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Opioid prescribing history prior to heroin overdose among commercially insured adults

Pooja Lagisetty[a,b,*], **Kun Zhang**[c], **Rebecca L. Haffajee**[d,i], **Lewei Allison Lin**[b,e], **Jason Goldstick**[f,g], **Rebecca Brownlee**[e], **Amy Bohnert**[b,j], **Marc R. Larochelle**[h]

[a]Department of Internal Medicine, University of Michigan, 1500 E Medical Center Drive, Ann Arbor, MI 48109, USA

[b]Center for Clinical Management and Research, Ann Arbor VA Hospital, 2215 Fuller Road, MS 152, Ann Arbor, MI 48105, USA

[c]Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC, 4770 Buford Highway, MS F62, Atlanta, GA 30341, USA

[d]Department of Health Management and Policy, University of Michigan School of Public Health, 1415 Washington Heights, Ann Arbor, MI 48109, USA

[e]Department of Psychiatry, University of Michigan, 1500 E Medical Center Drive, Ann Arbor, MI 48109, USA

[f]Injury Prevention Center, University of Michigan, 2800 Plymouth Road, Suite B10-G080, Ann Arbor, MI 48109, USA

[g]Department of Emergency Medicine, University of Michigan, 1500 E Medical Center Drive, Ann Arbor, MI 48109, USA

[h]Clinical Addiction Research and Education Unit at Boston University School of Medicine and Boston Medical Center, 801 Massachusetts Ave., 2nd Floor, Boston, MA 02118, USA

[i]RAND Corporation

[j]Department of Anesthesiology, University of Michigan, 1500 E Medical Center Drive, Ann Arbor, MI 48109, USA

Abstract

Background: Since 2010, heroin-related overdoses have risen sharply, coinciding with policies to restrict access to prescription opioids. It is unknown if patients tapered or discontinued off

[*]Corresponding author at: 2800 Plymouth Rd, Bldg 16 Rm 243, Ann Arbor, MI 48109, USA. lagiset@med.umich.edu (P. Lagisetty).

Contributors

All authors included in the manuscript contributed in a meaningful way to the study design, analysis, interpretation, writing, and/or editing.

Declaration of competing interest

An author who is a CDC employee (KZ) was involved in the design and analysis. Experts on CDC subject matter provided feedback for accuracy and clarity but were not otherwise involved in the study.

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.2020.108061.

prescription opioids transitioned to riskier heroin use. This study examined opioid prescribing, including long-term opioid therapy (LTOT) and discontinuation, prior to heroin overdose.

Methods: We used retrospective longitudinal data from a national claims database to identify adults with an emergency or inpatient claim for heroin overdose between January 2010 and June 2017. Receipt of opioid prescription, LTOT episodes, and discontinuation of LTOT were measured for the period of one year prior to heroin overdose.

Results: We identified 3183 individuals (53.2% age 18–25; 70.0% male) with a heroin overdose (incidence rate 4.20 per 100k person years). Nearly half (42.3%) received an opioid prescription in the prior 12 months, and 10.9% had an active opioid prescription in the week prior to overdose. LTOT at any time in the 12 months prior to overdose was uncommon (12.8%) among those with heroin overdoses, especially among individuals 18–25 years old (3.5%, $P < 0.001$). LTOT discontinuation prior to overdose was also relatively uncommon, experienced by 6.7% of individuals aged 46 and over and 2.5% of individuals aged 18–25 years ($P < 0.001$).

Conclusions: Prior to heroin overdose, prescription opioid use was common, but LTOT discontinuation was uncommon and observed primarily in older individuals with the lowest heroin overdose rates. Further study is needed to determine if these prescribing patterns are associated with increased heroin overdose.

Keywords

Opioid; Heroin; Overdose; Prescription; Discontinuation; Taper

1. Introduction

In the early 2000s, drug-related overdose deaths were largely attributed to prescription opioids (Hall et al., 2008; Hedegaard et al., 2017; Rudd et al., 2016). However, since 2010, there has been a sharp increase in the rate of heroin-related overdoses (Hedegaard et al., 2015; Rudd et al., 2014). Overdose deaths involving heroin increased more than four-fold since 2010 (Hedegaard et al., 2018). This rise in heroin-related overdoses coincided with multiple national efforts and polices to restrict supply and access to prescription opioids (Executive Office of the President of the United States, 2011). In March 2016 the Centers for Disease Control and Prevention (CDC) released the Guideline for Prescribing Opioids for Chronic Pain (Dowell et al., 2016). These efforts led many to question whether patients facing restricted access as a result of tapering or discontinuation of their prescription opioids may be converting to riskier heroin use (Powell et al., 2019; Compton et al., 2016a). Studies examining policies such as pill mill laws and mandatory checking Prescription Drug Monitoring Programs on heroin-related overdoses have showed mixed results, whereas multiple ecological studies exploring the temporal relationship between changes in opioid prescribing and heroin-related overdoses have found that decreased opioid prescribing was temporally associated with increases in heroin related overdoses (Dasgupta et al., 2014; Larochelle et al., 2015; Meiman et al., 2015). However, opioid prescribing trajectories among individuals who experience a heroin overdose are unknown.

Pathways to heroin use at an individual level may vary by age and/or birth cohort (Wall et al., 2018). In one observational study of roughly 3000 participants, heroin users who

initiated use in the 1960s stated that their introduction to opioids was through heroin itself as a teenager. However, in this same analysis, the majority of those who initiated heroin use in the 2010 decade self-reported initiating opioid use with prescription opioids as an adult (Cicero et al., 2014). As of 2017, rates of heroin-related overdoses were largest in the 18–25 and 26–34 year old cohorts (CDC, 2018), yet the vast majority of people receiving prescription opioids are older (Campbell et al., 2010; Parsells et al., 2008). Older cohorts who are prescribed more opioids may have a different trajectory to heroin use and overdose from prescription opioid use compared to younger cohorts. Updated individual-level studies that consider developmental differences in heroin use epidemiology are needed to elucidate these trends.

In this study, we used insurance claims to examine the prevalence and prescribing patterns of prescription opioids in a national cohort of individuals experiencing a treated heroin-related overdose between 2010, when both opioid prescribing plateaued and heroin overdoses began to increase (Rudd et al., 2014), and 2017. We hypothesized that opioid prescribing prior to heroin overdose would vary by age group. In addition, to better explore the link between prescription opioid discontinuation and conversion to heroin use, we examined the overall prevalence of opioid discontinuation in individuals receiving long-term opioid therapy and its temporal relationship with heroin overdose.

2. Methods

2.1. Sample

We used the Optum's de-identified Clinformatics® Data Mart Database containing 40, 364, 301 member enrollment records, medical claims, and prescription claims from January 2009 through June 2017. This database captures health data from commercial insurance claims for members spanning all 50 states, the District of Columbia, and Puerto Rico. Inpatient, outpatient, and pharmacy claims reported by providers and pharmacies are verified and de-identified prior to inclusion in Clinformatics™ Data Mart. Medicare Advantage beneficiaries with both medical and prescription drug coverage are included in the dataset. Compared to the total United States population, Clinformatics™ Data Mart is over representative of the South and West, as well as older individuals.

The sample was restricted to patients aged 18 and older who experienced and were treated for a heroin overdose. We excluded individuals without 365 days of continuous enrollment in both medical and pharmaceutical coverage prior to the heroin overdose to provide a minimum of a 365-day observation window for baseline characteristics and opioid prescribing trajectories (Tables 1–3).

2.2. Heroin overdose

We identified heroin overdose events using inpatient or emergency department claims with a diagnosis of heroin poisoning using codes 965.02, E850.0, T.40.1 × 1A, T40.1 × 4A (Table 1 in the Supplement[1]) (ISW, 2012). Multiple claims with overlapping dates or dated < 2 days from one another were considered a single event.

2.3. Opioid prescribing

As our primary exposure of interest, we examined all opioid prescriptions identified by NDC codes using a list developed by the Centers for Disease Control and Prevention (CDC, 2019). We excluded liquid opioid antitussive formulations not indicated for pain as well as intravenous formulations. We included buprenorphine transdermal patches used for treatment of chronic pain, and we excluded buprenorphine sublingual tablets and films indicated for treatment of opioid use disorder (OUD).

We calculated the daily morphine milligram equivalent (MME) dose for each opioid prescription using the applicable CDC conversion rate, prescription strength, quantity supplied, and days supplied (CDC, 2019). We excluded prescription claims missing any of these variables (0.03%). We distributed the MME evenly over the days supplied beginning on the fill date for all prescriptions including those for LTOT. We considered any subsequent dispensing of an opioid with an identical generic name, strength, and release type during the last 7-day supply of a prior dispensing to be a refill and adjusted the start date of the subsequent prescription forward. However, in the event that a prescription was consistently refilled early (≥3 consecutive early fills), we allowed the third and subsequent fills to overlap with prior fills and summed the MME during periods of overlap. This process prevented refill coverage dates from extending far beyond the date of the last recorded fill. We considered individuals to have an active opioid prescription on a given date with an MME greater than zero when distributing opioids dispensed over the days supply for each prescription as described above.

Long-term opioid therapy (LTOT) episodes were defined as periods of at least 84 days in duration during which a patient received 3 or more opioid prescription fills (Larochelle et al., 2016). The prescriptions had to be filled at least 21 days apart, with a minimum of 84 total days supplied. Any treatment periods not meeting these conditions were considered to be short-term. A gap in supply of 15 or more days indicated the end of a long-term episode, and enrollees were considered to have experienced a discontinuation from LTOT if no subsequent episodes met the outlined criteria. Discontinuation from LTOT did not preclude subsequent short-term treatment periods. For a patient to be classified as receiving LTOT in a given timeframe (90 or 365 days prior to overdose), we required one or more days during that timeframe to be within an episode of LTOT.

2.4. Comorbidities

Medical comorbidities were identified using ICD-9 and ICD-10 diagnosis codes in the 365 days prior to heroin overdose. Pain diagnoses (Table 2 in the Supplement[2]) were categorized into abdominal pain, back and neck pain, cancer-related pain, chest pain, general chronic pain, headache, injuries and acute pain, other musculoskeletal pain, and neuropathic pain. The initial list of codes came from a prior study (Larochelle et al., 2016). Two internal medicine physicians (authors PL and MRL) independently reviewed the list to confirm that all diagnoses included painful syndromes or diseases and were appropriately categorized.

[1]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org.
[2]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org.

Medical and psychiatric diseases (e.g. substance use disorders, depression, and sleep apnea) that have been previously associated with opioid use and overdose and may play a role in clinician decision-making with respect to opioid prescribing were also included (Table 3 in the Supplement[3]) (Brooner et al., 1997; Darke et al., 2006; Ronan and Herzig, 2016; Vozoris et al., 2016).

2.5. Analysis

We categorized patients into three age groups based on age at the time of overdose: 18–25, 26–45, and 46+ years. We calculated heroin overdose rates per 100,000 person years, stratifying by age, sex, race/ethnicity, geographic region, and whether the individual had commercial insurance, Medicare advantage and younger than 65 years old, or Medicare advantage and older than 65 years. We compared the distribution of medical and psychiatric comorbidities by age groups using Pearson's chi-squared tests.

We described history of any opioid prescription in the 7, 30, 90, 180 or 365 days prior to the heroin overdose. Among members with an opioid prescription in the year prior, the mean peak daily dosage during that time was calculated. Similarly, average daily dose in the week prior to an overdose event was calculated. We also examined the mean and median number of opioid fills and average LTOT episode length in the year prior. We determined the number of patients who discontinued LTOT within 90 days and 365 days prior to a heroin overdose and also counted the number of overdoses occurring within an episode of LTOT. Differences in prescribing patterns by age groups (overall and for LTOT) were assessed through chi-squared tests and one-way analysis of variance. All analyses were conducted using SAS 9.4 (SAS Institute Inc.; Cary, North Carolina). The University of Michigan Institutional Review Board granted IRB approval for this project. The Boston University Medical Campus Institutional Review Board determined that this study was not human subjects research.

3. Results

Between January 2010 and June 2017, 5460 people were treated for a heroin overdose. Of this sample, 3183 had continuous enrollment for the 12 months preceding the overdose and served as our final study cohort (Table 4 in the Supplement[4]). Those that did not have 12 months of continuous enrollment were younger, less likely to be white, and had higher rates of overdose than those with continuous enrollment. The overall heroin overdose rate in those who met criteria for continuous enrollment was 4.20 overdoses per 100,000 person-years. Men had a higher rate of overdose compared to women (6.11/100,000 person-years; 95% CI, 6.01–6.22/100,000 person-years versus 2.43/100,000 person-years; 95% CI, 2.33–2.53/100,000 person-years). Individuals aged 18–25 had the highest rate of overdose (21.30/100,000 person-years; 95% CI, 21.08–21.52/100,000 person-years). Rates of overdose were highest in Whites (4.81/100,000 person-years; 95% CI,4.72–4.89/100,000 person-years) and Blacks (3.98/100,000-person-years; 95% CI, 3.74–4.22/100,000 person-years) (Table 1).

[3]Ibid.
[4]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org.

Prevalence of pain was high across all age groups (70.7%), with 85.9% of those with heroin overdose above the age of 46 having a pain diagnosis (Table 2). The youngest cohort of 18–25 year olds had the highest prevalence of substance use disorder (66.6%) with over half of the entire age cohort having diagnosis for an OUD prior to the treated heroin overdose (56.3%). In contrast, only 34.8% of older individuals had a diagnosis of OUD ($P < 0.001$). Over half (56.4%) of the entire cohort had a diagnosis for a mental health disorder, 12.4% had had a prior non-heroin drug overdose, and 10.4% had a prior diagnosis of suicidality (Table 2 in the Supplement[5]).

Individuals above the age of 46 were most likely to have had an opioid prescribed in the year preceding a heroin overdose (61.5%) compared to 49.7% in patients aged 26–45 and 30.6% in those aged 18–25 years old ($p < 0.001$) (Table 3) in the Supplement[6]). Among LTOT recipients, 45.3% of individuals aged 46 and older discontinued LTOT during the 12 months prior to overdose, which represents 14.8% of all patients within this age group. In comparison, 70% of individuals aged 18–25 years old discontinued LTOT in the year prior to overdose, although this represents just 2.5% of all 18–25 year-olds with a heroin overdose.

4. Discussion

In this study of adults with treated heroin overdoses, past year receipt of an opioid prescription was relatively common (42.3%). The use of LTOT and discontinuation of LTOT were both relatively uncommon (12.8% and 6.7% respectively), especially for younger adults. Although LTOT and discontinuation of LTOT in the year prior to heroin overdose were relatively uncommon in absolute terms, the question of whether discontinuation results in transition to heroin use or overdose on heroin for some patients merits further study.

Patterns of prescription opioid use history differed by age. Individuals older than 46 were twice as likely to have an opioid prescribed in the year prior to a heroin overdose compared to those 18–25 years old. LTOT was especially unusual in younger individuals and most of the individuals having their LTOT discontinued prior to an overdose were older than 46 years. The higher prevalence of LTOT discontinuation in persons > 46 years old could suggest potential transition from prescription opioids to heroin is more common in this age cohort than in younger cohorts, or might just reflect the fact that LTOT was more common in this age group. Another possible explanation is that discontinuation is more common in this age due to increased comorbidities and/or drug interactions that could lead to discontinuation. Patients may discontinue opioids for multiple reasons, ranging from agreed upon treatment course, involuntary discontinuation due to misuse, or patient-centered tapers when risks of therapy may outweigh the benefits (Lovejoy et al., 2017; Martin et al., 2011). Therefore, causality cannot be established with respect to whether the discontinuation led to heroin use or misuse led to discontinuation.

[5]Ibid.
[6]Ibid.

In addition, our commercially insured cohort was much less likely to have an OUD diagnosis associated with a claim preceding the overdose (49%) compared to a previously published Medicaid sample (83%) (Frazier et al., 2017). This difference has been shown in prior studies looking at national rates of OUD by insurance type (Davenport and Matthews, 2018). This disparity could reflect a lower burden of disease in commercially insured populations but may also reflect sociodemographic bias in diagnosing addiction. Regardless, many of the individuals with a heroin overdose may have had an OUD diagnosis that was not recorded as a part of any medical encounter over a year, reflecting a missed opportunity to diagnose and engage this population in treatment prior to a potentially fatal event. Pain conditions, however, were highly prevalent across all age groups.

Our study had multiple limitations. First, our sample is a commercially insured population that included dependents up to age 25 and individuals with Medicare Advantage plans and is likely largely employed, so our results may not be generalizable to other populations. The requirement of a 12 month continuous enrollment period allowed for consistent opportunity to measure opioid use in the period leading up to the overdose, but may have introduced a selection bias for the sample because those that were not enrolled for 12 months were different from those who did meet this criterion for inclusion. This dataset also does not capture overdoses in patients that lose insurance prior to a heroin event, or heroin overdoses that were not treated and billed to the insurer, which may include overdoses that never reach professional medical attention. Billing codes for heroin-related overdoses are very sensitive and specific (Green et al., 2019). However, this analysis did combine both overdoses due to heroin alone and those due to heroin with other substances. Use of diagnosis codes in claims data is subject to potential misclassification. We only captured prescriptions and LTOT discontinuation in the year prior to the overdose. Theoretically, a prescription opioid exposure a few years earlier could also lead to potential transitions to heroin, and result in a heroin overdose only years later. Future studies will need to examine this association as well as study whether tapering without discontinuation could potentially be associated with heroin overdoses. Finally, our analysis focused on describing patterns of medical prescription opioid use and heroin overdose. We did not examine pathways of non-medical prescription opioid use to heroin overdose, outside of those with a diagnosed opioid use disorder, which have been described previously (Compton et al., 2016b).

In conclusion, receipt of prescription opioids was common in the year preceding heroin overdose. However, discontinuation of LTOT prior to heroin overdose was uncommon and largely observed among older individuals, the age cohort with the lowest rate of heroin overdose. Further study is needed to determine if observed patterns of opioid prescribing, and in particular opioid discontinuation, are associated with increased risk of heroin overdose.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Brooner RK, King VL, Kidorf M, Schmidt CW Jr., Bigelow GE, 1997 Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. Arch. Gen. Psychiatry 54, 71–80. [PubMed: 9006403]

Campbell CI, Weisner C, Leresche L, Ray GT, Saunders K, Sullivan MD, Banta-Green CJ, Merrill JO, Silverberg MJ, Boudreau D, Satre DD, Von Korff M, 2010 Age and gender trends in long-term opioid analgesic use for noncancer pain. Am. J. Public Health 10, 2541–2547.

Centers for Disease Control and Prevention, 2018 Annual Surveillance Report of Drug-related Risks and Outcomes- United States.

Centers for Disease Control and Prevention. 2019 https://www.cdc.gov/drugoverdose/resources/data.html (Accessed 24.06. 19).

Cicero TJ, Ellis MS, Surratt HL, Kurtz SP, 2014 The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. JAMA Psychiatry 71, 821–826. [PubMed: 24871348]

Compton WM, Jones CM, Baldwin GT, 2016a Relationship between nonmedical prescription-opioid use and heroin use. N. Engl. J. Med 374, 154–163. [PubMed: 26760086]

Compton WM, Jones CM, Baldwin GT, 2016b Nonmedical prescription-opioid use and heroin use. N. Engl. J. Med 374, 1296.

Darke S, Kaye S, Duflou J, 2006 Systemic disease among cases of fatal opioid toxicity. Addiction 101, 1299–1305. [PubMed: 16911729]

Dasgupta N, Creppage K, Austin A, Ringwalt C, Sanford C, Proescholdbell SK, 2014 Observed transition from opioid analgesic deaths toward heroin. Drug Alcohol Depend. 145, 238–241. [PubMed: 25456574]

Davenport S, Matthews K, 2018 In: Paper MW (Ed.), Opioid Use Disorder in the United States: Diagnosed Prevalence by Payer, Age, Sex, and State. Millman. https://www.milliman.com/-/media/Milliman/importedfiles/uploadedFiles/insight/2018/opioid_use_disorder_prevalence.ashx.

Dowell D, Haegerich TM, Chou R, 2016 CDC guideline for prescribing opioids for chronic pain-United States. JAMA 315, 1624–1645. [PubMed: 26977696]

Executive Office of the President of the United States, 2011 Epidemic: Responding to America's Prescription Drug Abuse Crisis.

Frazier W, Cochran G, Lo-Ciganic WH, Gellad WF, Gordon AJ, Chang CH, Donohue JM, 2017 Medication-assisted treatment and opioid use before and after overdose in Pennsylvania Medicaid. JAMA 318, 750–752. [PubMed: 28829862]

Green CA, Perrin NA, Hazlehurst B, Janoff SL, DeVeaugh-Geiss A, Carrell DS, Grijalva CG, Liang C, Enger CL, Coplan PM, 2019 Identifying and classifying opioid-related overdoses: a validation study. Pharmacoepidemiol. Drug Saf 28, 1127–1137. [PubMed: 31020755]

Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Crosby AE, Paulozzi LJ, 2008 Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA 300, 2613–2620. [PubMed: 19066381]

Hedegaard H, Chen LH, Warner M, 2015 Drug-poisoning deaths involving heroin: united States, 2000–2013. NCHS Data Brief 1–8.

Hedegaard H, Warner M, Minino AM, 2017 Drug overdose deaths in the United States, 1999–2016. NCHS Data Brief 1–8.

Hedegaard H, Miniño AM, Warner M, 2018 Drug overdose deaths in the United States, 1999–2017. NCHS Data Brief 1–8.

Injury Surveillance Workgroup 7, 2012 Consensus Recommendations for National and State Poisoning Surveillance. https://cdn.ymaws.com/www.safestates.org/resource/resmgr/imported/ISW7%20Full%20Report_3.pdf.

Larochelle MR, Zhang F, Ross-Degnan D, Wharam JF, 2015 Rates of opioid dispensing and overdose after introduction of abuse-deterrent extended-release oxycodone and withdrawal of propoxyphene. JAMA Intern. Med 175, 978–987. [PubMed: 25895077]

Larochelle MR, Liebschutz JM, Zhang F, Ross-Degnan D, Wharam JF, 2016 Opioid prescribing after nonfatal overdose and association with repeated overdose. Ann. Intern. Med 165, 376–377.

Lovejoy TI, Morasco BJ, Demidenko MI, Meath TH, Frank JW, Dobscha SK, 2017 Reasons for discontinuation of long-term opioid therapy in patients with and without substance use disorders. Pain 158, 526–534. [PubMed: 28192376]

Martin BC, Fan MY, Edlund MJ, Devries A, Braden JB, Sullivan MD, 2011 Long-term chronic opioid therapy discontinuation rates from the TROUP study. J. Gen. Intern. Med 26, 1450–1457. [PubMed: 21751058]

Meiman J, Tomasallo C, Paulozzi L, 2015 Trends and characteristics of heroin overdoses in Wisconsin, 2003–2012. Drug Alcohol Depend. 152, 177–184. [PubMed: 25935735]

Parsells KJ, Cook SF, Kaufman DW, Anderson T, Rosenberg L, Mitchell AA, 2008 Prevalence and characteristics of opioid use in the US adult population. Pain. 138, 507–513. [PubMed: 18342447]

Powell D, Alpert A, Pacula RL, 2019 A transitioning epidemic: how the opioid crisis is driving the rise in hepatitis C. Health Aff. 38, 287–294.

Ronan MV, Herzig SJ, 2016 Hospitalizations related to opioid abuse/dependence and associated serious infections increased sharply, 2002–12. Health Aff. 35, 832–837.

Rudd RA, Paulozzi LJ, Bauer MJ, Burleson RW, Carlson RE, Dao D, Davis JW, Dudek J, Eichler BA, Fernandes JC, Fondario A, Gabella B, Hume B, Huntamer T, Kariisa M, Largo TW, Miles J, Newmyer A, Nitcheva D, Perez BE, Proescholdbell SK, Sabel JC, Skiba J, Slavova S, Stone K, et al., 2014 Increases in heroin overdose deaths - 28 states, 2010 to 2012. MMWR Morb. Mortal. Wkly. Rep 63, 849–854. [PubMed: 25275328]

Rudd RA, Aleshire N, Zibbell JE, Gladden RM, 2016 Increases in drug and opioid overdose deaths–United States, 2000–2014. MMWR Morb. Mortal. Wkly. Rep 64, 1378–1382. [PubMed: 26720857]

Vozoris NT, Wang X, Fischer HD, Gershon AS, Bell CM, Gill SS, O'Donnell DE, Austin PC, Stephenson AL, Rochon PA, 2016 Incident opioid drug use among older adults with chronic obstructive pulmonary disease: a population-based cohort study. Br. J. Clin. Pharmacol 81, 161–170. [PubMed: 26337922]

Wall M, Cheslack-Postava K, Hu MC, Feng T, Griesler P, Kandel DB, 2018 Nonmedical prescription opioids and pathways of drug involvement in the US: generational differences. Drug Alcohol Depend. 182, 103–111. [PubMed: 29220668]

Table 1

Sociodemographic characteristics of patients treated for heroin overdose (n = 3183) in the U.S. Clinformatics® Data Mart Database (2010–2017) (N = 40, 364, 301).

Characteristic	Overall N (%)	Incidence rate per 100,000 person-years	95% CI for incidence rate
Overall	3183	4.20	(4.13–4.27)
Sex			
Male	2228 (70.0)	6.11	(6.01–6.22)
Female	955 (30.0)	2.43	(2.33–2.53)
Age, years			
18 to 25	1694 (53.3)	21.30	(21.08–21.52)
26 to 45	764 (24.0)	2.04	(1.91–2.17)
46 and over	725 (22.8)	0.69	(0.60–0.78)
Mean (S.D.)	33.42 (15.1)		
Race			
Asian	27 (0.8)	0.81	(0.47–1.15)
Black	265 (8.3)	3.98	(3.74–4.22)
Hispanic	232 (7.3)	2.90	(2.68–3.12)
White	2383 (74.9)	4.81	(4.72–4.89)
Unknown	276 (8.7)	3.35	(3.14–3.57)
Census division			
East North Central	826 (26.0)	7.69	(7.50–7.88)
East South Central	145 (4.6)	5.52	(5.13–5.90)
Middle Atlantic	316 (9.9)	5.97	(5.70–6.24)
Mountain	280 (8.8)	3.77	(3.54–4.00)
New England	166 (5.2)	6.61	(6.22–7.00)
Pacific	244 (7.7)	2.44	(2.25–2.64)
South Atlantic	669 (21.0)	3.80	(3.65–3.95)
West North Central	309 (9.7)	3.99	(3.77–4.22)
West South Central	220 (6.9)	2.04	(1.85–2.22)
Unknown	8 (0.3)	0.74	(0.14–1.33)
Plan type			
Commercial	2551 (80.1)	4.69	(4.61–4.78)
Medicare, under age 65	514 (16.1)	19.78	(19.39–20.16)
Medicare, age 65 and over	118 (3.7)	0.63	(0.48–0.77)

Table 2

Patient diagnoses recorded in the year prior to a treated heroin overdose, by patient age at the time of overdose (N = 3183).

Characteristic	Age 18 to 25 N = 1694 N (%)	Age 26 to 45 N = 764 N (%)	Age 46 and over N = 725 N (%)	Overall N = 3183 N (%)	x^2 *P*-value
Pain diagnoses	1066 (62.9)	560 (73.3)	623 (85.9)	2249 (70.7)	< 0.001
Abdominal pain	395 (23.3)	228 (29.8)	304 (41.9)	927 (29.1)	< 0.001
Back and neck pain	429 (25.3)	295 (38.6)	385 (53.1)	1109 (34.8)	< 0.001
Cancer and cancer pain	41 (2.4)	55 (7.2)	117 (16.1)	213 (6.7)	< 0.001
Chest pain	203 (12.0)	133 (17.4)	245 (33.8)	581 (18.3)	< 0.001
General chronic pain	89 (5.3)	115 (15.1)	246 (33.9)	450 (14.1)	< 0.001
Headache	233 (13.8)	135 (17.7)	132 (18.2)	500 (15.7)	0.005
Injuries and acute pain	582 (34.4)	324 (42.4)	347 (47.9)	1253 (39.4)	< 0.001
Other musculoskeletal pain	554 (32.7)	348 (45.5)	442 (61.0)	1344 (42.2)	< 0.001
Neuropathic pain	45 (2.7)	55 (7.2)	133 (18.3)	233 (7.3)	< 0.001
Mental health disorders	952 (56.2)	447 (58.5)	396 (54.6)	1795 (56.4)	0.209
Anxiety disorder	672 (39.7)	322 (42.1)	262 (36.1)	1256 (39.5)	0.064
Mood disorder	728 (43.0)	356 (46.6)	318 (43.9)	1402 (44.0)	0.165
Schizophrenic disorder	22 (1.3)	27 (3.5)	29 (4.0)	78 (2.5)	< 0.001
Other nonpsychotic mental health disorders	157 (9.3)	57 (7.5)	46 (6.3)	260 (8.2)	0.004
Medical comorbidities	90 (5.3)	84 (11.0)	239 (33.0)	413 (13.0)	< 0.001
Infectious diseases	55 (3.2)	35 (4.6)	93 (12.8)	183 (5.7)	< 0.001
Obstructive pulmonary disorder	2 (0.1)	10 (1.3)	113 (15.6)	125 (3.9)	< 0.001
Renal failure	31 (1.8)	23 (3.0)	80 (11.0)	134 (4.2)	< 0.001
Sleep apnea	8 (0.5)	27 (3.5)	58 (8.0)	93 (2.9)	< 0.001
Substance use disorders	1129 (66.6)	439 (57.5)	372 (51.3)	1940 (60.9)	< 0.001
Alcohol use disorder	424 (25.0)	164 (21.5)	159 (21.9)	747 (23.5)	0.036
Cannabis use disorder	417 (24.6)	105 (13.7)	47 (6.5)	569 (17.9)	< 0.001
Cocaine use disorder	237 (14.0)	109 (14.3)	78 (10.8)	424 (13.3)	0.086
Opioid use disorder	953 (56.3)	355 (46.5)	252 (34.8)	1560 (49.0)	< 0.001
Sedative, hypnotic or anxiolytic substance use disorder	293 (17.3)	81 (10.6)	36 (5.0)	410 (12.9)	< 0.001
Other substance use disorder	729 (43.0)	235 (30.8)	175 (24.1)	1139 (35.8)	< 0.001
Non-heroin overdoses	202 (11.9)	86 (11.3)	106 (14.6)	394 (12.4)	0.102

Characteristic	Age 18 to 25 N = 1694 N (%)	Age 26 to 45 N = 764 N (%)	Age 46 and over N = 725 N (%)	Overall N = 3183 N (%)	x^2 *P*-value
Non-heroin opioid overdose	75 (4.4)	33 (4.3)	52 (7.2)	160 (5.0)	0.023
Other and unspecified overdoses	224 (13.2)	112 (14.7)	108 (14.9)	444 (13.9)	0.534
Suicidality	167 (9.9)	88 (11.5)	77 (10.6)	332 (10.4)	0.155
Suicidal ideation	155 (9.1)	81 (10.6)	68 (9.4)	304 (9.6)	0.158
Suicide or self-harm	38 (2.2)	19 (2.5)	15 (2.1)	72 (2.3)	0.604

Table 3

Opioid prescribing history in the year prior to a treated heroin overdose, by patient age at the time of overdose (N = 3183).

Characteristic	Age 18 to 25 N = 1694 N (%)	Age 26 to 45 N = 764 N (%)	Age 46 and over N = 725 N (%)	Overall N = 3183 N (%)	*P*-value
Any opioid prescribed in prior:					
7 days	55 (3.2)	88 (11.5)	203 (28.0)	346 (10.9)	< 0.001
30 days	100 (5.9)	146 (19.1)	243 (33.5)	489 (15.4)	< 0.001
90 days	195 (11.5)	200 (26.2)	308 (42.5)	703 (22.1)	< 0.001
180 days	320 (18.9)	278 (36.4)	366 (50.5)	964 (30.3)	< 0.001
365 days	519 (30.6)	380 (49.7)	446 (61.5)	1345 (42.3)	< 0.001
Peak daily dosage in prior 365 days[a]					< 0.001
1 to < 20 MME	26 (5.0)	16 (4.2)	19 (4.3)	62 (4.6)	
20 to < 50 MME	230 (44.3)	122 (32.1)	114 (25.6)	483 (35.9)	
50 to < 90 MME	124 (23.9)	80 (21.1)	79 (17.7)	295 (21.9)	
90 + MME	118 (22.7)	145 (38.2)	226 (50.7)	505 (37.5)	
Number of prescriptions filled within prior 365 days					
Overall mean (SD)[b]	0.75 (1.27)	1.45 (1.93)	1.67 (1.92)	1.13 (1.66)	< 0.001
Overall median (IQR)[b]	0 (0–1)	1 (0–2)	1 (0–3)	1 (0–2)	< 0.001
Among those prescribed mean (SD)[a]	1.77 (1.42)	2.50 (1.94)	2.59 (1.83)	2.20 (1.74)	< 0.001
Among those prescribed median (IQR)[a]	1 (1–2)	2 (1–3)	2 (1–3)	2 (1–3)	< 0.001
Average daily dosage in the week of overdose[c]					0.011
1 to < 20 MME	22 (40.0)	21 (23.9)	36 (17.7)	79 (22.8)	
20 to < 50 MME	16 (29.1)	25 (28.4)	59 (29.1)	100 (28.9)	
50 to < 90 MME	5 (9.1)	18 (20.5)	34 (16.8)	57 (16.5)	
90+ MME	11 (20.0)	24 (27.3)	75 (37.0)	110 (31.8)	
LTOT in the past 365 days	60 (3.5)	110 (14.4)	236 (32.6)	406 (12.8)	< 0.001
Active LTOT at time of overdose (episode overlapped with the last week)[b]	18 (1.1)	46 (6.0)	129 (17.8)	193 (6.1)	< 0.001
LTOT discontinued within 90 days prior to overdose[b]	4 (0.24)	26 (3.4)	37 (5.1)	67 (2.1)	< 0.001
LTOT discontinued within 365 days prior to overdose[b]	42 (2.5)	64 (8.4)	107 (14.8)	213 (6.7)	< 0.001

Characteristic	Age 18 to 25 N = 1694 N (%)	Age 26 to 45 N = 764 N (%)	Age 46 and over N = 725 N (%)	Overall N = 3183 N (%)	*P*-value
Length of LTOT episode during the year, days, mean (SD)[d]	107.2 (105.0)	185.8 (119.7)	230.1 (119.0)	199.9 (124.7)	< 0.001
Length of LTOT episode during the year, days, median (IQR)[d]	84.5 (16.0–139.8)	199.0 (90.0–281.3)	247.0 (134.0–348.0)	214.0 (90.0–331.5)	< 0.001

[a]Among those with a prescription opioid claim in 365 days prior to overdose.

[b]Among all individuals in age group.

[c]Among those with a prescription opioid claim in 7 days prior to overdose.

[d]Among those receiving LTOT in 365 days prior to overdose.