

# Considerations and Determinants of Discharge Decisions among Prenatal Substance Exposed Infants

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Tre D. Gissandaner<sup>1</sup> , Alainna Wen<sup>2,\*</sup>, Jordan A. Gette<sup>3,\*</sup>, Kristin J. Perry<sup>4,\*</sup>, Lauren M. Mutignani<sup>5,\*</sup>, Timothy Regan<sup>6,\*</sup>, Lacy Malloch<sup>7</sup>, Lauren C. Tucker<sup>7</sup>, Clint B. White<sup>8</sup>, Taylor B. Fry<sup>7</sup>, Crystal S. Lim<sup>9</sup>, and Robert D. Annett<sup>10</sup>

## Abstract

Limited research has examined a comprehensive set of predictors when evaluating discharge placement decisions for infants exposed to substances prenatally. Using a previously validated medical record data extraction tool, the current study examined prenatal substance exposure, infant intervention (i.e., pharmacologic, or non-pharmacologic), and demographic factors (e.g., race and ethnicity and rurality) as predictors of associations with discharge placement in a sample from a resource-poor state ( $N = 136$ ; 69.9% Non-Hispanic White). Latent class analysis (LCA) was used to examine whether different classes emerged and how classes were differentially related to discharge placement decisions. Logistic regressions were used to determine whether each predictor was uniquely associated with placement decisions. Results of the LCA yielded a two-class solution comprised of (1) a Low Withdrawal Risk class, characterized by prenatal exposure to substances with low risk for neonatal abstinence syndrome (NAS) and non-pharmacologic intervention, and (2) a High Withdrawal Risk class, characterized by a high risk of NAS and pharmacologic intervention. Classes were not related to discharge placement decisions. Logistic regressions demonstrated that meth/amphetamine use during pregnancy was associated with greater odds of out of home placement above other substance types. Future research should replicate and continue examining the clinical utility of these classes.

## Keywords

prenatal substance exposure, child protective services, latent class analysis, infant pharmacologic intervention, neonatal abstinence syndrome

## Introduction

Substance use during pregnancy is surprisingly common and is associated with a host of deleterious effects on the fetus (for review see [Cook et al., 2017](#)). Alarming, nearly 400,000 to 440,000 out of 4 million newborns are prenatally exposed to alcohol, tobacco, cannabis, and illicit drugs in the United States (U.S.) every year ([Young et al., 2009](#)). A nationally representative survey from the Substance Abuse and Mental Health Services Administration (SAMHSA; U.S. Department of Health and Human Services [HHS], 2020a) indicates that, among pregnant persons aged 15–44 years, 9.6% had used tobacco products, 9.5% had ingested alcohol, 5.4% had used cannabis, and approximately 1% had used illicit drugs within the prior month. Despite these concerning rates, pregnant persons may be less likely to disclose substance use to health care providers or seek intervention due to punitive policies, thereby increasing the likelihood of negative infant outcomes such as, neonatal abstinence syndrome (NAS; [Goodman et al., 2019](#)).

<sup>1</sup>Department of Psychiatry, Columbia University Irving Medical Center, New York, NY, USA

<sup>2</sup>Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, Los Angeles, CA, USA

<sup>3</sup>Center of Alcohol and Substance Use Studies, Rutgers, the State University of New Jersey, New Brunswick, NJ, USA

<sup>4</sup>Edna Bennett Pierce Prevention Research Center, Pennsylvania State University, University Park, PA, USA

<sup>5</sup>Department of Psychiatry, University of Rochester Medical Center, Rochester, NY, USA

<sup>6</sup>Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

<sup>7</sup>Department of Pediatrics, University of Mississippi Medical Center, Jackson, MS, USA

<sup>8</sup>Forrest General Hospital, Hattiesburg, MS, USA

<sup>9</sup>Department of Health Psychology, University of Missouri, Columbia, MO, USA

<sup>10</sup>University of New Mexico Health Sciences Center, Albuquerque, NM, USA

\*These authors contributed equally to this work

## Corresponding Author:

Tre D. Gissandaner, Department of Psychiatry, Columbia University Irving Medical Center, 1051 Riverside Drive, New York, NY 10032-3784, USA.  
Email: [tg2838@cumc.columbia.edu](mailto:tg2838@cumc.columbia.edu)

NAS is a postnatal withdrawal syndrome that occurs in infants after chronic in utero exposure to substances. NAS is most associated with opioid use (illicit or prescribed); however, substances like nicotine, alcohol, methamphetamine, and prescribed psychiatric medications (e.g., benzodiazepines, SSRIs) also produce symptoms consistent with NAS (Anbalagan & Mendez, 2022). Clinically, NAS presents with a constellation of symptoms that can include tremors and convulsions, eating difficulties (uncoordinated suck/swallow reflex), tight muscle tone, breathing difficulties, diarrhea, and excessive crying (Jansson & Patrick, 2019). Symptoms of NAS usually occur within the first 48 hours but can present up to a week after birth (Anbalagan & Mendez, 2022). Though NAS and Neonatal Opioid Withdrawal Syndrome (NOWS) have been used interchangeably, research has made a distinction between the two, with NOWS describing opioid-only withdrawal symptoms (Patrick et al., 2020).

Typically, treatment of NAS begins with non-pharmacologic interventions such as breastfeeding (Welle-Strand et al., 2013), swaddling (Mangat et al., 2019), parent-infant rooming-in (Holmes et al., 2016), and low stimulation environments (i.e., dark, quiet rooms), which yield beneficial outcomes. While these interventions may be common among newborns (e.g., around 80% of newborns are breastfed at some point; CDC, 2022), they are particularly helpful in cases of NAS. If these interventions are ineffective, then pharmacologic treatment is indicated. Between 50%–80% of NAS cases are treated with medications, frequently with opioid agonists like morphine, methadone, and buprenorphine (Wachman & Werler, 2019; Young et al., 2021). Although in utero opioid exposure is highly linked to NAS (Siu & Robinson, 2014), the decision to administer medications depends on the severity of symptomology, rather than exposure to any specific class of substance (Mangat et al., 2019). Administration of these medications shows beneficial outcomes such as shorter and less severe hospitalizations post-delivery (Backes et al., 2012; Johnson et al., 2003; Kelly et al., 2015). Important, yet currently unknown, is how pharmacologic intervention delivery impacts the parent-child dyad post-delivery, including potential infant discharge placement decisions such as out-of-home placement by Child Protective Services (CPS).

Substance use in pregnancy is as a key predictor of CPS involvement (for reviews see Austin et al., 2022; Canfield et al., 2017). Infants diagnosed with substance exposure are 5 times more likely to have CPS involvement and 11 times more likely to be placed in foster care as opposed to infants without prenatal substance exposure (Prindle et al., 2018). The overarching goal of all CPS involvement is to ensure children are safe (Barth, 1999). In general, CPS involvement in such cases is to prevent risk for several negative outcomes associated with prenatal substance exposure, such as child maltreatment (Austin et al., 2022) and hospitalization later in childhood related to negative environmental or neurobiological effects (Witt et al., 2017). On the other hand, CPS out of home placement has been associated with childhood attachment disorders (Baldwin et al., 2019), physical abuse

within residential care settings (Euser et al., 2014), and more mental health disorders in adulthood relative to the general population (Seker et al., 2021). Therefore, CPS must weigh the potential benefits and risks of their placement decisions. Empirically understanding factors that predict these placements for infants exposed to substances in utero is of the utmost importance.

Still, states vary in their approach and responsiveness to prenatal substance exposure. For example, 24 states currently have laws that define substance use while pregnant as child abuse. In Mississippi, where the current study took place, substance use during pregnancy is not considered a crime nor is it considered child abuse. Healthcare workers are neither mandated to test nor report suspected prenatal exposure (Guttmacher Institute, 2022; HHS, 2020b). Rather, CPS reporting is likely influenced by hospital policy and/or a provider's clinical judgement.

CPS placement decisions are based on a myriad of factors, one of which may be the type of substance an infant has been exposed to in utero. Prior research shows that pregnant persons who engaged in cocaine, meth/amphetamine, opioid, or injection drug use were likelier to lose custody of their children compared to other types of substance use (Austin et al., 2022; Canfield et al., 2017; Prindle et al., 2018). However, the type of substance infants are exposed to in utero is not consistently related to future child abuse or neglect (Deutsch et al., 2020), highlighting the importance of considering contextual factors in tandem with substance use typology.

Racial/ethnic discrimination is one contextual factor that can determine which pregnant persons get screened (Harp & Bunting, 2020). For example, Black persons are likelier to be screened for drug use while pregnant, experience CPS involvement after giving birth, and victimized by anti-drug policies (Harp & Bunting, 2020; Kemper et al., 2021). Moreover, differences between race and substance use typology can predict CPS involvement. For example, Rebbe et al. (2019) showed pregnant persons who use alcohol and have Black infants were likelier to have CPS involvement compared to those who use opioids and have White infants.

Another factor associated with substance use typology and risk for child custody loss is whether a parent resides in an urban or rural environment. Drugs like nicotine and opioids have higher consumption rates in rural areas, whereas alcohol has a higher consumption rate in urban areas (Jumah, 2016; Roberts et al., 2016). One study found pregnant persons in rural areas presenting for opiate treatment were likelier to endorse polysubstance use (i.e., use of two or more drugs in combination) relative to those from urban settings (Shannon et al., 2010). Between 2007 and 2016, pregnant persons in rural areas had greater increases in drug use, with the greatest increase in meth/amphetamine and tobacco use, relative to those from urban areas (Jarlenski et al., 2020). Therefore, pregnant persons in rural areas may be at increased risk for specific types of drug use, namely nicotine, amphetamine, and opioid use.

## Current Study

Examining the influence of substance use typology, race/ethnicity, and rural/urban environment is critical, as prior research has shown that these variables impact child maltreatment (e.g., Maguire-Jack & Kim, 2021; Smith et al., 2021). Although, less research has considered their importance in placement decisions in the context of NAS (Prindle et al., 2018). Examining their influence, using NAS as a proxy for in utero substance exposure, is essential to understanding the factors that impact infants' out of home placements. Moreover, this study applied a person-centered analytic approach to determine whether individuals form subgroups, a novel approach to assessing subgroups of prenatal substance exposure. A person-centered analytic approach allowed for identification of specific profiles of substance exposures and demographic characteristics that could offer utility in understanding placement decisions more holistically. That is, one or two substance exposures or demographic characteristics may not comprehensively capture risk of child removal, but rather there are specific profiles of these factors that provide more precise associations with discharge placement decisions.

The current study addressed these gaps in the literature across three aims. Aim 1 utilized a person-centered analytic approach to determine whether individuals form subgroups based on a set of related variables — substance use typology, demographic factors, and NAS intervention within our sample. Aim 2 evaluated whether emergent subgroups differentially predicted discharge placement decisions. Finally, Aim 3 identified predictors uniquely associated with discharge placement decisions using a variable-centered approach. Based on evidence from two systematic reviews (i.e., Austin et al., 2022; Canfield et al., 2017), we hypothesized that prenatal cocaine, meth/amphetamine, and opioid exposure would be associated with greater odds of an out of home placement. Additionally, we hypothesized that infants from rural areas and infants with Black birthing parents would have greater odds of experiencing out of home placement. (Harp & Bunting, 2020; Kemper et al., 2021; Maguire-Jack & Kim, 2021; Smith et al., 2021).

## Method

### Procedure and Participants

This study was conducted with the help of two collaborating hospitals in the southern U.S. with level three and level four neonatal intensive care units. A waiver of informed consent was granted by the Institutional Review Boards of both hospitals. We used clinical information routinely collected from the medical records of pregnant patients and their infants born between July 1, 2015, and June 30, 2018. Participants were identified through medical record review from which the data were also extracted. Medical record data extraction was completed using a tool developed for a multi-site study of neonatal opioid withdrawal

syndrome (NOWS) within the NIH-funded ACT NOW collaborative (see Young et al., 2021 for details). The original aim of the ACT NOW collaborative was to broadly determine variations in care for infants with NOWS during a one-year interval. The current study sought to expand the data collection interval to 3 years to more broadly characterize trends that may have existed with one part of the southern U.S., encompassing a largely rural and minority population. Trained research staff completed the data extraction.

Study inclusion criteria included infant  $\geq 36$  weeks of gestational age<sup>1</sup> and at least one of the following: 1) NAS infant scoring within 120 hours of delivery; 2) patient history of opioid use as noted in the patient's or infant's medical record; or 3) patient and/or infant positive opioid toxicology screen as noted in the patient's or infant's medical record. Exclusion criteria included 1) major birth defects (e.g., heart defects); 2) any respiratory support after 72 hours of life; 3) neonatal encephalopathy; 4) neonatal seizure disorder; 5) need for surgical intervention; and 6) treatment with opioids not for NAS.

The medical record data extraction tool identified 136 parent-infant dyads as meeting inclusion criteria (see Figure 1). Non-Hispanic White pregnant persons comprised the largest proportion of the sample (69.9%;  $n = 95$ ), followed by Non-Hispanic Black pregnant persons (26.5%;  $n = 36$ ), Hispanic-White pregnant persons (2.2%;  $n = 3$ ), and Hispanic pregnant persons (0.7%;  $n = 1$ ) with 0.7% ( $n = 1$ ) of the sample missing data for race and ethnicity (coded as missing). Infant gestational age at birth ranged from 36–41 weeks ( $M = 38.07$ ,  $SD = 1.19$  weeks). The infants were 52.2% male. Infants were exposed, on average, to 2.81 substance types ( $SD = 1.27$ ). See Table 1 for demographic characteristics.

## Measures

### Dependent Variable

### Infant Discharge Outcome

The data collection form included a question asking where the infant was discharged or transferred. Response categories included 1) home with parent(s); 2) home with a relative; 3) home with foster parent; and 4) other, specify (open ended response). Open-ended responses included “adoption,” “CPS custody,” and “treatment facility with a parent.” Given the variability of the responses, a binary variable with categories of “discharged with a parent” and “not discharged with a parent” was created.

## Independent Variables

### Intervention

Non-pharmacologic intervention plus pharmacologic intervention (e.g., morphine dose) versus non-pharmacologic

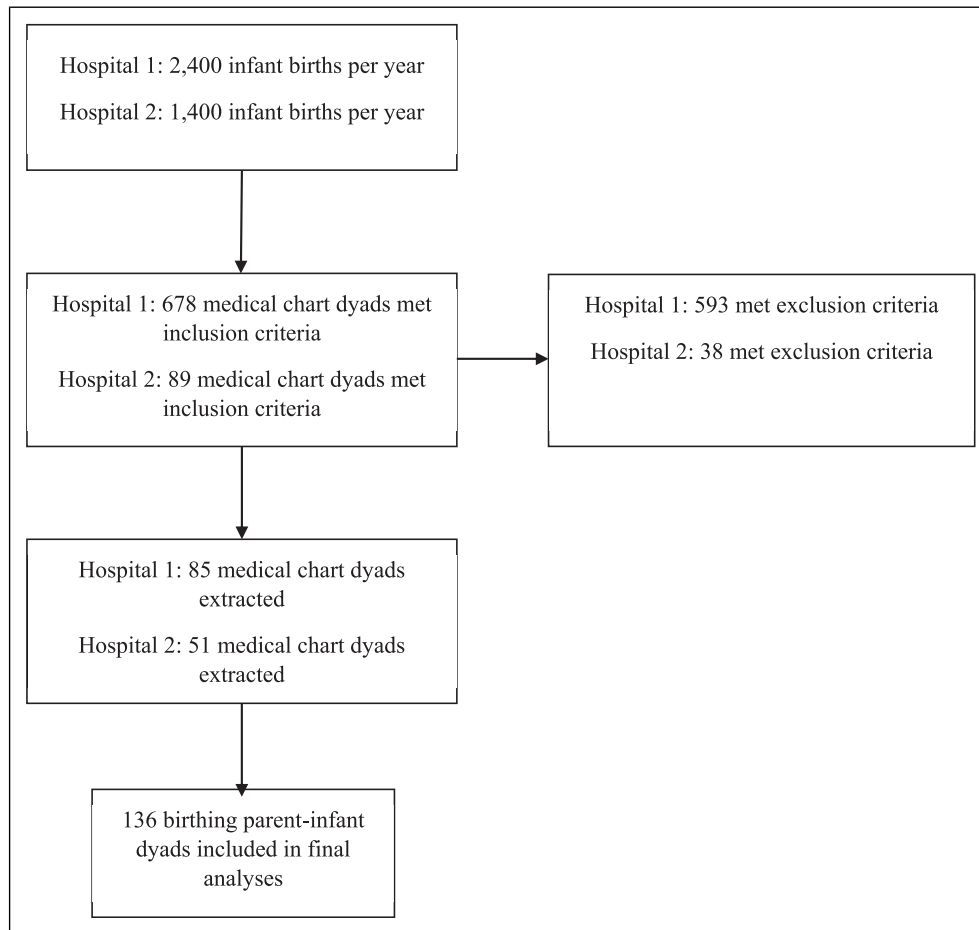


**Figure 1.** Flow diagram summary of the medical chart screening process. Hospital 1: 678 medical chart dyads met inclusion criteria. *Note.* Medical record data extraction was completed from the medical records of birthing parents and their infants born between July 1, 2015, and June 30, 2018.

intervention only (e.g., swaddling) was determined by an item from the data collection form that asked to indicate the type of NAS intervention received at the hospital. All participants received at least non-pharmacologic intervention. Responses were recoded into a binary pharmacologic intervention variable consisting of 1) non-pharmacologic alone and 2) non-pharmacologic plus pharmacologic.

## Substance Exposure

Substance exposure was determined by birthing parent positive toxicology screening and/or parent's history of substance use during pregnancy indicated in the medical chart<sup>2</sup>. Specific substances recorded included categories of 1) alcohol; 2) meth/amphetamines; 3) cocaine; 4) opioids (buprenorphine, hydrocodone, hydromorphone, methadone, oxycodone, and opioids not otherwise specified); 5) hallucinogens (cannabis and PCP); 6) nicotine; 7) heroin; and 8) non-scheduled substances (e.g., benzodiazepines, SSRIs). Each substance category was used to create a binary variable for that substance

with categories of “no exposure by history/screening” and “exposure by history/screening.”

## Rurality

Zip code and Rural-Urban Commuting Area (RUCA) conversion tables (RUCA Codes, 2020) were used to determine the rurality of participants. RUCA codes ranged from 1 = Metropolitan area core to 10 = Rural areas. RUCA codes 1–3 were considered “urban” and RUCA codes 4–10 were considered “rural.”

## Race and Ethnicity

Race was determined by indicating birthing parent race and ethnicity on the data collection form. Due to the low frequency of responses reported above, analyses were limited to Non-Hispanic White (henceforth, White) and Non-Hispanic Black (henceforth, Black) birthing parents to reduce heterogeneity. Therefore, a binary race and ethnicity variable was created.

**Table 1.** Demographic Characteristics and Descriptive Statistics.

| Birthing Parent and Infant Characteristics       | Overall (N = 136) | Hospital 1 (n = 85) | Hospital 2 (n = 51) | $t/X^2$ (p-value) |
|--------------------------------------------------|-------------------|---------------------|---------------------|-------------------|
| Gestational age (weeks) <i>M</i> ( <i>SD</i> )   | 38.07 (1.19)      | 37.94 (1.89)        | 38.29 (1.17)        | −1.69 (.09)       |
| Female                                           | 47.79%            | 51.76%              | 41.18%              | 1.43 (.23)        |
| Male                                             | 52.21%            | 48.24%              | 58.82%              |                   |
| Race and ethnicity                               |                   |                     |                     |                   |
| Non-Hispanic Black                               | 26.47%            | 33.33%              | 18.00%              | 3.65 (.06)        |
| Non-Hispanic White                               | 69.85%            | 66.67%              | 82.00%              |                   |
| Opioid exposure                                  |                   |                     |                     |                   |
| No                                               | 25.74%            | 34.12%              | 11.76%              | 8.33 (<.01)       |
| Yes                                              | 74.26%            | 65.88%              | 88.24%              |                   |
| Meth/amphetamine exposure                        |                   |                     |                     |                   |
| No                                               | 64.71%            | 56.47%              | 78.43%              | 6.73 (<.05)       |
| Yes                                              | 35.29%            | 43.53%              | 21.57%              |                   |
| Hallucinogen exposure                            |                   |                     |                     |                   |
| No                                               | 64.71%            | 58.82%              | 74.51%              | 3.43 (.06)        |
| Yes                                              | 35.29%            | 41.18%              | 25.49%              |                   |
| Alcohol exposure                                 |                   |                     |                     |                   |
| No                                               | 86.76%            | 87.06%              | 86.27%              | 0.02 (.90)        |
| Yes                                              | 13.24%            | 12.94%              | 13.73%              |                   |
| Nicotine exposure                                |                   |                     |                     |                   |
| No                                               | 34.56%            | 34.12%              | 35.29%              | 0.02 (.90)        |
| Yes                                              | 65.44%            | 65.88%              | 64.71%              |                   |
| Heroin exposure                                  |                   |                     |                     |                   |
| No                                               | 93.38%            | 90.59%              | 98.04%              | 2.86 (.09)        |
| Yes                                              | 6.62%             | 9.41%               | 1.96%               |                   |
| Cocaine exposure                                 |                   |                     |                     |                   |
| No                                               | 84.56%            | 80.00%              | 92.16%              | 3.61 (.06)        |
| Yes                                              | 15.44%            | 20.00%              | 7.84%               |                   |
| Non-scheduled exposure                           |                   |                     |                     |                   |
| No                                               | 64.71%            | 68.24%              | 58.82%              | 1.24 (0.27)       |
| Yes                                              | 35.29%            | 31.76%              | 41.18%              |                   |
| Total substance exposures <i>M</i> ( <i>SD</i> ) | 2.81 (1.27)       | 2.91 (1.31)         | 2.65 (1.20)         | 1.18 (.24)        |
| Pharmacological intervention                     |                   |                     |                     |                   |
| No                                               | 67.65%            | 87.06%              | 35.29%              | 39.03 (<.0001)    |
| Yes                                              | 32.35%            | 12.94%              | 64.71%              |                   |
| Discharged home                                  |                   |                     |                     |                   |
| No                                               | 26.47%            | 30.59%              | 19.61%              | 1.97 (.16)        |
| Yes                                              | 73.53%            | 69.41%              | 80.39%              |                   |
| Rurality (RUCA code)                             |                   |                     |                     |                   |
| Urban                                            | 69.12%            | 54.12%              | 94.12%              | 23.89 (<.0001)    |
| Rural                                            | 30.88%            | 45.88%              | 5.88%               |                   |

Note. Race and ethnicities of pregnant persons not included in the overall analyses: Hispanic-White (2.2%;  $n = 3$ ), Hispanic (0.7%;  $n = 1$ ), and 0.7% ( $n = 1$ ) of the sample missing data for race and ethnicity. Differences by hospital were determined by  $t$ -tests for continuous variables (i.e., gestational age and total substance exposures), and chi-square tests for dichotomous variables. Non-scheduled Exposure = non-scheduled substances (e.g., Benzodiazepines, SSRIs, and antidepressants). RUCA = Rural-Urban Commuting Area.

## Analytic Approach

Descriptive statistics were calculated in SAS Studio 3.8 (SAS Institute Inc.). Means and standard deviations were calculated for continuous variables, and frequency and percentages were calculated for categorical variables (see Table 1). Differences by hospital were determined by  $t$ -tests for continuous variables (i.e., gestational age and total

substance exposures), and chi-square tests for dichotomous variables. To determine class solutions based on indicators of birthing parent substance use, demographic background, and intervention type (Aim 1), latent class analysis (LCA) was conducted using the *poLCA* package in R (Linzer & Lewis, 2011). LCA is a person-centered approach, identifying subgroups of individuals (i.e., classes) using a set of specified indicators (McCutcheon, 1987). Bayesian

**Table 2.** Percent Endorsement of Substance Exposure, Rurality, Race and Ethnicity, and Pharmacologic Intervention by Class Membership.

|                            | Low Withdrawal Risk, % | High Withdrawal Risk |
|----------------------------|------------------------|----------------------|
| Opioid exposure            | 41.25                  | 95.70%               |
| Meth/amphetamine exposure  | 46.00                  | 28.34%               |
| Hallucinogen exposure      | 57.48                  | 20.89%               |
| Alcohol exposure           | 20.32                  | 8.63%                |
| Nicotine exposure          | 53.03                  | 73.50%               |
| Heroin exposure            | 2.67                   | 9.18%                |
| Cocaine exposure           | 29.09                  | 6.58%                |
| Non-scheduled exposure     | 30.67                  | 38.30%               |
| Rurality (RUCA Code)       |                        |                      |
| Urban                      | 62.95                  | 73.12%               |
| Rural                      | 37.05                  | 26.88%               |
| Race and ethnicity         |                        |                      |
| White                      | 44.08                  | 90.79%               |
| Black                      | 55.92                  | 9.21%                |
| Pharmacologic intervention |                        |                      |
| No                         | 100                    | 46.64%               |
| Yes                        | 0.00                   | 53.36%               |

Note. Non-scheduled Exposure = Non-scheduled substances (e.g., Benzodiazepines, SSRIs, and antidepressants). RUCA = Rural-Urban Commuting Area. All infants received non-pharmacologic intervention.

Information Criterion (BIC; Schwarz, 1978) was used to determine the optimal class solution, as simulation studies reported BIC as the most reliable fit index (Nylund et al., 2007). Entropy (Wang et al., 2017) was also used to determine subgroup classification (i.e., how distinct the identified classes are from one another). Relative to other study models, lower BIC values indicate better fit and higher entropy values indicate better subgroup classification.

Following the determinations of optimal class solutions, participants were classified into their most likely class and a chi-square analysis was conducted to determine the association between class and infant discharge outcome (Aim 2). Finally, to evaluate a variable-centered approach (Aim 3), univariate and multivariate logistic regression models were used to examine the associations between substance exposure, demographic background, and intervention type in predicting the infant's outcome at discharge (i.e., home with parent(s) versus not). Odds ratios were used to determine the change in the odds of placement decisions based on one-unit increases in each predictor variable. Additionally, predictors by hospital site interactions were included in initial models to account for hospital site variance. These terms revealed no significant predictor by site interactions ( $ps > .07$ ), suggesting that the sites did not differ in the way the independent variables related to the dependent variables. Thus, combining the hospital's data and removing the interaction terms for analyses was appropriate. Missing data were accounted for using maximum likelihood estimation in the SAS Studio and R software packages.

## Results

### Class Solutions and Infant Discharge Outcome

LCA models were conducted for two-, three-, and four-class models. Comparisons of fit indices yielded an optimal two-class solution (BIC = 1684.61, entropy = 5.80), which had better fit with the data compared to the three-class solution (BIC = 1695.87, entropy = 5.62), and four-class solution (BIC = 1726.83, entropy = 5.51). The resulting two classes differed in substance exposure, rurality, race and ethnicity, and pharmacologic intervention (Table 2). Based on these differences, the two resulting classes were named High Withdrawal Risk (HWR) and Low Withdrawal Risk (LWR). The HWR class was comprised of a greater proportion of infants exposed to heroin, nicotine, opioids, and non-scheduled substances (e.g., SSRIs, benzodiazepines), all of which have been linked to NAS ( $n = 82$ ). The LWR class was comprised of a greater proportion of infants exposed to meth/amphetamines, cocaine, alcohol, and hallucinogens, which have not been linked to NAS ( $n = 54$ ). Notably, relevant to distinguishing the classes, most of the HWR class infants received pharmacologic intervention plus non-pharmacologic care, whereas all LWR class infants received non-pharmacologic care only. Moreover, a much greater portion (90.79%) of the HWR group were White, and a slightly greater portion (55.92%) of the LWR group were Black. Lastly, both classes had greater proportions of urban than rural residences. See Table 2 for the proportions of each indicator by class membership. Chi-square analysis showed no significant

association between class membership and infant discharge outcome,  $\chi^2(1) = .08$ ,  $p = .78$ .

## Predictors of Infant Discharge Outcome

Univariate binomial logistic regression analysis conducted separately for each indicator showed a significant association between meth/amphetamine exposure and infant discharge outcome. Specifically, meth/amphetamine exposure was associated with 2.33 times greater odds of out of home placement compared to no meth/amphetamine exposure (OR = 2.33, 95% CI = 1.07, 5.10;  $p < .05$ ; Table 3). This association remained significant when a multivariate binomial logistic regression analysis was conducted with the addition of other indicators, OR = 2.63; 95% CI = 1.02, 6.76;  $p < .05$  (Table 4). Univariate and multivariate findings for other indicators were non-significant, all  $ps > .12$ .

## Discussion

Using a sample of patients with a history of substance use during pregnancy, this study employed a person-centered analytic approach to identify distinct subgroups distinguished by infant prenatal substance exposure (e.g., cocaine use, nicotine use), intervention type (i.e., pharmacologic plus non-pharmacologic, or non-pharmacologic only), and demographic factors (e.g., race and rurality). We then used these classes to predict the odds of infants being discharged to their biological parents versus out of home placement. Finally, using a variable-centered approach, we investigated how unique substance exposures, intervention type, and demographic factors influenced placement decisions in a series of univariate and multivariate logistic regressions.

Results of univariate regressions indicated that meth/amphetamine was the only substance type that was significantly associated with infant discharge placement. Further, including each substance in a multivariate model (to provide information about which substance(s) were impacting discharge placement) revealed that meth/amphetamine exposure was the sole substance impacting infant discharge outcome. Specifically, infants exposed to meth/amphetamine use had 2.63 times greater odds of out of home placement above and beyond other substances and combination of substances. This is congruent with prior research and with our hypothesis that prenatal meth/amphetamine exposure would be associated with placement decisions (i.e., Austin et al., 2022; Prindle et al., 2018). However, it is interesting to note that only meth/amphetamine exposure was significantly related to placement outcomes despite extant literature denoting deleterious effects of prenatal exposure for several of the substances examined (e.g., cocaine, opioids; Austin et al., 2022; Canfield et al., 2017). Intervention type for infants was also not associated with placement decisions in regression analyses. It is possible that there are variables

**Table 3.** Univariate Models of Substance Use Exposure, Rurality, and Race and Ethnicity Predicting Infant Placement.

|                            | OR (95% CI)      | p-value |
|----------------------------|------------------|---------|
| Opioid exposure            | 0.72 (.31–1.67)  | .44     |
| Meth/amphetamine exposure  | 2.33 (1.07–5.10) | .03*    |
| Hallucinogen exposure      | 1.45 (0.66–3.17) | .35     |
| Alcohol exposure           | 1.08 (0.36–3.28) | .89     |
| Nicotine exposure          | 1.84 (0.78–4.33) | .16     |
| Heroin exposure            | 1.42 (0.34–6.02) | .63     |
| Cocaine exposure           | 1.48 (0.55–4.03) | .44     |
| Non-scheduled exposure     | 1.45 (0.66–3.17) | .35     |
| Rurality (RUCA Code)       | 0.98 (0.43–2.34) | .96     |
| Race and ethnicity         | 0.55 (0.22–1.40) | .21     |
| Pharmacologic intervention | 1.49 (0.67–3.29) | .33     |

Note. \* $p < .05$ ; Substance exposure variables are coded such that 0 = no exposure, 1 = exposure. For Rurality, 0 = urban, 1 = rural. For Race and Ethnicity, 0 = White, 1 = Black. For Pharmacologic Intervention, 0 = no, 1 = yes. For infant placement, 0 = with birthing parent, 1 = other (i.e., CPS custody, adoption, foster care, or with other family member). Non-scheduled Exposure = non-scheduled substances (e.g., Benzodiazepines, SSRIs, and antidepressants). RUCA = Rural-Urban Commuting Area.

**Table 4.** Multivariate Model of Substance Use Exposure, Rurality, and Race and Ethnicity Predicting Infant Placement.

|                            | AOR (95% CI)     | p-value |
|----------------------------|------------------|---------|
| Opioid exposure            | 0.60 (.21–1.75)  | .35     |
| Meth/amphetamine exposure  | 2.63 (1.02–6.76) | .04*    |
| Hallucinogen exposure      | 1.54 (0.61–3.90) | .36     |
| Alcohol exposure           | 0.68 (0.18–2.49) | .55     |
| Nicotine exposure          | 1.51 (0.57–3.96) | .40     |
| Heroin exposure            | 1.69 (0.34–8.30) | .52     |
| Cocaine exposure           | 1.53 (0.47–4.95) | .48     |
| Non-scheduled exposure     | 1.40 (0.62–3.58) | .37     |
| Rurality (RUCA Code)       | 1.40 (0.55–3.56) | .48     |
| Race and ethnicity         | 0.64 (0.19–2.12) | .46     |
| Pharmacologic intervention | 2.24 (0.81–6.19) | .12     |

Note. \* $p < .05$ ; Substance exposure variables are coded such that 0 = no exposure, 1 = exposure. For Rurality, 0 = urban, 1 = rural. For Race and Ethnicity, 0 = White, 1 = Black. For Pharmacologic Intervention, 0 = no, 1 = yes. For infant placement, 0 = with birthing parent, 1 = other (i.e., CPS custody, adoption, foster care, or with other family member). Non-scheduled Exposure = non-scheduled substances (e.g., Benzodiazepines, SSRIs, and antidepressants). RUCA = Rural-Urban Commuting Area.

related to both the likelihood of meth/amphetamine use (e.g., lower-income, insecure housing; Carrillo Beck et al., 2022; Rommel et al., 2015) and placement decisions that were not accounted for in the present analyses. Similarly, it is possible indicators of severity, rather than intervention type, are better predictors of placement (e.g., observed withdrawal symptoms in infants, compliance of parents with a treatment plan, etc.). Future work should examine if these relations hold after accounting for social and socio-demographic indicators of use.

Results of the LCA yielded a two-class solution comprised of a HWR class and a LWR class. The HWR class was characterized by higher rates of endorsement of exposure to heroin, nicotine, opioids, and non-scheduled substances (e.g., SSRIs, benzodiazepines) compared to the LWR class, and these substances have been previously linked to infant withdrawal symptoms and the escalation of NAS symptoms (Kliegman et al., 2020; Levy & Spino, 1993). In contrast, the LWR class was characterized by higher endorsement rates of prenatal exposure to substances such as meth/amphetamine, cocaine, alcohol, and hallucinogens (predominantly cannabis), which have not been linked to the exacerbation of NAS withdrawal symptoms in the literature (see Kliegman et al., 2020). Though these substances have been linked to long-term deleterious outcomes for the infant, (e.g., Heindel & Vandenberg, 2015) evidence does not suggest their exposure leads infants to experience withdrawal symptoms after delivery.

The LWR and HWR classes were also distinguished by intervention type. Specifically, the LWR class received non-pharmacologic intervention alone in 100% of cases (i.e., 0% received a pharmacologic intervention). This is contrasted with the HWR class, in which 53.36% received both pharmacologic and non-pharmacologic intervention and 46.64% received a non-pharmacologic intervention alone. Class characteristics on intervention type are consistent with previous research suggesting that pharmacologic interventions (typically opioids) are used in more severe withdrawal cases involving higher symptom counts (Mangat et al., 2019). In the case of less severe or absent withdrawal symptoms, which may be more common in the LWR class, it is likely that non-pharmacologic interventions are used over pharmacologic interventions. Beyond parental substance use typology and infant intervention type, demographic differences between classes emerged as well. Namely, the HWR class was more likely to identify as White and live in urban areas. Given that the HWR class was also characterized by high non-scheduled drug exposure (e.g., benzodiazepines, SSRIs), demographic differences may be consistent with a recent literature review suggesting individuals who identify as White are more likely to engage in prescription drug misuse compared to individuals who identify as being from a racial or ethnic minority group (Peteet, 2019). Future research should directly examine prescription drug misuse in diverse samples to bolster these findings.

LWR and HWR class membership was not significantly associated with whether an infant was discharged to their biological parent or to an out of home placement. This finding was unexpected given that the HWR group generally appeared to represent a more severe presentation of NAS, and it may be expected that greater severity would be associated with greater odds of removal from their parent's custody. One potential explanation for this pattern is the role of medication-assisted therapy (MAT). MAT is a relatively common treatment for opioid use disorder, particular among pregnant persons.

SAMHSA statistics estimate that 48.5% of pregnant persons admitted with reported heroin use and 36.9% of pregnant persons admitted with non-heroin opioid use received MAT as part of their treatment plan (HHS, 2012). In this sample, per the intervention protocol and reporting laws in the state of data collection, patients who were deemed stable on MAT (typically Methadone or Buprenorphine) who did not endorse any illicit substance use in pregnancy typically would not have had a CPS referral placed. However, infants exposed to these MAT substances have a higher likelihood of severe withdrawal symptoms. As such, the role of MAT may partially explain the absence of a significant link between the HWR and placement decisions.

Further, this sample is comprised of only pregnant persons who screened positive for substance use. It is possible that in this sample, contextual variables that were unrelated to substance use, such as patient family support or previous CPS involvement (Canfield, 2017), become more salient in clinical decision-making regarding placement decisions. It is important to note that our work found similar rates of infants exposed to substances being discharged to home (73.5%) as that of previous multi-site findings (75.8%; Young et al., 2021), suggesting that the findings of the present study were not due to differences in rates of placement decisions. Future research is needed to replicate the latent classes found here and, provided classes are replicated, examine the clinical utility of LWR and HWR classes; for example, studies can use parental substance use typology, engagement in MAT, and infant intervention type to predict post-hospital discharge outcomes for infant-parent dyads. Further examination and replication of these latent classes is important as identification of at-risk groups can result in more targeted and effective interventions.

It is interesting to compare the class solution and the univariate regressions as they relate to placement decisions. Specifically, as noted above, substances that are associated with risk of physiological withdrawal for the infants (e.g., opioids, nicotine) formed the HWR class; however, despite this increased risk, membership in the HWR class were not more likely to be placed outside of the birthing parent's care. Conversely, at the variable-level, only meth/amphetamine exposure related to placement decisions, even though exposure to meth/amphetamines was not associated with infant withdrawal symptoms or the need for meth/amphetamine driven pharmacologic intervention.

Research suggests that, despite the low withdrawal risk associated with meth/amphetamine exposure in utero (Smith & Santos, 2016), there are a host of environmental and developmental risk factors for infants and children in homes in which a caregiver engages in methamphetamine use (e.g., cognitive and developmental delays, increased prevalence of abuse and neglect; Messina et al., 2014; Perez et al., 2022). Further, there may be increased perceptions among professionals and the public that methamphetamines are the "worst" drug (e.g., Messina et al., 2014; Carlson et al., 2012; Zernike, 2005). Notably, the present finding is congruent with a review

by Austin et al. (2022) that found children with caregivers using methamphetamines were more likely to be removed by child welfare than children with caregivers engaging in other illicit substances. Further, children in homes with caregiver methamphetamine use received higher “priority” scores by child welfare despite having lower prevalence of child abuse compared to homes in which the caregiver used alcohol-only (Carlson et al., 2012). Taken together, it appears that meth/amphetamines may factor more strongly into placement decisions because of increased environmental risk coupled with perceptions about methamphetamine rather than the immediate withdrawal risk associated with other substances.

This study had several strengths regarding methodological design and novel contributions to the literature. First, we employed both person- and variable-centered approaches in addressing our aims, with the LCA providing an exploratory, person-centered approach, and the regressions providing a variable-centered approach. This combination of approaches allowed for a comprehensive examination of both relations among unique variables and subgroups of cases. Additionally, this study addressed an important gap in the literature that investigated the individual relations between substance type and placement decisions (Prindle et al., 2018). Finally, in addition to infants being considered a vulnerable population; pregnant persons have been argued to be both a vulnerable and understudied population (e.g., van der Zande et al., 2017). Therefore, a focus on these populations is a notable strength of this work.

Although our study had several notable strengths, there were also limitations. Importantly, our study was conducted using a previously validated medical record data extraction tool which may have restricted the information obtained. For example, we could not capture all possible constructs associated with placement decision-making including previous CPS involvement, which has been associated with current CPS involvement in cases of infant NAS (Canfield et al., 2017). Additionally, we were unable to assess for differences in the home environment (e.g., income, marital status) and county-level CPS decision processes (e.g., documentation, placement decision criteria). Similarly, this study did not assess details of discharge placement correlated with long-term outcomes, such as whether the placement was voluntary or mandatory, length of stay, and whether the placement was kinship or foster care placement. This study was also unable to include common indicators of substance use severity such as continuous measures of frequency and amount of exposure.

As discussed above, MAT for opioid-use disorder could be an important confound to consider regarding discharge placement. Approximately, 74% of birthing parents in the present sample were identified to have opioid exposure; therefore, information regarding birthing parent participation in MAT alongside opioid exposure would help elucidate its role in placement decisions. This could also be improved by

sampling strategies that ensure opioid exposure is better distributed within the sample population. In addition to limitations regarding available variables, the current study is limited in our ability to generalize results outside of Mississippi, as substance use patterns and CPS responses differ by state (Guttmacher Institute, 2022; HHS, 2020b; HHS, 2020c). Though it is a strength that our study focused on a high-risk population, results may also not generalize to other samples, such as pregnant persons not identified as high risk for substance use. Our sample size is also relatively small, although comparable to other studies using LCA as an analytic strategy (e.g., Karlson et al., 2020). Future studies should look to replicate our findings in larger state and nationally representative samples.

Both our preliminary findings and study limitations inform future research on NAS interventions, discharge placement decisions, long-term outcomes, and sociodemographic differences. First, replication of study results, particularly the indicated latent class structure, are warranted in larger and more diverse samples (e.g., different geographical regions, risk level, etc.). Second, studies that examine the effectiveness of specific intervention types such as pharmacologic versus non-pharmacologic (e.g., behavior or parenting-related) are needed. Third, given this study’s limited variables available for assessment, future research should focus on multimethod and multi-informant approaches in which multiple variables are used to capture multifaceted constructs such as substance use and placement decisions. For instance, future studies can include variables associated with substance use severity such as frequency and quantity to better capture various dimensions of substance exposure. Similarly, studies investigating various aspects of discharge placement decisions, including environmental and contextual factors influencing placement and post-placement outcomes, will be important future directions. Finally, future research should extend the sociodemographic differences found in the current study and examine how demographic characteristics are linked to clinical factors (e.g., types of substance used) and outcomes (e.g., placement decisions). Research has demonstrated profound variations in care (e.g., toxicology screening, initiation of pharmacologic interventions, length of hospital stays) of substance-exposed infants that likely influences infant outcomes (Young et al., 2021). This highlights the necessity for research to provide generalizable evidence that can inform development of uniform and standard practices, including policy changes to support and increase identification of substance-exposed infants, subsequent referrals, communication with CPS, and connection to family supports (e.g., plans of safe care).

## Conclusion

In sum, this study found that meth/amphetamine use during pregnancy, above and beyond the use of other substances, was

associated with higher odds of the infant not being discharged home with their parent(s). We also provide preliminary support for classes of prenatal substance exposure that can be defined as (1) prenatal exposure to substances with a low risk of NAS and non-pharmacologic intervention alone and (2) prenatal exposure to substances with a high risk of NAS and combined pharmacologic and non-pharmacologic intervention. Interestingly, classes were not related to post-hospital discharge placement decisions. Replication of these study findings are needed. Future research should continue to examine the relations between parental substance use, early interventions, and placement decisions to inform the effectiveness of early interventions and to reduce deleterious effects for the infants and parent(s).

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### ORCID iD

Tre D. Gissandaner  <https://orcid.org/0000-0001-7462-8798>

### Notes

1. The  $\geq 36$ -week gestation inclusion criterion was established to not confound prematurity with substance exposure or other confounding factors (e.g., birth defects). The intention of the study was to understand the effect of NAS while minimizing other factors associated with prematurity.
2. The data collection form included substance exposure response options of “no exposure,” “history,” “maternal positive toxicology screen,” and “both history and positive toxicology screen.” Coding of substance exposure for this study was selected due to irreconcilable inconsistencies with how exposure was determined for each substance. Particularly, birthing parent alcohol exposure could only be determined by “history” as toxicology screening for alcohol is unlikely to be positive at the time of birth due to alcohol having a shorter half-life compared to other substances. Relatedly,

the distribution of the responses varied from substance to substance with some substances heavily skewed toward one information type or another. For example, the distribution of birthing parent nicotine exposure was as follows: “history” = 63%, “maternal positive toxicology screen” = 2%, “no exposure” = 35%, “both history and positive toxicology screen” = 0%). While the distribution of birthing parent methamphetamine exposure was: “history” = 2%, “maternal positive toxicology screen” = 17%, “no exposure” = 80%, “both history and positive toxicology screen” = 1%). In totality, to ensure consistency across all participants, we elected to combine information about history and toxicology screen and not distinguish between the two where it would be difficult to detect meaningful associations.

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