Associations of Depression with Opioid Use Among Pregnant Individuals, and Rural-Urban Differences in the Relationships: An Analysis of PRAMS Data

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Abstract

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Background: Depression during pregnancy affects approximately 15–20% of pregnancies and is associated with poor maternal and infant outcomes, including increased risk for preterm birth and inadequate prenatal care. It is also linked to adverse health behaviors, including opioid use. While research has documented associations of depression with opioid use during pregnancy, limited work has examined how this relationship may differ based on geographic residence. Individuals in rural areas face distinct barriers, such as limited access to healthcare, greater stigma, and increased isolation, that may impact both depression and substance use patterns. This study aimed to investigate association of depression with opioid use during pregnancy and whether rural versus urban residence modifies the association.

Methods: This cross-sectional study used 2016–2022 data from Phase 8 of the Pregnancy Risk Assessment Monitoring System (PRAMS), a population-based survey of individuals who recently gave birth. We included respondents (N = 44,048) from 17 jurisdictions that asked about both depression and opioid use, representing a weighted total of 1,760,357 individuals. Depression during pregnancy and opioid use were self-reported. Residence was classified as rural or urban. Survey-weighted logistic regression models estimated odds ratios (ORs) for the association between depression and opioid use. Analyses adjusted for maternal age,

race/ethnicity, education, and household income. Rural/urban status stratified models and models with an interaction term were used to examine effect modification.

Results: Depression during pregnancy was reported by 19.6% of participants. Participants with depression were younger, had lower education, and were more likely to live in rural areas and low-income households, compared with participants who did not report depression. Opioid use was reported by 11.4% of individuals with depression, compared to 5% without depression. Participants with depression had two-fold higher odds of opioid use during pregnancy compared with participants without depression (adjusted OR = 2.02; 95% CI: 1.61–2.55). Although the depression-opioid use association appeared slightly stronger among rural residents (adjusted OR = 2.06; 95% CI: 1.62-2.62), compared with association among urban residents (adjusted OR = 1.82; 95% CI: 1.54-2.17), the interaction term between depression and rural/urban status was not statistically significant ($p > 0.05$).

Conclusion: Depression is strongly associated with increased odds of opioid use during pregnancy, highlighting the need for integrated mental health and substance use screening and treatment during prenatal care. While the observed association was stronger among rural residents, geographic residence did not significantly modify the depression-opioid association. Expanded investment in maternal mental health infrastructure and policies can promote equitable access to care across geographic settings.

Background

Depression during pregnancy, a significant public health concern that complicated about 15-20% of pregnancies in 2020, is associated with adverse infant (e.g., preterm birth and low birth weight) and maternal outcomes (e.g., poor nutrition, inadequate prenatal care, and delayed recognition of labor signs).[1] Depression during pregnancy is also associated with adverse health behaviors and related chronic diseases, such as Opioid Use Disorder (OUD). According to the Centers for Disease Control and Prevention (CDC), approximately 7% of pregnant individuals reported using prescription opioids in 2019, and of those, 21% reported misuse.[3] Data from the 2017 National Survey on Drug Use and Health (NSDUH) indicate that 6.5% of pregnant women reported illicit use of prescription opioids or heroin in the past year, and 1.3% reported use in the past month.[4] Opioid dependence during pregnancy is linked to a range of adverse maternal and neonatal outcomes, including increased risk of maternal mortality, preterm birth, and extended hospital stays.[5]

Previous studies have reported associations of depression with opioid use during pregnancy. Findings from studies among participants of the National Survey on Drug Use and Health as well as the Environmental Influences on Child Health Outcomes Program have indicated that pregnant individuals with depression have 2.15- and 2.42-fold higher risk of opioid use,respectively, compared with pregnant individuals without depression.[6–8] However, limited work has examined potential differences in associations across populations and whether structural and contextual factors modify the association.

There is growing recognition that rural and urban differences may play a role in the relationship between mental health outcomes and substance use behaviors during pregnancy.[9–11] Research suggests that individuals living in rural areas may face higher rates of depression compared to those in urban areas, potentially due to reduced access to healthcare resources, fewer mental

health providers, greater stigma, and increased social isolation.[12] One study using Pregnancy Risk Assessment Monitoring System (PRAMS) data found that rural women in the U.S. had a 21% higher risk of depression compared to urban women, even after adjusting for demographic factors.[13] In addition, a separate study found that a greater proportion of rural pregnant women reported illicit opiate use.[14] However, to our knowledge, no study has examined whether geographic residence modifies the association between depression and opioid use during pregnancy.

This study seeks to address this critical gap in our understanding of the relationship between depression and opioid use during pregnancy. We hypothesized that pregnant individuals who report experiencing depression will have significantly higher odds of reporting opioid use compared to those who do not. We also hypothesized that depression during pregnancy would be more prevalent among those living in rural areas (defined as rural vs. urban residence), and that the association between depression and opioid use would be stronger among rural residents than urban residents. Study findings can help inform design and implementation of targeted interventions, equitable health care strategies, and geography-specific resource allocation efforts for pregnant individuals experiencing depression and/or opioid use. Ultimately, this work aims to contribute to improved maternal and child health outcomes through informed, context-sensitive policy and practice.

Methods

Study Design and Setting

This cross-sectional study used data from the Pregnancy Risk Assessment Monitoring System (PRAMS) Phase 8 (2016–2022). PRAMS is a population-based surveillance system developed by the Centers for Disease Control and Prevention (CDC) in collaboration with state, tribal, and territorial health departments. It collects standardized, site-specific data on maternal attitudes, behaviors, and experiences before, during, and shortly after pregnancy.[15] PRAMS includes individuals who have recently had a live birth,identified through state birth certificate records. PRAMS uses stratified random sampling to ensure the inclusion of underrepresented populations, with sampling strata defined by variables such as race/ethnicity or birth weight. Selected individuals were contacted 2 to 6 months postpartum through mailed surveys, with telephone follow-up for nonrespondents.

Study Population

The current study included respondents who completed the core PRAMS questionnaire and supplemental questions related to opioid use. Phase 8 jurisdictions that administered questions on both depression and opioid use include Arkansas, Arizona, Washington D.C., Indiana, Kansas, Kentucky, Missouri, Montana, North Dakota, Nevada, Puerto Rico, South Dakota, South Dakota Tribal, Vermont, Wisconsin, and West Virginia. Among respondents residing in these jurisdictions, approximately 98% completed the opioid supplement questions. The final analytic sample included 44,048 participants across the 17 participating sites, representing a total population of 1,760,357. This analysis was conducted using de-identified PRAMS data and

was determined to be exempt from Institutional Review Board (IRB) oversight under University of Washington guidelines.[16]

Data Collection

Data for this study were collected through the standardized PRAMS methodology.[15,17] The PRAMS core questionnaire gathers self-reported data on a range of maternal and infant health topics, including prenatal care, maternal stress, substance use, and postpartum experiences. In 2019, PRAMS introduced a supplemental opioid module at select sites, allowing for more detailed assessment of opioid use during pregnancy. The opioid supplement includes questions on types of opioids used, source of the drugs, timing of use during pregnancy, and whether the use was medically supervised. All survey responses are weighted to account for complex sampling design, nonresponse, and noncoverage, ensuring representativeness of the source population.

Exposure, Outcome, and Effect Modifier Assessment

The primary exposure of interest was self-reported depression during pregnancy, measured by the PRAMS question: *"During your most recent pregnancy, did you have any of the following health conditions?"* Participants who responded "Yes" to "depression" were classified as having experienced depression during pregnancy. The primary outcome was self-reported opioid use during pregnancy, assessed through the PRAMS question: *"During your most recent pregnancy, did you take or use any of the following drugs for any reason?"* Participants who reported use of any of the following substances were classified as having used opioids during pregnancy: (1) medications for opioid use disorder (e.g., methadone, naloxone, buprenorphine/Subutex/Suboxone), (2) prescription opioids (e.g., hydrocodone/Vicodin, oxycodone/Percocet, codeine), or (3) illicit opioids (e.g., heroin). Geographic residence was

assessed as a potential effect modifier. It was classified based on the National Center for Health Statistics (NCHS) urban-rural classification scheme, which categorizes counties as urban or rural based on metropolitan status and population size.[18]

Covariates

All covariates were identified a priori due to their potential associations with both the exposure and the outcome and were included in adjusted models to control for confounding. Based on previous literature related to maternal mental health and substance use during pregnancy, a set of sociodemographic characteristics were considered as potential covariates. These included maternal age, race/ethnicity, education level, and household income.[19–21] Maternal age was included as a continuous variable. Race/ethnicity was categorized based on self-reported Hispanic ethnicity and maternal race. Participants were categorized as Non-Hispanic White, Non-Hispanic Black, Non-Hispanic American Indian, Non-Hispanic Asian/Pacific Islander, Non-Hispanic Other/Multiple, or Hispanic (any race). No participants identified as Alaska Native, therefore this group was not included in the analysis. Maternal education was categorized as ≤8th grade, 9–12 without a diploma, high school graduate or GED, some college or associate degree, and bachelor's degree or higher. Household income was calculated as a percentage of the Federal Poverty Level (FPL), using reported household size and income in accordance with the U.S. Department of Health and Human Services (HHS) poverty guidelines for each survey year (2016–2023).[22] The resulting FPL ratio was categorized as <100% FPL, 100–199% FPL, 200–399% FPL, or ≥400% FPL.

Statistical Analysis

Data were analyzed using survey-weighted logistic regression models to account for the complex sampling design. All analyses incorporated appropriate strata, weights, and finite population corrections.

Descriptive statistics were used to characterize the study population. The association between depression during pregnancy and opioid use during pregnancy was examined using unadjusted and adjusted survey-weighted logistic regression models that estimated odds ratios (OR) and corresponding 95% confidence intervals (CIs). Covariates in adjusted models included maternal age, race and ethnicity, education level, and household income. We assessed the association between rural/urban residence and depression during pregnancy using prevalence ratio (PR) estimates (and corresponding 95% CIs) from Poisson regression models with robust standard errors. To assess whether depression-opioid use associations differ by rural/urban residence, we fitted stratified adjusted logistic regression models for rural and urban populations separately. We also fitted an adjusted logistic regression model that included terms for the exposure (depression), outcome (opioid use), and an interaction term for rural/urban residence and depression. The interaction term p-value cutoff ($p\text{-value} < 0.05$) was used to test for statistical significance of the interaction.

All analyses were conducted using R version 4.5.0 and the sryvr package. An alpha=0.05 was used to assess statistical significance in analyses.

Results

Table 1 presents weighted demographic and socioeconomic characteristics of the study population, stratified by depression status during pregnancy. Overall, 19.6% of respondents reported experiencing depression during pregnancy. Individuals reporting depression were slightly younger (mean age 27.2 years) compared to those without depression (mean age 29.0 years). A slightly higher and lower proportion of pregnant individuals with depression identified as Non-Hispanic White (76% vs. 71%) and Hispanic (7.7% vs. 11%), respectively. Individuals with depression reported lower educational attainment, with 14.8% (vs. 10.5%) having less than a high school diploma or GED and only 18% (vs. 39%) having Bachelor's or higher degree. A higher proportion of those with depression (64%) lived in low income households, compared to those without depression (42%). While most participants lived in urban areas (71%), a greater proportion of individuals with depression lived in rural settings (35%) relative to those without depression (27%).

Opioid use during pregnancy was nearly twice as common among those reporting depression (11.4%) compared to those without (5%) (**Table 2**). In unadjusted models, depression during pregnancy was significantly associated with increased odds of any opioid use during pregnancy (unadjusted OR = 2.45; 95% CI: 2.28, 2.63; $p < 0.001$). The association was slightly attenuated but remained statistically significant in adjusted models (adjusted OR = 2.02 ; 95% CI: 1.61, 2.55; $p < 0.001$). Rural/urban residence was not significantly associated with depression (adjusted PR = 0.97, 95% CI: 0.91–1.04; $p = 0.41$). In stratified, unadjusted logistic regression models, the increased odds of any opiod use during pregancy related to depression during pregnancy were slightly higher among rural residents (unadjusted OR = 2.56; 95% CI: 2.08, 3.17; $p < 0.001$) compared to associations among urban residents (unadjusted OR = 2.33; 95% CI: 2.0, 2.7; $p < 0.001$) (**Table 3**). These associations were slightly attenuated but remained statistically significant after adjustment for covariates. Associations were slightly stronger among

rural residents (adjusted OR = 2.06; 95% CI: 1.62, 2.62; $p < 0.001$) compared to similar association among urban residents (adjusted OR = 1.82; 95% CI: 1.54, 2.17; $p < 0.001$). However, the interaction term between rural/urban residence and depression, in overall models with interaction terms, was not statistically significant in both unadjusted ($p = 0.485$) and adjusted ($p = 0.503$) models (all p-values for interactions < 0.05).

Discussion

In the current study, we found that depression during pregnancy was strongly associated with higher odds of any opioid use during pregnancy. In adjusted models, pregnant individuals with depression had twice the odds of reporting opioid use compared to those without depression (OR: 2.02; 95% CI: 1.61–2.55). There was no significant difference in the prevalence of depression between rural and urban residents (PR = 0.97, 95 % CI 0.91–1.04). Although the association between depression and opioid use appeared stronger among rural residents, compared with urban residents, there was no statistically significant evidence that geographic residence modified this relationship.

Numerous population-based studies have documented a strong association between depression during pregnancy and opioid use, with research consistently showing that pregnant individuals experiencing depression are more likely to use opioids compared to those without depression.[6,7] Additional studies have found that depressive symptoms are linked to higher rates of postpartum substance and polysubstance use, as well as increased opioid use after delivery.[23,24] While prior research has highlighted differences in opioid use between rural and urban populations, few have specifically examined whether the relationship between depression and opioid use varies by geographic residence. Some evidence suggests that urban populations may have higher rates of substance misuse linked to earlier initiation and polysubstance use, while social and economic factors influencing opioid overdose may differ between rural and urban areas.[25,26]

In line with past literature, our analysis of a large, population-based dataset confirms a strong positive association between depression during pregnancy and opioid use. However, unlike some previous studies, we did not find statistically significant differences in this relationship between rural and urban residents after accounting for demographic and socioeconomic factors.

This discrepancy may be due to differences in study design, sample selection, and measurement of geographic residence, as well as evolving trends in opioid prescribing and mental health services.[27,28]

The stronger observed associations between depression and opioid use among rural residents, compared with similar associations among urban residents, in both unadjusted and adjusted models, may reflect unique challenges faced by rural populations, such as limited access to mental health and substance use treatment services, greater social isolation, and heightened stigma surrounding both conditions.[11,29,30] These factors could exacerbate the co-occurrence of depression and opioid use in rural settings. While the interaction term was not statistically significant, possibly due to limited power and relatively small differences across rural and urban strata, the patterns observed in both unadjusted and adjusted models were similar, with stronger associations in rural settings. Despite its small size, however, the rural-urban difference in the associaitons may still have significant practical implications. Using a broad rural versus urban classification may overlook important differences within counties, such as access to healthcare or social support, making it harder to detect accurately differences in how depression and opioid use are related. Temporal changes in healthcare services and opioid prescribing patterns during the study period may also have contributed to narrowing disparities. These findings highlight the complexity of geographic influences on maternal mental health and substance use, and underscore the need for more nuanced measures of place and longitudinal data to fully understand these dynamics.

A key strength of this study is its use of a large, population-based sample from PRAMS, which enabled analysis of depression and opioid use during pregnancy across diverse geographic and demographic groups. The use of standardized, state-level data and survey weights enhances

the representativeness and generalizability of findings to the broader population of individuals who recently gave birth.

However, this study has several potential limitations. First, PRAMS relies on self-report data, which may introduce recall bias or social desirability bias, particularly regarding opioid use and depression, as stigma may lead to underreporting or misclassification. Additionally, the cross-sectional nature of PRAMS limits the ability to establish causality between depression and opioid use during pregnancy. The classification of geographic residence at the county level may not fully capture the diversity of rural experiences, as access to healthcare and social resources varies widely within rural populations. Another limitation is the presence of unmeasured confounders, such as trauma history, mental health conditions, and intimate partner violence, which may influence both depression and opioid use. In addition, state-level variability in PRAMS participation, healthcare access, policies around reporting and responding to substance use in pregnancy, and opioid prescribing practices could affect our findings. We did not include state as a covariate in our models, limiting our ability to account for potential confounding due to contextual factors that vary across states. Although PRAMS survey weights are calculated at the state level to ensure representativeness within each state, they do not address variability between states. Lastly, generalizability is a concern, as PRAMS does not capture all pregnant individuals, particularly those who are unstably housed, not receiving prenatal care, or those who may not participate in the survey due to other social or logistical barriers.

Our findings support the need for integrated models of prenatal care that screen for and treat depression alongside substance use. Routine mental health screening and early referral to behavioral health services should be prioritized within prenatal care settings. Improving access to mental health care, particularly in rural areas where services are often limited, may help lower both depression and substance use during pregnancy. From a policy perspective, investing in

maternal mental health infrastructure, such as expanding telehealth services in rural areas, could help reduce geographic disparities in access to care. Expanding Medicaid coverage to include comprehensive mental health and substance use treatment during pregnancy and beyond may also help address unmet needs.

Future research should use longitudinal designs and improved measures of depression and opioid use to better understand their relationship during pregnancy. Studies that examine trauma, co-occurring mental health conditions, and healthcare access could help clarify the link between substance use and depression. Qualitative research may also offer important insights into barriers to care, especially for structurally marginalized groups. In conclusion, our findings demonstrate a strong association between depression during pregnancy and opioid use, particularly among rural residents. Public health and clinical programs should aim to integrate mental health and substance use treatment, expand screening efforts, and invest in systems-level strategies that promote equitable care for pregnant individuals and their infants.

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Table 1: Selected Participant Demographic and Socioeconomic Characteristics

Characteristic	Total Population (N = 1,760,357)[1,2]	No Depression (N = 1,415,337)[1,2]	Depression (N = 345,020)[1,2]
Maternal Age (Mean (SD))	28.6 (5.5)	27.2 (5.6)	29.0 (5.5)
Race/Ethnicity			
Hispanic (any race)	197,663 (11%)	26,641 (7.7%)	171,022 (12%)
Non-Hispanic American Indian	24,411 (1.4%)	5,875 (1.7%)	18,536 (1.3%)
Non-Hispanic Asian/PI	53,573 (3.0%)	3,273 (1.0%)	50,299 (3.6%)
Non-Hispanic Black	175,439 (10.0%)	32,492 (9.4%)	142,947 (10%)
Non-Hispanic Other/Multiple	56,396 (3.2%)	13,944 (4.1%)	42,453 (3.0%)
Non-Hispanic White	1,249,005 (71%)	261,711 (76%)	987,294 (70%)
Education			
≤8th grade	54,004 (3.1%)	6,253 (1.8%)	47,752 (3.4%)
9–12, no diploma	143,533 (8.2%)	43,792 (13%)	99,741 (7.1%)
Bachelor's or higher	605,441 (35%)	62,777 (18%)	542,664 (39%)
High school/GED	466,214 (27%)	120,646 (35%)	345,568 (25%)
Some college/Associate	482,720 (28%)	110,226 (32%)	372,495 (26%)
Income			
High	439,685 (26%)	44,626 (14%)	395,059 (30%)
Low	772,755 (47%)	206,394 (64%)	566,360 (42%)
Middle	447,419 (27%)	73,729 (23%)	373,690 (28%)
Geographic Residence			
Rural	504,655 (29%)	119,173 (35%)	385,481 (27%)
Urban	1,255,702 (71%)	225,846 (65%)	1,029,856 (73%)

[1] Maternal Age presented as Mean (SD); all other values are weighted n (%)
[2] Weighted population estimates representing the analytic population. The unweighted sample size is 44,048.

Table 2: Association Between Depression and Opioid Use During Pregnancy

Depression Status	No Opioid Use[1]	Opioid Use[1]	Unadjusted OR (95% CI)	P-value	Adjusted[2] OR (95% CI)	P-value
No Depression	1,344,517 (95%)	70,820 (5%)	Reference	_ _	Reference	_ _
Depression	305,622 (88.6%)	39,397 (11.4%)	**2.45 (2.28 – 2.63)**	**<0.001**	**2.02 (1.61 – 2.55)**	**<0.001**

[1] Weighted population estimates representing the analytic population. The unweighted sample size is 44,048.
[2] Adjusted for maternal age, race/ethnicity, education, and household income.

Table 3: Effect Modification by Rural/Urban Residence

Residence	Depression Status[1]	No Opioid Use[1]	Opioid Use	Unadjusted OR (95% CI)	P-value	Adjusted[2] OR (95% CI)	P-value
Rural	No Depression	363,676 (94.3%)	21,806 (5.7%)	Reference	_ _	Reference	_ _
	Depression	103,315 (86.7%)	15,858 (13.3%)	2.56 (2.08, 3.17)	<0.001	2.06 (1.62, 2.62)	<0.001
Urban	No Depression	980,841 (95.2%)	49,015 (4.8%)	Reference	_ _	Reference	_ _
	Depression	202,307 (89.6%)	23,539 (10.4%)	2.33 (2.00, 2.70)	<0.001	1.82 (1.54, 2.17)	<0.001

[1] Weighted population estimates representing the analytic population. The unweighted sample size is 44,048

[2] Adjusted for maternal age, race/ethnicity, education, and household income.

Note: The formal test for interaction between depression and rural/urban residence was not statistically significant (p-value < 0.05) in unadjusted (p = 0.485) and adjusted (p = 0.503) models.