Drug and Alcohol Dependence 202 (2019) 185–190

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Opioid-related hospitalizations in Pennsylvania: A latent class analysis

Stephen J. Liu[a,*], Christina Mair[a], Thomas J. Songer[a], Elizabeth E. Krans[b,c], Abdus Wahed[a], Evelyn Talbott[a]

[a] University of Pittsburgh, Graduate School of Public Health, 130 DeSoto St, Pittsburgh, 15261 PA, USA
[b] University of Pittsburgh, Department of Obstetrics, Gynecology and Reproductive Sciences, 300 Halket Street, Pittsburgh, 15213 PA, USA
[c] Magee-Womens Research Institute, 204 Craft Avenue, Pittsburgh, 15213 PA, USA

ARTICLE INFO

Keywords:
Opioid use disorder
Opioid overdose
Latent class analysis
Polysubstance use

ABSTRACT

Background: Opioid abuse is associated with substantial morbidity and often results in hospitalization. Despite this, patient-level factors associated with opioid-related hospitalizations are not well understood.
Methods: We used the Pennsylvania Health Care Cost Containment Council dataset (2000–2014) to identify opioid-related hospitalizations using primary and/or secondary ICD-9-CM hospital discharge codes for opioid use disorder (OUD), opioid poisoning, and heroin poisoning. Latent class analyses (LCA) of patient-level factors including sociodemographic characteristics, pregnancy, alcohol, tobacco, other substance use, and psychiatric disorders were used to identify common patterns within hospitalizations.
Results: Among 28,538,499 hospitalizations, 430,569 (1.5%) were opioid-related. LCA identified five latent class (LC) patient groups associated with opioid-related hospitalizations: pregnant women with OUD (LC1); women over 65 with opioid overdose (LC2); OUD, polysubstance use and co-occurring psychiatric disorders (LC3); patients with opioid overdose without co-occurring polysubstance use (LC4); and African American patients with OUD and co-occurring cocaine use (LC5). LC3 was the largest latent class (58.2%) with annual hospitalizations doubling over time.
Discussion: Among patients with opioid-related discharges, we identified five subpopulations among this sample. These findings suggest increased outpatient OUD treatment, mental health service support for patients with co-occurring psychiatric disorders and polysubstance use to prevent overdose and hospitalization.

1. Introduction

The prevalence of opioid use disorder (OUD) has reached epidemic proportions in the United States (Han et al., 2015; Substance Abuse and Mental Health Services Administration, 2016). In 2017, an estimated 11.4 million Americans misused opioids in the past year, including prescription opioids and heroin (Substance Abuse and Mental Health Services Administration, 2017). Due to rising rates of morbidity and mortality associated with opioid abuse, opioid-related hospitalizations in the United States (US) have increased substantially. Between 2001 and 2012, over 600,000 prescription opioid and heroin overdose-associated hospital admissions occurred across the US with an associated increase in annual hospitalization costs of more than $700 million (Hsu et al., 2017).

Pennsylvania has the 3rd highest drug overdose death rate in the United States and has observed an increasing rate of opioid-related hospitalizations, especially in rural compared to urban counties from 2000 to 2014 (Centers for Disease Control and Prevention, National Vital Statistics System/ Mortality 2019; PA Health Care Cost Containment Council (PHC4), 2014). Pennsylvania ranks 9th in the nation in prescribing rate of long-acting pain relievers and above the median for prescription of opioid pain relievers (OPR) and high dose OPR (Paulozzi et al., 2014). Overall, there were 3500 opioid overdose-related hospitalizations recorded in 2017 due to pain medication overdose or heroin overdose (PA Health Care Cost Containment Council (PHC4), 2018). Evolving national patterns of opioid use are also reflected in Pennsylvania's overdose death rates. Synthetic opioids including fentanyl are now responsible for a 65% increase in PA drug overdose deaths from 2015 to 2017 (Ciccarone, 2019; Drug Enforcement Agency Philadelphia division, University of Pittsburgh 2018).

Despite high healthcare costs associated with opioid use, patient-level factors predictive of opioid-related hospitalizations remain poorly understood. Existing evaluations (Fulton-Kehoe et al., 2015; Mosher et al., 2014; Zedler et al., 2014) have identified several factors– chronic opioid therapy, use of other drugs, COPD, depression, hypertension, opioid dependence, and psychiatric disorders– associated with an increased risk of opioid hospitalizations and overdoses. However, these studies utilized multiple logistic regression and other descriptive

* Corresponding author.
E-mail address: STL45@pitt.edu (S.J. Liu).

https://doi.org/10.1016/j.drugalcdep.2019.05.009
Received 9 January 2019; Received in revised form 2 May 2019; Accepted 2 May 2019
Available online 19 July 2019
0376-8716/

methods which have a limited ability to accurately evaluate multifactorial risk and properly perform subgroup analyses. In contrast, latent class analysis (LCA) categorizes events or individuals into distinct classes based upon observed patterns in the data (Monga et al., 2007). Previous studies implementing LCA have largely focused on characterizing the heterogeneity of opioid-using populations from different data sources. Evaluations of national survey data found that opioid users fall into 2–4 latent classes based on increasing severity of OUD or other drug use (Castaldelli-Maia et al., 2016; Ghandour et al., 2008; Wu et al., 2011). In an evaluation of illicit drug users from a multi-site cohort study, Monga et al. described 3 classes of persons who use illegal opioids, including concurrent use of prescription Tylenol, non-injection drug use, and the most severe class of persons who use heroin and cocaine (Monga et al., 2007).

Using an LCA approach may be particularly important for opioid-related hospitalizations due to the need to categorically account for a complex group of factors that contribute to OUD and overdose. Thus, we utilized the Pennsylvania Health Care Cost Containment Council (PHC4), a dataset containing information from all 239 hospitals and 284 freestanding ambulatory surgery centers in Pennsylvania (PA Health Care Cost Containment Council (PHC4), 2014, 2018), to a) describe patient-level characteristics associated with opioid-related hospitalizations in a state with one of the highest burdens of opioid-related morbidity and mortality and b) describe how these classes have changed over time. Our findings will help target interventions for high-risk subgroups among a diverse population of individuals with OUD.

2. Data and methods

2.1. Data sources

Inpatient hospital discharge records from 2000 to 2014 were obtained from the PHC4, a state agency charged with collecting information from all 239 hospitals and 284 freestanding ambulatory surgery centers in Pennsylvania, excluding information from Veteran's Affairs (VA) and federal government institutions (PA Health Care Cost Containment Council (PHC4), 2014, 2018). The following patient groups were excluded from the analysis: 1) cancer-related discharges (10.2% of all PHC4 hospitalizations); 2) discharges for children ages 8 years or younger (10.3%); and 3) discharges for persons who resided outside of Pennsylvania (4.8%). The final analytic sample (n = 430,569) included all inpatient hospital records with opioid-related primary, secondary (first 8 fields), and/or E-code (external cause of injury) discharges. ICD-9-CM codes were used to create the following opioid-related categories: heroin overdoses (965.01, E850.0), non-heroin opioid overdoses (965.00, 965.09, E850.2), OUD (304.00–304.03, 304.70–304.73, 305.50–305.53) and adverse effects in therapeutic opioid use (code E935.2). Each hospitalization could be associated with multiple, non-exclusive opioid-related categories. The analysis was approved by the Institutional Review Board at the University of Pittsburgh.

2.2. Covariates

Demographics assessed in PHC4 records included patient age, sex, race, and urbanicity of the county of residence. Age was categorized into the following groups: 9–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84, and 85+ years. Race was categorized as White, African American, Asian/Pacific Islander/Native Hawaiian, American Indian/Alaskan Native, Other/Multiple, and Unknown. Urbanicity of the county of residence of the subjects was determined by the 2013 NCHS Urban-Rural Classification Scheme (Ingram and Franco, 2014) and divided into: Large central metro, Large fringe metro, Medium metro, Small metro, Micropolitan, and Noncore. Opioid-related diagnostic codes were identified using ICD-9-CM codes (listed in Appendix Table A) in the primary and/or the first 8 secondary discharge fields. Diagnostic codes used to create the latent classes included pregnancy, alcohol, tobacco, marijuana, cocaine, and barbiturate use, and psychiatric disorders (including anti-social personality disorder, anxiety, bipolar disorder, major depressive disorder, psychosis).

Table 1
Characteristics of hospital discharges by opioid-related diagnosis codes, Pennsylvania.2000–2014.

Sample characteristics	*Hospitalizations with an ICD-9 opioid-related diagnosis code N = 430,569*	*Hospitalizations without an ICD-9 opioid-related diagnosis codes N = 21,267,337*
Age Group		
9-14 yrs	619 (0.1%)	317,992 (1.5%)
15-24 yrs	71,313 (16.6%)	1,629,262 (7.7%)
25-34 yrs	118,592 (27.5%)	2,239,729 (10.5%)
35-44 yrs	93,998 (21.8%)	2,059,539 (9.7%)
45-54 yrs	80,855 (18.8%)	2,580,866 (12.1%)
55-64 yrs	34,857 (8.1%)	2,902,623 (13.7%)
65-74 yrs	14,444 (3.4%)	3,275,617 (15.4%)
75-84 yrs	10,691 (2.5%)	3,922,214 (18.4%)
85+ yrs	5198 (1.2%)	2,339,316 (11%)
Sex		
Male	242,906 (56.4%)	8,729,392 (41.1%)
Female	187,626 (43.6%)	12,533,924 (58.9%)
Pregnancy	20,119 (4.7%)	2,229,389 (10.5%)
Race		
White	329,073 (76.4%)	16,891,665 (79.5%)
African American	57,108 (13.3%)	2,834,980 (13.3%)
Asian/Pac Is/ Hawaiian	837 (0.2%)	130,830 (0.6%)
American Ind/AK Native	2770 (0.6%)	32,166 (0.2%)
Other/Multiple	23,845 (5.5%)	541,282 (2.6%)
Residence County Urbanicity		
Large central metro	177,898 (41.3%)	5,544,607 (26.1%)
Large fringe metro	100,142 (23.3%)	5,955,836 (28%)
Medium metro	98,555 (22.9%)	5,479,663 (25.8%)
Small metro	23,059 (5.4%)	1,713,520 (8.1%)
Micropolitan	23,392 (5.4%)	1,923,615 (9%)
Noncore	7523 (1.7%)	650,096 (3.1%)
Opioid use history		
Opioid use disorder (OUD)	367,538 (85.4%)	0 (0%)
Non-heroin opioid overdose	25,593 (5.9%)	0 (0%)
Heroin overdose	9384 (2.2%)	0 (0%)
Opioid Adverse Effects	39,686 (9.2%)	0 (0%)
Other substance use		
Tobacco	100,204 (23.3%)	2,449,668 (11.5%)
Cocaine	68,861 (16.0%)	278,664 (1.3%)
Alcohol use	36,720 (8.5%)	515,049 (2.4%)
Marijuana	32,709 (7.6%)	207,659 (1.0%)
Barbiturates	32,027 (7.4%)	35,725 (0.2%)
Amphetamines	1,946 (0.5%)	4787 (0.0%)
Medical co-morbidities		
Psychiatric disorder	138,176 (32.1%)	2,144,672 (10.1%)
HCV	68,143 (15.8%)	271,317 (1.3%)
HIV	10,263 (2.4%)	123,190 (0.6%)

2.3. Statistical analyses

First, demographic and medical characteristics were identified in the opioid-related hospital discharge data and compared to all hospitalizations without an opioid diagnosis code (Table 1). Next, LCA was performed on the analytic sample of the opioid-related hospitalizations using statistical software R version 3.3.1 (R Foundation for Statistical Computing) using the *poLCA* package, created for polytomous variable latent class analysis. Models were fit with an increasing number of classes (2 through 11) using input variables: OUD, non-heroin opioid

Table 2
Posterior probabilities [a] (%) for class membership in the 5-class model.

		Latent classes (percentage of analytic sample, n=430,569)[b]				
Variable	**Outcome**	**LC1 (4.7%)**	**LC2 (8.7%)**	**LC3 (58.2%)**	**LC4 (6.6%)**	**LC5 (21.8%)**
Age Group	9-14 yrs	0.0	0.9	0.1	0.4	0.0
	15-24 yrs	**34.4**	0.5	23.0	16.5	4.5
	25-34 yrs	**56.3**	1.0	33.3	20.2	20.6
	35-44 yrs	9.3	4.5	21.7	22.0	31.0
	45-54 yrs	0.1	9.2	16.3	26.2	**29.5**
	55-64 yrs	0.0	**18.4**	4.8	12.3	12.2
	65-74 yrs	0.0	**25.6**	0.7	2.3	2.1
	75-84 yrs	0.0	**26.6**	0.1	0.1	0.2
	85+ yrs	0.0	**13.3**	0.0	0.0	0.0
Sex	Male	0.0	32.1	59.1	49.4	**72.6**
	Female	**100.0**	**67.9**	40.9	50.6	27.4
Pregnancy		**94.0**	0.0	0.0	0.3	0.0
Race	White	83.4	**90.0**	**91.5**	82.0	35.0
	African American	9.2	6.3	1.7	11.7	**42.9**
	Asian/Pac Is/Hawaiian	0.2	0.3	0.2	0.3	0.2
	American Ind/AK Native	0.1	0.0	1.1	0.0	0.0
	Other/Multiple	1.8	0.9	2.7	2.8	15.0
	Unknown	5.3	2.4	2.8	3.2	6.8
Residence county	Large central metro	40.8	17.2	29.9	22.7	**80.9**
	Large fringe metro	24.7	28.1	30.0	29.0	4.5
	Medium metro	19.2	**32.8**	25.0	28.1	13.8
	Small metro	5.6	8.5	6.4	8.8	0.8
	Micropolitan	7.4	10.1	6.5	8.9	0.0
	Noncore	2.2	3.2	2.1	2.6	0.0
Opioid use disorder (OUD)		**95.7**	13.5	**100.0**	6.0	**99.2**
Non-heroin opioid overdose		0.1	**11.8**	1.2	**59.2**	0.7
Heroin overdose		0.2	0.0	1.7	**12.5**	1.5
Tobacco		12.7	5.7	29.4	22.1	18.5
Cocaine		12.5	0.0	15.3	3.6	**27.5**
Alcohol use		1.9	0.3	9.9	9.4	9.6
Marijuana		6.5	0.0	10.4	2.7	5.7
Barbiturates		3.6	0.1	10.3	0.9	6.4
Psychiatric Disorder		13.4	8.1	**42.7**	29.0	21.9

a. Cells that are **highlighted and bolded** are ≥10% higher than the overall sample of opioid hospitalizations.
b. Name of latent classes: LC1 "Pregnant women with OUD"; LC2 "Women over 65, with opioid overdose"; LC3 "OUD, polysubstance use and co-occurring psychiatric disorders"; LC4 "Opioid overdose without co-occurring polysubstance use".
LC5 "African American patients with OUD and co-occurring cocaine use".

overdose, heroin overdose, age, sex, race, urbanicity of the county of residence, pregnancy, alcohol, tobacco, marijuana, cocaine, barbiturate, and the presence of a psychiatric disorder. Selection for the appropriate number of LCs was determined by comparing the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Chi-squared goodness-of-fit test statistics among models. We took the most parsimonious model, checked the interpretations of class divisions to confirm the most appropriate number of classes, and chose the model that divided the hospitalizations into 5 distinct classes. We also examine the trend of different LC groups by year of discharge. All other statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Characteristics of cohort

Among 430,569 opioid-related hospitalizations, the majority were attributable to OUD (85%), with smaller percentages attributable to non-heroin opioid overdose (6%) and heroin overdose visits (2%). Patients with opioid-related admissions were more likely to be male (56%), white (76%), and from large central metro counties (41%) compared to patients without an opioid-related diagnosis (Table 1). When compared to the other age groups, most patients with an opioid-related hospitalization were aged 25–54 years (68%). The frequency of other co-morbid conditions, including polysubstance use and psychiatric disorders, were higher among patients with opioid-related hospitalizations compared to total hospitalizations during the study period.

3.2. Defining latent classes

The best-fitting LCA model identified 5 distinct groups of opioid-related hospitalizations (Table 2). While fit statistics improved with an increasing number of classes, the interpretive validity was best with 5 classes. Latent class 1 (LC1) was defined by a 94% probability of pregnancy, 15–34 years old, OUD, and very few other comorbidities. Latent class 2 (LC2) included discharges that had a higher than average probability of being associated with non-heroin opioid overdose (11.8%), white race, female sex, age ≥65 years old (~65% probability), and rural county of residence. Latent class 3 (LC3) was defined by discharges associated with OUD (100% probability), white race,

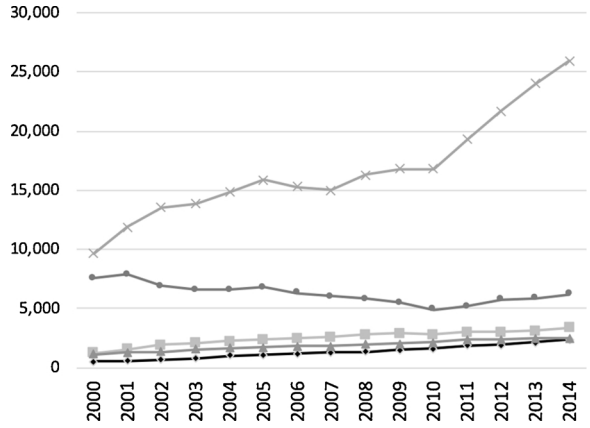

Fig. 1. Number of visits, trends of latent classes by year.2000–2014.
LC1: Pregnant women with OUD.
LC2: Women over 65, with opioid overdose.
LC3: OUD, polysubstance use and co-occurring psychiatric disorders.
LC4: Opioid overdose without co-occurring polysubstance use.
LC5: African American patients with OUD and co-occurring cocaine use.

psychiatric disorder diagnoses and co-occurring tobacco, marijuana, and barbiturate use disorders. Latent class 4 (LC4) represented discharges associated with overdose including non-heroin, opioid overdose (59% probability) and heroin overdose (12.5% probability), in addition to low probabilities of marijuana, cocaine, and barbiturate use disorders. Latent class 5 (LC5) represented discharges associated with OUD (99.2% probability), African American or other/multiple race, male sex, age > 35 years old, cocaine use, and tobacco use. Among these 5 classes, LC3 was the largest class representing 58% of all classified discharges followed by LC5 (21.8%) and non-heroin opioid overdose (LC2, 8.7%), and heroin overdose classes (LC4, 6.6%) were lower in overall class frequency.

3.3. Latent class time trends

Between 2000–2014, the number of opioid-related hospitalizations increased from 20,073 to 40,401. The number of hospitalizations by latent class varied over time (Fig. 1). LC3 (OUD, co-occurring psychiatric disorders, polysubstance use) made up the largest portion of our analytic sample and doubled over the study period from 9465 hospitalizations in 2000–25,950 hospitalizations in 2014, with the largest increase occurring between 2010–2014. The frequency of hospitalizations in LC1, LC2, and LC4 appeared to increase more gradually during the studied years, likely due to their smaller representation among the analyzed opioid-related hospitalizations. Despite an initial decline in frequency, LC5 hospitalizations also increased from 2010 to 2014.

4. Discussion

Opioid-related hospitalizations represent a significant healthcare event with substantial costs to both individuals and society. Our analysis provides an in-depth description of the likely characteristics of individuals affected by OUD who require hospitalization by identifying five distinct classes of opioid-related hospitalizations from 2000 to 2014. We determined that opioid-related hospitalizations commonly occur for pregnant women with OUD (LC1), older women over 65 years of age with non-heroin opioid overdoses (LC2), persons with OUD with co-occurring psychiatric disorders and polysubstance use (LC3), persons with heroin overdose (LC4), and African American persons with OUD and co-occurring cocaine use (LC5). Our analyses also identified a large increase in the number of opioid-related hospitalizations for LC3, which doubled between 2000–2014. The identification of patient-level characteristics associated with opioid-related hospitalizations has implications for treatment and prevention strategies and can help providers risk-stratify patient subgroups at high-risk for morbidity and mortality related to substance use.

Consistent with increased healthcare engagement during pregnancy, the LC1 grouping predominantly consisted of pregnant women with opioid-related diagnoses, which is a unique category not included in previous assessments that describe opioid-related healthcare utilization. While hospitalizations among pregnant women with OUD are predominantly due to birth, women with OUD are most likely to engage in healthcare services during pregnancy due to enhanced investment in maternal and neonatal health outcomes and expanded pregnancy-related insurance eligibility (Krans and Patrick, 2016; Olander et al., 2016). From 1999 to 2014, hospital births complicated by opioid use disorder increased from 1.5 to 6.5 per 1000 births per year (Haight et al., 2018).

LC2 consisted of higher probabilities of opioid overdose events as well as characteristics such as female and in older age groups. This is also a subpopulation of growing concern, since it has been reported that women ages 30–64 years have a crude rate of overall drug-related overdose deaths increased by 260% from 1999 to 2017 (VanHouten et al., 2019). During our study period, prescription opioids were the predominant drug class involved in drug overdose deaths, according to the National Vital Statistics System.

LC3 was the largest class identified in our analysis and identified increased morbidity associated with co-occurring psychiatric and other substance use disorders which increased significantly over time from 2000 to 2014. Reasons for the aforementioned increase may be because they represent the hallmark characteristics and discharge patterns of persons driving the opioid epidemic, including those using other drugs and having psychiatric disorders (Fulton-Kehoe et al., 2015; Oregon Health Authority, 2014). Despite the fact that persons who have psychiatric comorbidities are more likely to receive opioids (Sehgal et al., 2013), use of opioids may further compound problems for those with depressive disorders (American Psychiatric Association, 2013). Depression and/or anxiety are likely to increase the risk of substance use disorders, therefore making it necessary to adjust for mental health disorders when determining the risk of opioid use disorder in those who are prescribed opioids (Edlund et al., 2007).

LC5 was a class that consisted of African American patients with OUD and co-occurring cocaine use. Past literature from data of the 1980s and 1990s on OUD focused on middle age African American individuals with or without other substance use disorders (Kosten et al., 1986; Rounsaville and Kleber, 1985) and had causes of death that involve opioids, cocaine, and alcohol in combination (Coffin et al., 2003). Our results suggest that this class remains an issue in Pennsylvania after 2000, as it was the second-largest class identified.

Although other articles using National Survey on Drug Use and Health data and other databases that used LCA methods (Castaldelli-Maia et al., 2016; Ghandour et al., 2008; Wu et al., 2011) found smaller proportions of persons with OUD, co-morbid major depression, and substance abuse treatment, the analyses were performed on general opioid users representative of the US civilian population and not necessarily persons who were hospitalized. The latent classes determined in prior studies had slightly different input variables, with emphasis on sociodemographics and opioid types (Ghandour et al., 2008), depression, days using opioids (Wu et al., 2011), psychiatric disorders, doctor shopping, and how opioid was obtained (Castaldelli-Maia et al., 2016). However, each study found a latent class with an especially high amount of substance use and/or psychiatric disorder(s).

Other studies examine populations of persons hospitalized for opioid-related reasons that include prescription opioid use and overdoses and examine risk factors, co-morbidities, and deaths (Mosher et al., 2014; Zedler et al., 2014). However, compared to these hospital studies, our analysis accounts for a longer time period (2000–2014), a large non-veteran hospital sample, and includes heroin overdoses.

Our results should be interpreted while considering the following limitations. First, our study used visit-level hospital data, which may misrepresent the true prevalence of hospitalizations for patients due to insufficient data to link visits to individuals. In general, multiple hospital admissions are found in older patients and/or those with more severe conditions. Second, opioid-related hospitalizations were identified by ICD-9-CM diagnostic codes and may underestimate the true prevalence of hospitalizations due to opioid use (Owens et al., 2014). However, other studies have found that opioid ICD-9-CM codes have high specificity, despite low sensitivity (Rowe et al., 2016). Third, these data represent events where an opioid diagnosis code was in either a primary and/or secondary discharge diagnosis field. Inclusion of an opioid diagnosis code in a secondary field depends upon the viewpoints of attending medical personnel with regards to the role of opioid issues in that admission. We conducted a sensitivity analysis examining a subset of events with an opioid diagnosis code in only the primary discharge code field. There were 82,880 visits with opioid as a primary discharge code. The LCA performed on these primary opioid discharge visits yielded a slightly different LCA model that did not have a class of pregnant women like LC1 in the presented analysis. Fourth, the increases in fentanyl-related deaths since around 2006 are important drivers of drug overdoses in the United States (Gladden et al., 2016; O'Donnell et al., 2017). Our analysis of ICD-9-CM codes is not specific enough to distinguish how many hospitalizations are due to fentanyl use. Further investigation is needed on data using toxicology testing.

In addition, latent class analyses have inherent limitations, especially because of the subjective nature of selecting the appropriate model which was not entirely based on the lowest fit statistic values. Models with different numbers of classes could have changed the characteristics of the classes. It is also important to note that latent classes were named to note the indicators that have higher probabilities compared to the general hospitalized population captured in PHC4. These should be described with the understanding that not all visits within a latent class share identical characteristics (Lanza et al., 2007).

With the rising burden of OUD and drug overdoses, it is important to recognize that the characteristics of those affected are not identical. We identified 5 distinct groups within all opioid-related hospital admissions in Pennsylvania over 15 years. The identification of latent classes has implications for treatment and prevention strategies for morbidity and mortality for opioid-related issues to help curb the opioid epidemic.

Contributors

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property. We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from STL45@pitt.edu.

Declaration of Competing Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2019.05.009.

References

American Psychiatric Association, 2013. Opioid Use Diagnostic Criteria. American Psychiatric Association, Washington, D.C.

Castaldelli-Maia, J.M., Andrade, L.H., Keyes, K.M., Cerdá, M., Pilowsky, D.J., Martins, S.S., 2016. Exploring the latent trait of opioid use disorder criteria among frequent nonmedical prescription opioid users. J. Psychiatr. Res. 80, 79–86.

Centers for Disease Control and Prevention, National Vital Statistics System/Mortality, 2019. Drug Overdose Deaths. Centers for Disease Control and Prevention, Atlanta, GA.

Ciccarone, D., 2019. The triple wave epidemic: supply and demand drivers of the US opioid overdose crisis. Int. J. Drug Policy(Feb 1). https://doi.org/10.1016/j.drugpo.2019.01.010. pii: S0955-3959(19)30018-0 [Epub ahead of print].

Coffin, P.O., Galea, S., Ahern, J., Leon, A.C., Vlahov, D., Tardiff, K., 2003. Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990-98. Addiction 98, 739–747.

Drug Enforcement Agency Philadelphia division, University of Pittsburgh, 2018. The Opioid Threat in Pennsylvania. Drug Enforcement Agency, Philadelphia, PA.

Edlund, M.J., Sullivan, M., Steffick, D., Harris, K.M., Wells, K.B., 2007. Do users of regularly prescribed opioids have higher rates of substance use problems than nonusers? Pain Med. 8, 647–656.

Fulton-Kehoe, D., Sullivan, M.D., Turner, J.A., Garg, R.K., Bauer, A.M., Wickizer, T.M., Franklin, G.M., 2015. Opioid poisonings in Washington state Medicaid: trends, dosing, and guidelines. Med. Care 53, 679–685.

Ghandour, L.A., Martins, S.S., Chilcoat, H.D., 2008. Understanding the patterns and distribution of opioid analgesic dependence symptoms using a latent empirical approach. Int. J. Methods Psychiatr. Res. 17, 89–103.

Gladden, R.M., Martinez, P., Seth, P., 2016. Fentanyl law enforcement submissions and increases in synthetic opioid–involved overdose deaths— 27 States, 2013–2014. MMWR Morb. Mortal. Wkly. Rep. 65, 837–843.

Haight, S.C., Ko, J.Y., Tong, V.T., Bohm, M.K., Callaghan, W.M., 2018. Opioid use disorder documented at delivery hospitalization— United States, 1999–2014. MMWR Morb. Mortal. Wkly. Rep. 67, 845–849.

Han, B., Compton, W.M., Jones, C.M., Cai, R., 2015. Nonmedical prescription opioid use and use disorders among adults aged 18 through 64 years in the United States, 2003-2013. JAMA 314, 1468–1478.

Hsu, D., McCarthy, E., Stevens, J., Mukamal, K., 2017. Hospitalizations, costs, and outcomes associated with heroin and prescription opioid overdoses in the United States 2001–2012. Addiction 112, 1558–1564.

Ingram, D., Franco, S., 2014. 2013 NCHS urban-rural classification scheme for counties. Vital Health Stat. 2, 1–73.

Kosten, T.R., Gawin, F.H., Rounsaville, B.J., Kleber, H.D., 1986. Cocaine abuse among opioid addicts: demographic and diagnostic factors in treatment. Am. J. Drug Alcohol Abuse 12, 1–16.

Krans, E., Patrick, S., 2016. Opioid use disorder in pregnancy: health policy and practice in the midst of an epidemic. Obstet. Gynecol. 128, 4–10.

Lanza, S.T., Collins, L.M., Lemmon, D.R., Schafer, J.L., 2007. PROC LCA: a SAS procedure for latent class analysis. Struct. Equ. Model. A Multidiscip. J. 14, 671–694.

Monga, N., Rehm, J., Fischer, B., Brissette, S., Bruneau, J., El-Guebaly, N., Noël, L., Tyndall, M., Wild, C., Leri, F., Fallu, J.S., Bahl, S., 2007. Using latent class analysis (LCA) to analyze patterns of drug use in a population of illegal opioid users. Drug Alcohol Depend. 88, 1–8.

Mosher, H., Jiang, L., Sarrazin, M., Cram, P., Kaboli, P., Vander Weg, M., 2014. Prevalence and characteristics of hospitalized adults on chronic opioid therapy. J. Hosp. Med. 9, 82–87.

O'Donnell, J.K., Gladden, R.M., Seth, P., 2017. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by census region— United States, 2006–2015. MMRW Morb. Mortal. Wkly. Rep. 66, 897–903.

Olander, E.K., Darwin, Z.J., Atkinson, L., Smith, D.M., Gardner, B., 2016. Beyond the "teachable moment"— a conceptual analysis of women's perinatal behaviour change. Women Birth 29, e67–71.

Oregon Health Authority, 2014. Drug Overdose Deaths, Hospitalizations, Abuse and Dependency among Oregonians. Oregon Health Authority, Salem, OR.

Owens, P., Barrett, M., Weiss, A., Washington, R., Kronick, R., 2014. Hospital inpatient utilization related to the rate of hospital stays opioid overuse among adults, 1993–2012. HCUP Stat. Br. 177, 1–14.

Paulozzi, L.J., Mack, K.A., Hockenberry, J.M., 2014. Variation among states in prescribing of opioid pain relievers and benzodiazepines— United States, 2012. J. Safety Res. 51, 125–129.

PA Health Care Cost Containment Council (PHC4), 2018. Hospitalizations for Opioid Overdose – Population Differences PHC4 Website. PA Health Care Cost Containment Council, Harrisburg, PA.

PA Health Care Cost Containment Council (PHC4), 2014. Hospitalizations for Overdose of Pain Medication and Heroin. PA Health Care Cost Containment Council, Harrisburg, PA.

Rounsaville, B.J., Kleber, H.D., 1985. They differ from those seeking treatment? Arch.

Gen. Psychiatry 42, 1072–1077.
Rowe, C., Vittinghoff, E., Santos, G.-M., Behar, E., Turner, C., Coffin, P., 2016. Performance measures of diagnostic codes for detecting opioid overdose in the emergency department. Acad. Emerg. Med. 24, 475–483.
Sehgal, N., Colson, J., Smith, H.S., 2013. Chronic pain treatment with opioid analgesics: benefits versus harms of long-term therapy. Expert Rev. Neurother. 13, 1201–1220.
Substance Abuse and Mental Health Services Administration, 2017. Results from the 2017 National Survey on Drug Use and Health: Detailed Tables. Substance Abuse and Mental Health Services Administration, Rockville, MD.
Substance Abuse and Mental Health Services Administration, 2016. Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health. Substance Abuse and Mental Health Services Administration, Rockville, MD.
VanHouten, J.P., Rudd, R.A., Ballesteros, M.F., Mack, K.A., 2019. Drug overdose deaths among women aged 30–64 years— United States, 1999–2017. MMWR Morb. Mortal. Wkly. Rep. 68, 1–5.
Wu, L.-T., Woody, G.E., Yang, C., Pan, J.-J., Blazer, D.G., 2011. Abuse and dependence on prescription opioids in adults: a mixture categorical and dimensional approach to diagnostic classification. Psychol. Med. (Paris) 41, 653–664.
Zedler, B., Xie, L., Wang, L., Joyce, A., Vick, C., Kariburyo, F., Rajan, P., Baser, O., Murrelle, L., 2014. Risk factors for serious prescription opioid-related toxicity or overdose among veterans health administration patients. Pain Med. 15, 1911–1929.