Cross-Sectional Study

Latent Class Analysis of Maternal Comorbid Conditions among Hospitalized Pregnant Women Diagnosed with Opioid Use Disorders in North Carolina

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Background: Pregnant women are among the groups most affected by the United States opioid epidemic.

Objectives: To determine latent classes of maternal comorbidities, examine their relationship to opioid use disorder (OUD), and how they can predict hospital discharge status among hospitalized pregnant women with and without OUD.

Study Design: This is a cross-sectional study.

Setting: Hospitals in North Carolina.

Methods: A latent class analysis (LCA) was performed using 929,085 hospital discharge records from the 2000-2014 State Inpatient Databases for North Carolina. We defined OUD status and 24 maternal comorbid conditions based on International Classification of Diseases, Ninth Revision, Clinical Modification diagnostic codes and Clinical Classification Software codes, respectively. Discharge status was categorized as home, institution, or died. Binary and multinomial logistic regression models were constructed adjusting for demographic and hospital characteristics.

Results: LCA of maternal comorbid conditions resulted in 591,745 records belonging to Class 1 (birth complications) and 337,340 records belonging to Class 2 (pre-existing and pregnancy-related morbidities). Class 2 records less frequently belonged to patients with OUD than those without OUD, and more frequently to younger, Black/Hispanic/other race or ethnicity, and patients with a higher socioeconomic status who resided in large metropolitan areas. Non-Medicare primary payers were more likely among Class 2 records. Irrespective of OUD status, patients belonging to Class 2 were less likely to be discharged to an institution or be deceased, controlling for confounders.

Limitations: Administrative database; data clustering; misclassification bias; confounding bias; temporality; data-driven approach; generalizability.

Conclusions: Hospitalized pregnant women may be classified based on comorbid conditions into 2 latent classes ("birth complications" and "pre-existing and pregnancy-related morbidities"), with the former exhibiting greater OUD frequency than the latter. These findings can inform health care needs of populations with a high-risk for OUD.

Key words: Comorbidity, epidemic, health care, hospitalization, maternal, neonatal, perinatal, opioid use disorder.

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The effect of the opioid epidemic has reached a substantial proportion of the United States (US) population (1), with prescription opioid overdose deaths more than quadrupling between 1999 and 2015 (2-4). In 2016, there were approximately 11.8 million past-year opioid misusers, representing 4.4% of the total US population aged 12 or older (5,6). Recent studies suggest that pregnant women are among the most affected groups (7), with opioid use in pregnancy increasing 5-fold between 2000 and 2012 (8). This adds to the burden of substance use among pregnant women as the 2011 US National Survey on Drug Use and Health determined that 5% of pregnant women 15 to 44 years of age report using illicit drugs (9).

A similar trend of opioid use disorder (OUD) has been observed in North Carolina. For instance, there were 1,953 opioid-related deaths in the state in 2017 - a rate of 19.8 deaths per 100,000 persons compared to the national rate of 14.6 deaths per 100,000 (9,10). The unintentional poisoning mortality rate among pregnant women in North Carolina has also more than doubled since 2012, with a current overdose rate of 23.3 deaths per 100,000 due to prescription opioid analgesics including fentanyl, hydrocodone, methadone, and oxycodone (10,11).

Opioid dependence during pregnancy increases the risk of maternal and perinatal complications (12-14), adversely affecting the clinical management of an already vulnerable group of patients. Despite the significant health risks associated with OUD, discharge-level factors predictive of OUD-related hospitalizations remain poorly understood. Studies on this topic (15-17) have identified several factors – childhood trauma, chronic depressive disorder, a family history of substance use disorder, chronic medical condition, and hypertension – associated with an increased risk of OUD hospitalizations. However, these studies utilized descriptive methods and logistic regression modeling that have a limited ability to accurately evaluate patterns of comorbid conditions within affected patients.

By contrast, latent class analysis (LCA) categorizes events or patient groups into distinct classes based upon observed patterns in the data (18). Previous studies implementing LCA have largely focused on characterizing the heterogeneity of opioid-using populations from different data sources. For instance, evaluations of national survey data found that opioid users fall into 2-5 latent classes based on increasing severity of OUD or other drug use (19-22). In an evaluation of illicit drug users from a multisite cohort study, Monga et al (18) described 3 classes of persons who use illegal opioids, including the concurrent use of prescription acetaminophen, noninjection drug use, and the most severe class of persons who use heroin and cocaine. Using the Pennsylvania Health Care Cost Containment Council dataset, Liu et al (21) also identified 5 latent patient groups that were associated with opioid-related hospitalizations, one of which was pregnant women with OUD.

We used LCA analysis to examine and characterize patterns of maternal comorbid conditions among hospitalized pregnant women diagnosed with OUD in North Carolina. Using an LCA approach may be particularly important for OUD-related hospitalizations due to the need to categorically account for a complex group of factors that contribute to this disorder. Accordingly, we used the State Inpatient Databases (SID) for North Carolina, a database containing discharge-level records from 125 community hospitals as reported by the North Carolina Department of Health and Human Services (23), to a) determine distinct latent classes of maternal comorbid conditions, b) examine the relationship of OUD status with these latent classes, and c) examine how these latent classes predict discharge status among pregnant women who have and do not have OUD. With prescription opioid use among women of reproductive age increasing since the late 1990s, concern regarding the effect of OUD on maternal and neonatal health has grown. Our findings will help target interventions for high-risk subgroups among a diverse population of pregnant women with OUD.

Methods

Data Sources

Data included inpatient discharge records reported for community hospitals in North Carolina. Specifically, a retrospective analysis of all pregnancy-related hospital discharges was conducted using the SID for the years 2000-2014. The SID is a family of databases and software tools developed for the Healthcare Cost and Utilization Project (HCUP) (24) that includes inpatient discharge records from community hospitals in selected states. The SID files encompass all patients, regardless of payer, providing a unique view of inpatient care in a defined market or state over time. The stratified systematic random sampling method used by the SID ensures a more representative sample of discharges than a simple random sample would yield (24).

Study Variables

Hospital discharges for women who either were pregnant or had delivered were identified using the indicator variable "NEOMAT" (coded as 0 = "no", 1 = "yes") in the SID dataset. The NEOMAT indicator variable was created by HCUP to identify maternal and/or neonatal diagnosis records based on the International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) diagnosis (25). The ICD-9-CM has more than 14,000 diagnostic codes that are used in the context of the HCUP SID hospital discharge records. For accuracy and efficiency, we used a uniform and standardized coding system called the Clinical Classifications Software (CCS). The CCS collapses the ICD-9-CM codes into 679 clinically meaningful categories (26) that are more useful than individual ICD-9-CM codes for presenting descriptive statistics pertaining to maternal comorbidities. This analysis was approved by the Institutional Review Board at Western Carolina University.

Demographic variables were extracted using the SID database. Maternal age was categorized as < 18, 18-24, 25-29, 30-34, 35-39 and 40+ years, whereas race was categorized as White, Black, Hispanic, Asian or Pacific Islander, Native American or Other. Primary payer was defined into 3 categories, namely, public (Medicare/Medicaid), private, and other (Self-pay, No charge, Other). Relative median household income (in quartiles) was estimated by HCUP using the patient's zip code and served as a proxy for socioeconomic status. Hospital characteristics, such as hospital location (based on Metropolitan Statistical Area and Core Based Statistical Area) as well as year of admission were also included in these analyses. OUD status was defined as a dichotomous variable based on ICD-9-CM diagnostic codes, as previously described elsewhere (27). Discharge status was categorized as home, institution, or died.

Statistical Analysis

Latent Class Analysis

We applied LCA to investigate patterns, predictors and outcomes of maternal comorbid conditions among pregnant women diagnosed with OUD. LCA is an exploratory technique that inputs observed categorical variables and predicts class membership of observations based on values of these variables. LCA is often used to empirically determine discrete latent variables (constructs that are not observed directly) from a series of 2 or more discrete observed variables and form subgroups based on observations that appear to be similar (28). LCA provides 2 key outputs: the probability of class membership for each observation (conditional item probability parameter) and overall prevalence in each class (class probability parameter). Expectation Maximization Algorithm is used to calculate the class membership likelihood (29).

The process of likelihood estimation is iterative. In each iteration, the procedure algorithm attempts to improve the fit of the model such that expected class membership values get closer to observed class values based on the same identification codes. Choosing the appropriate number of distinct classes is a decision-making step in LCA. This decision is usually based on 2 criteria: statistical fit and substantive theory or interpretability of the classes. LCA provides a classification of cases with categorical indicators similar to factor analysis with continuous variables. However, LCA also provides the probability of a particular case belonging to a latent class that is solely data-driven. It is assumed that the observed manifest variables are independent of one another once conditioned on the latent variable (21,28). In the current study, the patients were assigned to the different classes based on their posterior probabilities for class membership for a particular discharge diagnosis profile.

Model Building and Analysis

All data analyses were performed using (STATA version 15, StataCorp LLC, College Station, TX). First, we estimated the prevalence rates of major comorbidity types, defined based on CCS codes with their 95% confidence intervals (CI). Next, LCA was performed on 24 highly prevalent comorbidities using Stata's generalized structural equation model estimation command, gsem. The selection for the appropriate number of latent classes (LCs) was determined by comparing the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and χ^2 goodness-of-fit test statistics among models. As such, we selected the most parsimonious model which divided hospitalizations into 2 distinct classes. Predictors of belonging to either latent class, including OUD status and patient- and hospital-level characteristics, were evaluated using binary logistic regression models, whereby adjusted odds ratios (OR) with their 95% CI were estimated. Similarly, latent classes were examined as predictors of discharge status among OUD and non-OUD hospital discharges, before and after controlling for patient and hospital characteristics, using multinomial logistic regression modeling whereby relative risk ratios with their 95% CI were

estimated. Two-sided statistical tests were conducted at $\alpha = 0.05$.

Results

Table 1 presents the prevalence rates of 24 maternal comorbid conditions that were identified among 929,085 eligible hospital discharge records for the purpose of LCA. As expected, the majority of these CCS codes were focused on preexisting chronic conditions as well as pregnancy-related maternal and neonatal complications, although some of these CCS codes were focused on clinical procedures rather than diagnoses. Prevalence rates ranged between 0.6% for patients who had "forceps delivery" and 89% for patients with a "normal pregnancy and/or delivery." The remaining comorbidities had prevalence rates that ranged between 2.4% and 47.8%.

As shown in Table 2, 591,745 (63.7%) of eligible records belonged to latent class one whereas 337,340 belonged to latent class 2. When the LCA was conducted, assuming 2 latent classes, the AIC, BIC, and χ^2 goodness-of-fit test statistics suggested that the model was a good fit to the data.

When comparing hospital discharge records that belonged to class 2 versus hospital discharge records that belonged to class one, we found that they were more or less likely to have received specific CCS codes. Specifically, class 2 records had lower odds than class one records for having "prolonged pregnancy," "fetopelvic disproportion or obstruction," "fetal distress and abnormal forces of labor," "polyhydramnios and other problems of the amniotic cavity," "umbilical cord complication," "obstetrics-related trauma to perineum and vulva," "forceps delivery," "other complications of birth or puerperium affecting management of mother"

Table 1. *Types of maternal comorbid conditions (n = 929,085).*

Condition #	Maternal Comorbidity Type	DX Classification Codes	Prevalence (95% Confidence Interval)
1	Immunizations and screening for infectious disease	10	0.211 (0.210 – 0.214)
2	Other nutritional; endocrine; and metabolic disorders	58	0.0492 (0.0488 – 0.0497)
3	Deficiency and other anemia	59	0.0925 (0.0919 – 0.0931)
4	Coagulation and hemorrhagic disorders	62	0.0164 (0.0161 – 0.0166)
5	Substance-related mental disorders	67	0.00805 (0.00787 – 0.00824)
6	Urinary tract infections	159	0.0188 (0.0185 – 0.0190)
7	Contraceptive and procreative management	176	0.0849 (0.0844 – 0.0855)
8	Other complications of pregnancy	181	0.478 (0.477 – 0.479)
9	Hemorrhage during pregnancy; abruptio placenta; placenta previa	182	0.0237 (0.0234 – 0.0241)
10	Hypertension complicating pregnancy; childbirth and puerperium	183	0.119 (0.118 – 0.120)
11	Early or threatened labor	184	0.094 (0.0938 – 0.0949)
12	Prolonged pregnancy	185	0.109 (0.108 – 0.110)
13	Diabetes or abnormal glucose tolerance complicating pregnancy; childbirth; or puerperium	186	0.078 (0.077 – 0.079)
14	Malposition; malpresentation	187	0.070 (0.069 – 0.071)
15	Fetopelvic disproportion; obstruction	188	0.0474 (0.0470 – 0.0479)
16	Previous C-section	189	0.143 (0.142 – 0.144)
17	Fetal distress and abnormal forces of labor	190	0.0878 (0.0872 – 0.0884)
18	Polyhydramnios and other problems of the amniotic cavity	191	0.122 (0.121 – 0.123)
19	Umbilical cord complication	192	0.194 (0.193 – 0.195)
20	OB-related trauma to perineum and vulva	193	0.340 (0.339 – 0.341)
21	Forceps delivery	194	0.00627 (0.00611 – 0.00643)
22	Other complications of birth; puerperium affecting management of mother	195	0.433 (0.432 – 0.434)
23	Normal pregnancy and/or delivery	196	0.890 (0.889 – 0.891)
24	Residual codes; unclassified	259	0.0439 (0.0435 – 0.0443)

Table 2. *Latent classes of maternal comorbid conditions (n = 929,085).*

	Class I (n=591,745)			Class II (n=337,340)		
Type	**B**	**95% CI**	***P***	**B**	**95% CI**	***P***
1	-1.089	-1.095, -1.082	< 0.0001	-1.758	-1.771, -1.754	< 0.0001
2	-3.561	-3.58, -3.542	< 0.0001	-2.389	-2.402, -2.376	< 0.0001
3	-2.512	-2.524, -2.501	< 0.0001	-1.986	-1.998, -1.975	< 0.0001
4	-4.408	-4.434, -4.381	< 0.0001	-3.729	-3.729, -3.704	< 0.0001
5	-5.307	-5.351, -5.263	< 0.0001	-4.324	-4.357, -4.292	< 0.0001
6	-5.839	-5.898, -5.781	< 0.0001	-3.074	-3.091, -3.057	< 0.0001
7	-3.407	-3.427, -3.390	< 0.0001	-1.586	-1.596, -1.576	< 0.0001
8	-.3142	-.3204, -0.308	< 0.0001	0.276	0.268, 0.285	< 0.0001
9	-4.893	-4.931, -4.855	< 0.0001	-2.945	-2.962, -2.929	< 0.0001
10	-2.353	-2.364, -2.342	< 0.0001	-1.574	-1.583, -1.563	< 0.0001
11	-2.920	-2.935, -2.905	< 0.0001	-1.631	-1.641, -1.621	< 0.0001
12	-1.566	-1.574, -1.558	< 0.0001	-4.796	-4.868, -4.723	< 0.0001
13	-2.849	-2.863, - 2.836	< 0.0001	-2.023	-2.035, -2.012	< 0.0001
14	-3.011	-3.027, -2.993	< 0.0001	-2.121	-2.135, -2.109	< 0.0001
15	-2.668	-2.679, -2.656	< 0.0001	-3.918	-3.956, -3.881	< 0.0001
16	-3.272	-3.295, -3.249	< 0.0001	-0.782	-0.7912, -0.773	< 0.0001
17	-2.041	-2.050, -2.032	< 0.0001	-3.070	-3.097, -3.044	< 0.0001
18	-1.872	-1.880, -1.863	< 0.0001	-2.149	-2.163, -2.136	< 0.0001
19	-1.044	-1.051, -1.037	< 0.0001	-2.328	-2.344, -2.311	< 0.0001
20	0.165	0.157, 0.172	< 0.0001	-3.969	-4.031, -3.907	< 0.0001
21	-4.642	-4.669, -4.613	< 0.0001	-6.907	-7.064, -6.750	< 0.0001
22	-0.260	-0.266, -0.254	< 0.0001	-0.279	-0.287, -0.271	< 0.0001
23	5.041	4.985, 5.096	< 0.0001	0.968	0.959, 0.978	< 0.0001
24	-3.395	-3.412, -3.379	< 0.0001	-2.711	2.726, -2.696	< 0.0001
Fit Statistics						
χ^2, Sign.	1.000					
AIC	5.22*10^6					
BIC	5.22*10^6					

Abbreviations: AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion

or "normal pregnancy and/or delivery," with odds ratios ranging between 0.018 and 0.96. By contrast, class 2 records had higher odds than class one records for "other nutritional, endocrine, and metabolic disorders," "deficiency and other anemia," "coagulation and hemorrhagic disorders," "substance-related mental disorders," "urinary tract infections," "contraceptive and procreative management," "other complications of pregnancy," "hemorrhage during pregnancy, abruptio placenta, placenta previa," "hypertension complicating pregnancy, childbirth, and the puerperium," "early or threatened labor," "diabetes or abnormal glucose tolerance complicating pregnancy, childbirth, or the puerperium," "malposition, mal-presentation" and "previous C-section," with odds ratios ranging between 28.21 and 1.85. Based on labels provided to these CCS codes, it appears that class one is focused on "birth complications" whereas class 2 is focused on "pre-existing and pregnancy-related morbidities" (Table 3).

Table 4 presents a multiple logistic regression model for OUD, patient and hospital characteristics as predictors of latent classes of maternal comorbid conditions. Taking class one records as a reference group, class 2 records were less likely to belong to OUD patients (OR = 0.43, 95% CI: 0.41 – 0.46). Similarly, class 2 records corresponded to younger patients and to patients who were more likely to be Black, Hispanic, or of another race. Whereas class 2 exhibited a higher

Table 3. *Relationship of comorbidities with latent classes (n = 929,085).*

DX Classification Codes	OR (95% Confidence Interval)
10	0.44 (0.43 – 0.44)
58	4.06 (3.98 – 4.14)
59	2.04 (2.02 – 2.08)
62	2.36 (2.28 – 2.44)
67	3.47 (3.31 – 3.64)
159	17.66 (16.78 – 18.58)
176	8.79 (8.63 – 8.95)
181	1.85 (1.84 – 1.86)
182	9.74 (9.40 – 10.11)
183	2.77 (2.74 – 2.81)
184	5.61 (5.52 – 5.70)
185	0.018 (0.017 – 0.019)
186	3.02 (2.97 – 3.07)
187	4.01 (3.94 – 4.08)
188	0.19 (0.18 – 0.19)
189	28.21 (27.65 – 28.77)
190	0.24 (0.24 – 0.25)
191	0.73 (0.72 – 0.74)
192	0.22 (0.22 – 0.23)
193	0.005 (0.005 – .005)
194	0.070 (0.062 – 0.080)
195	0.96 (0.95 – 0.97)
196	0.01 (0.009 – 0.01)
259	2.11 (2.06 – 2.15)

Table 4. *Predictors of latent classes of maternal comorbid conditions (n = 929,085).*

	Proportion	OR (95% CI) Class II vs Class I
OUD status:		
Yes	0.0047	0.43 (0.41 – 0.46)
No	0.995	Ref.
Patient and hospital characteristics		
Age (years):		
< 18	0.03	Ref.
18-24	0.32	0.66 (0.65 – 0.68)
25-29	0.28	0.47 (0.46 – 0.48)
30-34	0.23	0.37 (0.35 – 0.38)
35-39	0.11	0.27 (0.26 – 0.28)
40+	0.03	0.20 (0.19 – 0.21)
Race / Ethnicity:		
White	0.55	Ref.
Black	0.24	0.63 (0.62 – 0.64)

Table 4 (cont.). *Predictors of latent classes of maternal comorbid conditions (n = 929,085).*

	Proportion	OR (95% CI) Class II vs Class I
Race / Ethnicity:		
Hispanic	0.08	1.21 (1.19 – 1.23)
Asian or Pacific Islander	0.03	1.45 (1.41 – 1.49)
Native American	0.02	0.87 (0.84 – 0.90)
Other	0.08	1.28 (1.26 – 1.30)
Household income (quartile):		
1st	0.25	Ref.
2nd	0.24	1.06 (1.05 – 1.07)
3rd	0.24	1.15 (1.14 – 1.17)
4th	0.27	1.35 (1.33 – 1.37)
Urban-rural location:		
Large metropolitan areas with at least 1 million residents	0.24	Ref.
Small metropolitan areas with less than 1 million residents	0.52	1.06 (1.04 – 1.07)
Micropolitan areas	0.18	0.95 (0.94 – 0.96)
Not metropolitan or micropolitan	0.06	0.90 (0.88, 0.92)
Primary payer:		
Medicare	0.006	Ref.
Medicaid	0.48	1.82 (1.72 – 1.92)
Private insurance	0.44	2.68 (2.54 – 2.83)
Self-pay	0.036	1.36 (1.28 – 1.44)
No charge	--	--
Other	0.034	2.13 (2.00 – 2.26)
Year of admission:		
Before 2011	0.48	Ref.
2011 or later	0.52	1.04 (1.04 – 1.06)

socioeconomic status than class one, they were also more likely to reside in large metropolitan areas and to have been admitted during the time period from 2011 through 2014. All primary payers besides Medicare were more likely to belong in class 2.

Table 5 presents latent classes of maternal comorbid conditions as predictors of discharge status among OUD and non-OUD pregnancies. Overall, patients in class 2 were less likely than patients in class one to be discharged to an institution or to be deceased at discharge, after controlling for patient- and hospital-level characteristics. Furthermore, we found similar results among OUD and non-OUD pregnancies, with no

significant interaction effects between OUD status and latent class of maternal comorbid conditions.

Discussion

Our analysis of pregnancy-related discharge records in North Carolina from 2000 – 2014 reveals the clustering of fetomaternal events into 2 distinct groups. The larger group (latent class one), accounted for approximately 64% of pregnancy-related discharge records and showed higher odds of comorbid OUD, being white, older, and belonging to a lower socioeconomic class. Class one records were also more likely to have fetal complications and negative perinatal outcomes. This finding reflects what has been reported in most scientific studies, especially in terms of neonatal outcomes and the sociodemographic characteristics of pregnant women with comorbid OUD. For instance, Tolia and colleagues' analysis (30) of neonatal intensive care unit data for 33 states in the US for the years 2004 – 2013 shows an increase in neonatal withdrawal symptoms (NWS) resulting predominantly from in-utero exposure to opioids. The authors also found a large majority of the infants with NWS had mothers who were white.

Although whites are reported to have higher rates of opioid misuse, opioid overdose, and opioid-related deaths in general, a 2019 analysis of opioid overdose deaths in metropolitan areas of the US found ethnic minorities are equally affected (31). These researchers from the US Department of Health and Human Services examined the ethno-geographic distribution of opioid-related deaths from 2015-2017 using the new National Center for Health Statistics urban-rural classification scheme for US counties (31). The authors found that Blacks had the largest increases in opioid deaths among people in "large central metro areas" (inner cities) and "medium and small metro" areas; whites had the largest increases in areas designated "large fringe metros" (suburbs). As earlier mentioned, our study also found a difference in the odds of being in either latent classes based on income and health insurance status. Individuals of low-socioeconomic status and reliant on public insurance have been shown to be less likely to have access to medication-assisted treatment for opioid use disorder (32). Easy access to prescription opioids and difficulty accessing opioid treatment programs is common in economically disadvantaged women and portend higher opioid misuse rates with attendant negative perinatal outcomes such as prolonged labor and fetal distress.

Even though class 2 records represented only 36% of the study population, a few important issues emerged in this group, including a higher likelihood of having chronic medical problems affecting maternal health. Additionally, compared to class one, those in class 2 had higher odds of having preexisting and pregnancy-related morbidities and are more likely to be of a higher socioeconomic status, being residents in large metropolitan areas, and of not being publicly insured. The strong correlation with a previous Cesarean section (C-section) is particularly striking as the odds of this relatively common procedure in the US was 28 times higher among those in class 2 compared with class 1 records. To put things into perspective, approximately one-third of births in the US in 2018 were via C-section, which increases to about 40% among women aged 40 and older (33). The link between C-section and OUD remains uncertain. However, a recent study of over 308,000 deliveries (2008 – 2016) by investigators at the University of Michigan is revealing; the authors found approximately 72% of opioid-naïve women with Cesarean deliveries were prescribed opioid analgesics in 2016 (down from 76% in 2008), compared with 23.8% for mothers with vaginal deliveries (34). The implication of this prescription pattern, the investigators found, is that over 2% of the women with Cesarean deliveries (1.7% for vaginal deliveries) continued to use opioids. With approximately one-third of births in the US in 2018 reported to be via C-section, the current opioid prescribing practice may add to the existing burden of OUD among pregnant women (33).

Disposition outcomes also differed among the 2 latent classes of maternal comorbid conditions as those belonging to class 2 were less likely to have died or to be transferred to another facility at discharge, compared with those in class one. Given that preexisting

Table 5. *Latent classes of maternal comorbid conditions as predictors of discharge status, overall and according to OUD status.*

Latent Classes	Discharge Status [a]	
	Institution RRR (95% CI)	Died RRR (95% CI)
Class II vs Class I		
Overall	0.086 (0.081 – 0.092)	0.12 (0.07 – 0.20)
OUD	0.18 (0.11 – 0.26)	--#
Non-OUD	0.086 (0.081 – 0.091)	0.12 (0.073 – 0.20)

[a] All models were adjusted for patient and hospital characteristics and discharge status. "Home" was used as reference; # = Not enough data available to estimate relative risk ratios with their 95% confidence intervals; Abbreviations: CI=Confidence Interval, RRR=Relative Risk Ratio.

chronic medical conditions (especially of cardiovascular, infectious, and hemorrhagic origins) contribute more to the burden of pregnancy-related mortality in the US, it is unclear from our study why the odds of mortality was greater among those in class one (35). One plausible explanation is the more acute nature of admissions for patients belonging to class one versus class 2, given that fetal complications are likely to influence maternal health around the time of delivery.

Our findings should be interpreted with caution in light of several limitations. First, an administrative database that consists of patient- and hospital-level data elements typical of hospital discharge records was utilized, with limited information on physical examinations, laboratory tests and medications. Second, data clustering because of patient readmission to one of the participating hospitals could not be evaluated, without access to unique patient identifiers. Third, many study variables, including comorbid conditions, were defined based on ICD-9-CM or CCS codes, potentially leading to misclassification bias. Fourth, residual confounding by unmeasured or inadequately measured covariates may have led to biased measures of association. Fifth, this study design does not allow the establishment of temporality or causal relationships between exposure and outcome variables. Sixth, reliance on AIC, BIC, and other criteria can be considered a data-driven approach to choosing the number of classes and can potentially lead to overfitting, although the large sample size may have compensated for this data-driven approach. Finally, study results can only be generalized to hospitalized patients from North Carolina and potentially the US, with those seeking inpatient care having different characteristics from those who sought outpatient care.

In conclusion, pregnant women who are hospitalized may be classified based on their comorbid conditions into 2 groups, namely those with "birth complications" and those with "pre-existing and pregnancy-related morbidities," with the former group exhibiting greater odds of having OUD than the latter group. These findings may be useful for planning health care services in the context of hospitalized patients with OUD by informing health care providers about the health care needs of high-risk populations. Furthermore, predictive models linking these latent classes to health care utilization outcomes may aid health care professionals in clinical decision making. Due to the exploratory nature of our analyses and the complexity of maternal, perinatal, and neonatal complications, labeling a new patient as belonging to one of the 2 classes and consecutively predicting her clinical course may be difficult. By contrast, prediction of a clinical outcome using machine learning may be more efficient in the context of databases, whereby more detailed clinical characteristics are available. As such, prospective cohort studies are needed to confirm these exploratory findings.

Authors' Roles

Dr. Alemu conceptualized the original research study, obtained funding for conducting the study, performed statistical analysis, and drafted and revised the manuscript for intellectual content. Dr. Beydoun performed confirmatory statistical analyses, drafted specific sections of the manuscript and revised the manuscript for intellectual content; Dr. Olayinka performed literature reviews, drafted specific sections of the manuscript and revised the manuscript for intellectual content.

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