying by OUD overdose burden; yet, we continued to observe that buprenorphine capacity did not necessarily equate to lower NOWS rates. Past studies have highlighted the need for increased buprenorphine capacity based on local availability (Bedrick et al., 2020; Brown et al., 2018; S. Patrick, SW et al., 2019a), and our study provides a nuanced analysis of Missouri's treatment gap, suggesting that increased buprenorphine capacity is necessary but not sufficient to decrease NOWS rates in Missouri counties of greatest need. Against the backdrop of untreated and undertreated mental health conditions being common in people with OUD (Patrick et al., 2019b; Xu et al., 2023c), we found that mental health care clinician shortage was strongly associated with increased rates of NOWS across all tertiles of county-level overdose burden. Interestingly, all

Table 1
County Socioeconomic Characteristics.

County Characteristic	County Buprenorphine Capacity			p-value	Opioid Overdose Burden			p-value
	No	Low	High		Low	Medium	High	
Urban/Rural				<0.001				0.88
Urban	17 (21)	13 (76)	4 (24)		12 (32)	11 (28)	11 (29)	
Intermediate	33 (41)	3 (18)	5 (29)		11 (29)	15 (39)	15 (39)	
Rural	31 (38)	1 (6)	8 (47)		15 (39)	13 (33)	12 (32)	
PCPSA				0.58				0.13
No	9 (11)	1 (6)	0 (0)		6 (16)	3 (8)	1 (3)	
Yes	72 (89)	16 (94)	17 (100)		32 (84)	36 (15)	6 (16)	
MHPSA				0.20				0.84
No	14 (17)	2 (12)	0 (0)		4 (11)	6 (15)	6 (16)	
Yes	67 (83)	15 (88)	17 (100)		34 (89)	33 (85)	32 (84)	
Poverty (%)	17	15	20		17	17	17	
	(13, 20)	(11, 18)	(17, 21)		(13, 20)	(13, 20)	(13, 21)	
Unemployment (%)	3.3	3.1	3.2		3.0	3.1	3.6	
	(2.9, 3.9)	(2.9, 3.6)	(3.1, 4.4)		(2.8, 3.7)	(3.0, 3.7)	(3.1, 4.4)	
Manufacturing (%)	15	12	14		14	14	14	
	(11, 17)	(10, 14)	(11, 15)		(10, 16)	(10, 18)	(12, 17)	

Table 1: County Characteristics by buprenorphine capacity and opioid overdose burden. Categorical values are represented as n (%); Poverty, unemployment, and manufacturing rates are represented as median (Interquartile range).
PCPSA- primary care physician shortage area; MHPSA- mental health physician shortage areas.

Table 2
County-level rates of neonatal opioid withdrawal syndrome stratified by overdose rate. Middle tertile omitted for simplicity.

Variable	Rate of NOWS per 1000 live births	Negative Binomial Regression Stratified by Fatal and Nonfatal Overdose Rate in Reproductive Age Women	
		Lowest Tertile Counties IRR (95 % CI, p-value)	Highest Tertile Counties IRR (95 % CI, p-value)
Buprenorphine Capacity[c]	4.99	Ref	Ref
No capacity	6.99	2.13 (1.26, 3.59, $p = 0.005$)	0.69 (0.51, 0.95, $p = 0.02$)
Low capacity	7.51	1.23 (0.65, 2.32, $p = 0.53$)	1.56 (1.21, 2.03, $p<0.001$)
High capacity			
Urban/Rural			
Urban	6.54	Ref	Ref
Intermediate:	5.90	0.63 (0.29, 1.41, $p = 0.26$)	0.81 (0.61,1.07, $p = 0.13$)
Rural	7.44	1.16 (0.51, 2.66, $p = 0.72$)	0.50 (0.35, 0.73, $p<0.001$)
Covariates			
Mental Health Physician Shortage Area	4.47	Ref	Ref
No	6.72	1.92 (1.05, 3.53, $p = 0.04$)	1.75 (1.18–2.59, $p = 0.005$)
Yes			
Poverty			
Quartile 1	6.35	Ref	Ref
Quartile 2	4.45	0.77 (0.29, 2.00, $p = 0.59$)	0.91 (0.66–1.26, $p = 0.57$)
Quartile 3	5.73	0.97 (0.57, 1.64, $p = 0.91$)	0.67 (0.48–0.94, $p = 0.02$)
Quartile 4	11.31	2.14 (0.76, 6.01 $p = 0.15$)	1.49 (1.22–1.82, $p<0.001$)
Unemployment			
Quartile 1	5.45	Ref	Ref
Quartile 2	6.54	0.97 (0.45, 2.06, $p = 0.93$)	1.30 (1.07, 1.58, $p = 0.008$)
Quartile 3	7.39	0.65 (0.25, 1.65, $p = 0.36$)	1.78 (1.38, 2.30, $p<0.001$)
Quartile 4	7.34	1.67 (0.69, 4.04, $p = 0.25$)	1.70 (1.26, 2.29, $p<0.001$)
Manufacturing[b]			
Quartile 1	6.83	Ref	Ref
Quartile 2	6.56	1.13 (0.66, 1.96, $p = 0.65$)	1.13 (0.96,1.34, $p = 0.14$)
Quartile 3	5.35	0.64 (0.38, 1.08, $p = 0.09$)	0.80 (0.59,1.07, $p = 0.13$)
Quartile 4	6.28	0.66 (0.30, 1.44, $p = 0.30$)	1.25 (1.06,1.49, $p = 0.01$)

NOWS: neonatal opioid withdrawal syndrome; IRR: incidence rate ratio; CI: confidence interval; Ref: reference.
[a]Overdose rate is defined as the total instances of fatal and nonfatal overdoses occurring in women 15–45 among all women aged 15–45.
[b] Manufacturing is defined as the proportion of all jobs that are manufacturing.
[c] Buprenorphine capacity is defined as the county's capacity to provide buprenorphine to pregnant patients. No capacity indicates no clinicians in the county prescribe buprenorphine to pregnant women; the remaining counties were divided in half based on the ratio of the number of clinicians accepting pregnant patients to the number of births.

Missouri counties with high buprenorphine capacity were designated both primary care and mental health clinician shortage areas, but 17 % of Missouri counties considered to have adequate mental health clinicians did not have any clinicians who would provide buprenorphine to pregnant patients. This may be an indicator of the siloed healthcare system, as access to mental health clinicians does not necessarily translate to OUD treatment availability or vice versa (Novak et al., 2019).

We also sought to analyze the influence of rurality on NOWS rates. Historically, much attention surrounding the USA overdose endemic has focused on increases in drug-related poisonings and "diseases of despair" among rural and suburban people (Friedman et al., 2023). Yet, recent data has suggested that the demographics of the overdose crisis are shifting, with non-Hispanic Black women and people residing in urban areas of high Black-White segregation experiencing increasing rates of overdose (Banks et al., 2023). These trends are supported by data in these present analyses, showing that rural status did not correlate with increased NOWS burden even after controlling for socioeconomic factors and clinician presence. While this could very well represent changing trends in the overdose epidemic, it could also suggest that pregnant patients living in rural counties in Missouri with high overdose rates are traveling to other Missouri counties to give birth, resulting in lower NOWS rates in those high overdose risk rural Missouri counties. This is consistent with evidence that the majority of Missouri counties are lacking in maternity services (MoD, 2022). 47 % of Missouri counties qualify as maternity care deserts, meaning they have no obstetric clinicians and no health centers providing obstetric services, and 22.6 % of Missouri counties only have low or moderate access to these services (Novak et al., 2019). While many recent studies on OUD and NOWS have focused on the need for an increased number of clinicians in rural areas, there is still a significant need to improve access to care in urban areas, especially in Missouri counties with high OUD burden. Future studies could investigate how the distance pregnant patients must travel to receive buprenorphine and prenatal care varies by county.

In addition, previous research has demonstrated that urban and high-risk areas have higher numbers of OUD treatment and buprenorphine clinicians (Bedrick et al., 2020). Our results suggest this increase may still be inadequate to support these areas' disproportionately high OUD burden and deflect the downstream outcome of NOWS. This highlights the critical need for continued investment of research and resources into the treatment of OUD during pregnancy in both rural and urban communities with high rates of opioid overdoses and OUD burden, even if the number of local OUD clinicians and medication to treat OUD capacity is relatively high for the state. Importantly, how pregnant patients with OUD find accepting clinicians is unknown. Even if a county had a high capacity to care for pregnant patients, if these women are unaware of these resources, this capacity is effectively diminished.

4.2. *Limitations and strengths*

With regards to limitations, first, the study is limited in that causality cannot be established from observational data. Second, measurement error from the ascertainment of diagnostic codes cannot be ruled out. Third, NOWS rates are subject to variation in case definition and may capture withdrawal from co-occurring substances beyond solely opioid-related etiologies. Fourth, our analysis does not take buprenorphine caps into consideration, and inclusion on the publically-available prescriber directories is voluntary; this may contribute to underestimation of buprenorphine capacity. Furthermore, many people may travel to other Missouri counties for treatment, which cannot be captured by our data (Markus and Pillai, 2021).

Finally, there are several limitations that are related to generalizability. Our manuscript is focused on solely buprenorphine prescribing, as opposed to methadone. This is an important limitation, particularly in an era of increasing fentanyl contamination, because methadone may be a more effective treatment option than buprenorphine for people who experience difficulty initiating and remaining stable on buprenorphine (Silverstein et al., 2019). While shared decision-making to guide the selection of buprenorphine versus methadone is needed (Nguemeni Tiako et al., 2024), methadone can only be accessed via treatment centers, overseen by the Drug Enforcement Administration, where people are required to show up daily for supervised dosing (Work et al., 2023). The tightly-regulated methadone treatment system—where non-Hispanic Black people are overrepresented and White peers

underrepresented—contrasts sharply with the more flexible framework of office-based buprenorphine treatment, which are available for general practitioners to prescribe (Andraka-Christou, 2021; Hansen and Roberts, 2012; Jackson et al., 2022). Unfortunately, the lack of racial and ethnic diversity across 112 of Missouri's 115 counties limits our ability to robustly evaluate racialized differences in county-level NOWS rates and access to buprenorphine versus methadone; however, future studies should be conducted at a more granular level (i.e., census tract, zip code) to evaluate area-based differences in NOWS rates and access to buprenorphine versus methadone

Furthermore, our data is specific to the state of Missouri, where recent efforts to increase OUD treatment have focused on buprenorphine rather than methadone (Winograd et al., 2019). However, data has shown that "medication-first" initiatives to boost access to OUD have heavily focused on buprenorphine, suggesting that the data from Missouri is likely generalizable to many other regions of the USA (Banta--Green et al., 2022; Brady et al., 2021). Finally, while the present study was performed when the DATA 2000 X-waiver was still required, which may limit generalizability, the removal of the X-waiver has not been found to significantly increase buprenorphine prescribing rates,(Luo and Erikson, 2023; Stringfellow et al., 2023), suggesting that the lessons gained from data preceding X-waiver removal periods will likely still apply to the present.

With regards to strengths, our study provides a detailed assessment of county-level buprenorphine capacity in relation to NOWS rates using a "secret shopper" study design, a useful method for monitoring the real-world effectiveness of health policies. Previous studies have analyzed NOWS trends based on the distance to registered medication therapy clinicians;(Brown et al., 2018; UrbanInstitute, 2018) however, our recent analysis suggest the number of registered clinicians may over-represent capacity for buprenorphine treatment, as over 40 % of clinicians could not be reached or did not accept pregnant patients (Bedrick et al., 2020). Our study used the number of clinicians who *could* be reached and who indicated they accept pregnant patients, as opposed to numbers listed on the websites of publically available directories. This methodology allowed us to analyze NOWS rates using a more accurate representation of buprenorphine capacity. Other strengths include using standardized state data and comprehensive socioeconomic demographics to further characterize counties that could benefit the most from interventions, specifically using data from reproductive-aged women to best estimate prevalence and rates. Finally, our analysis is unique by incorporating stratification of opioid overdose burden to best understand the complex relationship of a county's buprenorphine capacity and socioeconomic demographics with resultant rates of NOWS.

5. Conclusions

In summary, we found that the vast majority of Missouri's 115 counties have no capacity for buprenorphine prescribing during pregnancy. Rurality and lower buprenorphine capacity did not significantly predict elevated rates of NOWS. Our results support the need for continued research and exploration of new predictors of OUD and NOWS risk to better target intervention strategies, as well as a need for ongoing aid to all communities struggling with OUD and its sequelae

CRediT authorship contribution statement

Bronwyn S. Bedrick: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Caroline Cary:** Data curation, Investigation, Writing – original draft, Writing – review & editing. **Carly O'Donnell:** Data curation, Investigation, Writing – review & editing. **Christine Marx:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – review & editing. **Hayley Friedman:** Data curation, Investigation, Writing – review & editing. **Ebony B. Carter:** Data curation, Investigation, Resources, Writing – review & editing. **Nandini Raghuraman:** Data curation, Investigation, Resources, Writing – review & editing. **Molly J. Stout:** Data curation, Investigation, Writing – review & editing. **Benson S. Ku:** Data curation, Investigation, Methodology, Validation, Visualization, Writing – review & editing. **Kevin Y Xu:** Data curation, Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Jeannie C. Kelly:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dadr.2024.100218.

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