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Short Communication

Cluster analysis to identify patient profiles and substance use patterns among pregnant persons with opioid use disorder

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ABSTRACT

The study objective was to identify distinct profiles of pregnant persons with opioid use disorder (PP-OUD) using cluster analysis and examine difference in substance use patterns between profiles. We examined data from 104 PP-OUD ≤ 32 weeks of gestation who were recruited into a behavioral health clinical trial at two academic medical centers. We used Partitioning Around Medoids analysis to identify clusters and explored patterns of substance use and substance use treatment between clusters using bivariate statistical tests and regression methods. We identified two distinct clusters of participants, including 'Group A' (n = 68; 65.4 %) and 'Group B' (n = 36; 34.6 %). Group A had fewer members who were not employed (38 % vs 58 %) and incarcerated (3 % vs 8 %) compared to Group B. Group A compared with Group B included more members with: a history of overdose (72 % vs 50 %); anxiety (85 % vs 25 %); ≥moderate pain (76 % vs 22 %); ≥moderate depression (75 % vs 36 %); ≥moderate drug use severity (94 % vs 78 %); and, more days of cannabis (mean: 6.2 vs 2.3 days), stimulant (mean: 4.5 vs 1.3 days), and injection heroin (mean: 1.3 vs 0 days) use in the past 30 days ($P < 0.05$ for all comparisons). Clusters of PP-OUD differed with respect to sociodemographic characteristics, mental health conditions, and substance use patterns. More research is needed to confirm identified profiles and assess treatment outcomes associated with cluster membership.

1. Introduction

The prolonged US opioid crisis has greatly impacted pregnant people. Rates of maternal opioid use disorder (OUD) documented at delivery increased 400 % from 1999 to 2014 and 131 % from 2010 to 2017 (Haight, Ko, Tong, Bohm, & Callaghan, 2018; Hirai, Ko, Owens, Stocks, & Patrick, 2021). While gold-standard treatments—formulations of methadone or buprenorphine combined with adjunctive behavioral therapies—are effective to improve outcomes of pregnant people with OUD (PP-OUD) (Klaman et al., 2017), OUD is a heterogenous disease with respect to addiction severity, comorbidities, and recovery progression (Carroll, 2021). This heterogeneity complicates care planning and delivery as not all individuals may respond similarly to recommended treatment. An important initial step in tailoring pharmacologic and behavioral treatments for PP-OUD is to begin to understand clinically-meaningful, similar subtypes of individuals with the disease. A

Abbreviations: PP-OUD, pregnant persons with opioid use disorder.

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more refined taxonomy of OUD in pregnancy would support identification of PP-OUD most likely to benefit from specific treatment plans and interventions. This exploratory study sought to empirically identify profiles of PP-OUD using cluster analysis, a multidimensional approach that partitions data into homogenous groups on the basis of selected characteristics (Romesburg, 2004), and examine differences between profiles in substance use and treatment patterns.

2. Materials and methods

2.1. Study design and population

This secondary analysis used data from the Optimizing Pregnancy and Treatment Interventions for Moms (OPTI-Mom) 2.0 study, a prospective clinical trial testing the efficacy of a patient navigator intervention to prevent return to illicit substance use among PP-OUD (Cochran et al., 2019). Briefly, participants were pregnant individuals, ≤32 weeks of gestation presenting with OUD at urban academic medical centers in Utah and Western Pennsylvania. Participants were recruited between April 2019- January 2022 and followed for 6 months postpartum. Institutional review boards of the medical centers approved the study. Validated standardized questionnaires were used to obtain information about overdose, pain, mental health, alcohol use, drug use, and treatment services (Table A1).

2.2. Measures

2.2.1. Overdose experiences, self and witnessed-drug (OESW-D) questionnaire

Lifetime prescription or illicit drug overdose was assessed using the Overdose Experiences, Self and Witnessed—Drug (OESWD) instrument (Fernandez et al., 2019). Participants were provided a description of the term 'overdose' and asked to report the number of overdose events they experienced in their lifetime and when they occurred, which we categorized into no overdose history, overdose (≥1) in their lifetime, and overdose (≥1) in the past year.

2.2.2. 36-Item short form health Survey (SF-36)

We assessed pain with the two-item Bodily Pain subscale of the 36-Item Short Form Health Survey (SF-36), a valid and reliable questionnaire for evaluating health-related quality of life (McHorney, Ware Jr, & Raczek, 1993; Ware Jr & Sherbourne, 1992). Pain items were scored on a scale of 0 (lowest) to 100 (highest). We then averaged component scores and dichotomized participant responses into minimum or no pain (<60) and moderate or more pain (≥60).

2.2.3. Primary care Evaluation of mental Disorders (PRIME-MD) patient health questionnaire (PHQ)

We used the PRIME-MD PHQ to assess anxiety (no (0) vs some (≥1) anxiety) and depression (mild or no (0–9), moderate (10–14), and severe (15–27) depression). The PRIME-MD PHQ screens for anxiety, depression, and other clinical and subthreshold disorders measured on the basis of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (Spitzer, Kroenke, Williams, Group, & Group, 1999; Spitzer et al., 2000).

2.2.4. Alcohol use disorders identification test-concise (AUDIT-C)

We evaluated alcohol misuse using a three-item alcohol screen, AUDIT-C, which is a reliable and valid screening test assessing the frequency and quantity of drinking during the past year (Bush et al., 1998). The AUDIT-C is scored from 0 to 12, with a score of ≥ 3 indicating alcohol misuse for women (Bradley et al., 2004).

2.2.5. Drug Abuse screen Test-10 (DAST-10)

We measured non-opioid drug use severity with the DAST-10, a valid and reliable 10-item brief drug screening questionnaire evaluating drug use, not including tobacco or alcohol use, in clinical or research settings (Skinner, 1982; Yudko, Lozhkina, & Fouts, 2007). Participants were asked to consider drugs other than opioids when responding to the questions. Their responses were dichotomized into no or low severity (<3) and moderate or above (≥3) severity non-opioid drug use.

2.2.6. Treatment services Review-6 (TSR-6)

We ascertained the number of days of mental health and substance use disorder (SUD) treatment services utilization using the TSR-6 instrument, which captures receipt of substance use support services in the past 28 days within the following domains: medical, employment/self-support, alcohol, drug, legal, family/social, and psychiatric (Cacciola et al., 2008).

2.2.7. Timeline followback (TLFB)

The TLFB method was used to measure number of days of drug use in the past 30 days for the following substances: prescription opioids, cannabis, stimulants, and heroin. Originally developed to collect retrospective reports of alcohol use (Sobell & Sobell, 1992), TLFB methodology validly detects illicit substance use in populations with SUDs (Hjorthøj, Hjorthøj, & Nordentoft, 2012).

2.2.8. Sociodemographic characteristics

Sociodemographic characteristics were captured via self-report and included: age; race; marital status; education; employment; region; incarceration during study period; and number of previous children.

2.3. Statistical analysis

We performed cluster analysis using sociodemographic and behavioral health characteristics (Table 1) and employed the Partitioning Around Medoids (PAM) method to identify underlying population clusters (Kaufman & Rousseeuw, 2008). We used to Gower distance to quantify the similarity between subjects and silhouette width, an internal validation metric that is an aggregated measure of how similar an observation is to its own cluster compared its closest neighboring cluster, to select the number of clusters for the final model (Gower, 1971; Rousseeuw, 1987). Table A2 in the supplement contains a more detailed description of the PAM methodology. PAM has been used successfully in healthcare research to identify clinical subtypes in opioid use, post-traumatic stress disorder, and depression (Brancati et al., 2019; Siegel, Laska, Lin, & Marmar, 2020; Sun et al., 2012).

We compared patterns of drug use severity and alcohol misuse between clusters using chi-squared tests and regression models. We compared days of drug use and SUD treatment in the past month between clusters using Student's t-tests and linear regression models. Group B was used as the reference in all models. Logistic regression estimates are presented as odds ratio (OR) and 95 % confidence intervals (CIs) and linear regression estimates are presented as regression coefficients (β) and 95 % CIs. We defined a significance level of 5 % for all statistical tests. Data were analyzed using R version 3.5.2.

3. Results

3.1. Cluster selection

After calculating silhouette width for clusters ranging from 2 to 10 for the PAM algorithm, we observed that 2 clusters yielded the highest value (Figure Al). We labeled the first cluster as 'Group A' (n = 68; 65.4 %) and the second cluster as 'Group B' (n = 36; 34.6 %).

3.2. Cluster identification

Group A was characterized by more individuals reporting a history of overdose (72 % vs 50 %), anxiety (85 % vs 25 %), ≥ moderate pain (76 % vs 22 %), and ≥ moderate depression (75 % vs 36 %) than Group B

Table 1
Characteristics of pregnant patients with opioid use disorder by cluster.

Characteristics	Cluster A (n = 68) N (%)	Cluster B (n = 36) N (%)
Sociodemographic		
Age, years		
18–34	59 (87)	31 (86)
35 and older	8 (12)	5 (14)
Race		
White	56 (82)	31 (86)
Other	9 (13)	5 (14)
Married		
No	54 (79)	24 (67)
Yes	13 (19)	12 (33)
Education		
High school or equivalent	45 (66)	20 (56)
More than high school	20 (29)	11 (31)
Employment		
Employed	42 (62)	13 (36)
Not Employed	26 (38)	21 (58)
Region		
Western Pennsylvania	48 (71)	10 (28)
Utah	20 (29)	26 (72)
Incarceration		
N	66 (97)	33 (92)
Y	2 (3)	3 (8)
Previous children		
0	16 (24)	11 (31)
≥1	51 (75)	25 (69)
Behavioral health		
History of overdose		
No overdose history	19 (28)	18 (50)
Overdose lifetime	17 (25)	7 (19)
Overdose in past year	32 (47)	11 (31)
Anxiety[a]		
No anxiety	10 (15)	27 (75)
Some anxiety	58 (85)	9 (25)
Bodily pain[b]		
Minimum or none	16 (24)	28 (78)
Moderate or more	52 (76)	8 (22)
Depression[c]		
Mild or no problem	17 (25)	23 (64)
Moderate	29 (43)	13 (36)
Severe	22 (32)	0 (0)
Days of mental health treatment in the last 28 days		
Mean (standard deviation)	0.75 (3.8)	0.24 (0.99)

[a] Anxiety was measured using the Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Health Questionnaire (PHQ) and dichotomized into no (0) vs some (≥1) anxiety.
[b] Bodily pain was assessed with the 36-Item Short Form Health Survey (SF-36) and dichotomized into minimum or none (<60) vs moderate or more (≥60).
[c] Depression was measured with the PRIME-MD PHQ and categorized into mild or no (0–9), moderate (10–14), and severe (15–27) depression. Note: Data presented as N (%) unless otherwise noted.

(Table 1). Group A had fewer members who were married (19 % vs 33 %), not employed (38 % vs 58 %), incarcerated (3 % vs 8 %), and in Utah (29 % vs 72 %) compared to Group B. There were no differences between clusters with respect to age, race, and education.

3.3. Clusters and substance use

Fewer individuals in Group A than Group B reported low severity of non-opioid drug use (6 % vs 19 %; $P = 0.04$; OR = 0.25, 95 % CI = 0.06–0.90) (Table 2). Most individuals in Group A and Group B reported no alcohol misuse (79 % vs 89 %; $P = 0.16$; OR = 0.40, 95 % CI = 0.08–1.32). Group A compared to Group B had significantly more days of cannabis (mean = 6.2, SD = 10.2 vs mean = 2.3, SD = 5.2; $P = 0.02$; β = 3.77, 95 % CI = 0.14–7.41) and stimulant (mean = 4.5, SD = 7.8 vs mean = 1.3, SD = 5.1; $P = 0.02$; β = 3.16, 95 % CI = 0.27–6.01) use in the past 30 days. While Group A compared to Group B had higher mean days of opioid (mean = 6.4, SD = 9.3 vs mean = 3.1, SD = 7.8; $P = 0.08$; β = 3.26, 95 % CI = -0.39–6.91) or heroin (mean = 17.2, SD = 11.8 vs mean = 13.5, SD = 12.5; $P = 0.15$; β = 3.72, 95 % CI = -1.28–8.72) use in the past 30 days, these differences did not achieve statistical significance. Group A had higher mean days of injection heroin use than Group B (mean = 1.2, SD = 4.7 vs mean = 0.0, SD = 0.0; $P = 0.04$). There was no difference between groups in SUD treatment in the past 28 days (mean = 10.1, SD = 10.2 vs mean = 10.9, SD = 11.4; $P = 0.80$; β = -0.83, 95 % CI = −6.99–5.32).

Table 2
Differences in substance use patterns between clusters.

	Cluster A (n = 68) N (%)	Cluster B (n = 36) N (%)	P value[a]	OR (95% CI)
Non-opioid drug use severity[b]			0.04	
Low severity	4 (6)	7 (19)		0.25 (0.06, 0.90)
Moderate or above severity	64 (94)	28 (78)		Ref
Alcohol misuse[c]			0.16	
No alcohol misuse	54 (79)	32 (89)		0.40 (0.08, 1.32)
Alcohol misuse	13 (21)	3 (11)		Ref
	Cluster A (n = 68) Mean (SD)	Cluster B (n = 36) Mean (SD)	P value[a]	β (95% CI)
Days of opioid use in the last 30 days[d]	6.4 (9.3)	3.1 (7.8)	0.07	3.26 (-0.39, 6.91)
Days of cannabis use in the last 30 days	6.2 (10.2)	2.3 (5.2)	0.02	3.77 (0.14, 7.41)
Days of stimulant use in the last 30 days	4.5 (7.8)	1.3 (5.1)	0.02	3.16 (0.27, 6.01)
Days of heroin use in the last 30 days	17.2 (11.8)	13.5 (12.5)	0.15	3.72 (-1.28, 8.72)
Days of injection heroin use in the last 30 days	1.2 (4.7)	0 (0)	0.04	
Days of drug/alcohol treatment in the last 28 days	10.1 (10.2)	10.9 (11.4)	0.80	−0.83 (-6.99, 5.32)

[a] P values obtained using chi-squared tests for categorical data and Student's t-tests for continuous data and considered significant at $p < 0.05$.
[b] Non-opioid drug use severity measured with a 10-item brief drug screening questionnaire, Drug Abuse Screening Test (DAST-10), and dichotomized into low severity (<3) and moderate or above severity (≥3) drug use.
[c] Alcohol misuse was assessed with a 3-item alcohol screen, Alcohol Use Disorders Identification Test-Concise (AUDIT-C), and categorized into no alcohol misuse (<3) and alcohol misuse (≥3).
[d] Includes prescription opioids, street methadone, and street buprenorphine. Note: Categorial variables presented as N (%) and continuous variables presented as mean (SD) OR = odds ratio, CI = confidence interval, SD = standard deviation, β = regression coefficient.

4. Discussion

We identified two distinct patient profiles among PP-OUD by using multidimensional, clustering methods. Group A compared to Group B was characterized by a higher prevalence of multimorbid mental health conditions and more likely to engage in and have more severe poly-substance use, particularly of non-opioid substances. In addition, we observed differences in certain sociodemographic characteristics, including marital status, employment, and incarceration, between clusters. These findings signal that there may be distinct comorbidity profiles among PP-OUD and provide an initial understanding of heterogeneity in OUD among pregnant populations.

Our results augment what is presently known about the link between mental health disorders and substance use patterns in pregnant persons. Cannabis use is more common among US pregnant individuals with than

without depression (Goodwin et al., 2020). Anxiety and depression are more common among US pregnant people who use opioids with other illicit substances than among those who use opioids alone (Metz, Brown, Martins, & Palamar, 2018). Psychiatric conditions, use of psychotropic medications, and use of opioids are more likely among women who use stimulants in pregnancy than among those without such use (Huybrechts et al., 2018). There were also unanticipated findings. A larger proportion of Group A than Group B reported employment. This finding was unexpected given that mental health and employment status can have a negative mutually reinforcing effects such that poor mental health may be a significant predictor of low- or un-employment, which may in turn be associated with depression, anxiety, and suicide (Milner, Page, & LaMontagne, 2014). In addition, a lower proportion of Group A reported incarceration than Group B. Although incarceration provides stability in a controlled environment and can be a stabilizing for many individuals (Dumont, Brockmann, Dickman, Alexander, & Rich, 2012), release from incarceration and community reentry is a time of heightened risk for OUD treatment discontinuation, relapse, and overdose (Russell et al., 2022). More work is needed to clarify the relationships between mental health, substance use, and incarceration among PP-OUD.

While this research is an important initial step toward identifying clinically distinct subtypes of OUD in pregnancy, future studies should validate clusters and assess treatment outcomes associated with cluster membership. Doing so would enable researchers and clinicians to identify patients at risk of poor treatment and health outcomes and tailor treatment planning and delivery accordingly. As one example, OUD-affected pregnancies are designated as high-risk and frequently managed in facilities that can provide the required level of specialized care, which often includes comprehensive, integrated services consisting of multidisciplinary teams providing obstetric care, addiction treatment, counseling, behavioral health care, case management, and/or social work in one location (Johnson, 2019). This type of care model has been found to decrease drug use and improve perinatal outcomes among PP-OUD (Goodman et al., 2022; Martinez & Allen, 2020; Obstetricians & Gynecologists, 2017). Simultaneously, it is resource intensive, costly, and may not be needed for all individuals entering treatment. Future work in this direction could provide an empirical basis for determining which patients may benefit from intensive specialized services and which could successfully receive care in lower acuity settings.

4.1. Strengths and limitations

This study possesses marked strengths—including accounting for multidimensional patient characteristics, which promotes clinician understanding of the whole patient—and also has limitations. The clustering algorithm was applied to a narrow population of PP-OUD seeking treatment at large, academic medical centers. While participants are similar to PP-OUD receiving treatment at other academic medical center and community-based care settings (Goodman et al., 2022; Mullins et al., 2020), these findings are potentially not generalizable to the broader population of PP-OUD not seeking care. Moreover, the clustering algorithm yielded results based on the inclusion of data for individuals voluntarily participating in a large clinical trial. We cannot say at this point whether the clusters identified here are the optimal taxonomy of OUD in pregnancy. Clusters would likely change based on the inclusion of additional individuals or a more diverse population.

4.2. Conclusions

We identified two distinct profiles of PP-OUD that differed with respect to sociodemographic characteristics, mental health conditions, and substance use patterns. More research is needed to confirm identified profiles and assess treatment outcomes associated with cluster membership.

This study's findings may be used to support the development of a more refined taxonomy of OUD in pregnancy, eventually enabling precision treatment strategies.

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Declaration of Competing Interest

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

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.abrep.2023.100484.

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