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U.S. Prescribing Trends of Fentanyl, Opioids, and Other Pain Medications in Outpatient and Emergency Department Visits from 2006-2015

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Abstract

The United States is currently facing an epidemic of opioid-related deaths, increasingly associated with fentanyl use. Our objective was to characterize rates of fentanyl, general opioid and non-opioid pain medication prescription at a national level in both outpatient and emergency department settings. We used a retrospective cross-sectional research design using data from the 2006–2015 National Ambulatory Medical Care Surveys and National Hospital Ambulatory Medical Care Surveys. Between 2006–2015, 66,987 (17.4%) of 390,538 office-based outpatient visits (nationally-representative of 961 million visits) and 134,953 (45.0%) of 305,570 ED visits (nationally-representative of 130 million visits) listed a pain medication prescription. The

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proportion of all outpatient visits in which any pain medication was prescribed increased from 15.0% in 2006–2007 to 20.5% in 2014–2015 ($p<0.001$). The proportion of all outpatient visits in which any fentanyl product was prescribed remained stable at 0.3% and 0.4% ($p=0.32$), but increased among ED visits from 0.5% to 1.1% ($p=0.006$). In contrast, the proportion of all outpatient visits in which any opioid product was prescribed increased from 6.6% to 9.7% ($p<0.001$), but remained relatively stable among ED visits from 26.2% to 24.4% ($p=0.07$). Non-opioid pain medication prescription increased in both settings, from 9.7% to 13.7% ($p<0.001$) in the outpatient setting and from 25.6% to 27.6% ($p=0.02$) in the ED setting between 2006–2007 and 2014–2015, respectively. To address current opioid crisis, both clinical and public health interventions are needed, such as targeted education outreach on evidence-based opioid prescribing and non-opioid alternatives.

Keywords

opioid; fentanyl; NSAID; prescribing

1. Introduction

The United States is currently facing an opioid epidemic, which began in the mid-1990s with increased pharmaceutical marketing, as well as promotion by both hospital accrediting bodies and official medical societies (Kolodny et al., 2015). Emergency department (ED) visits for opioid overdoses rose 30% across the country from July 2016 through September 2017 (Centers for Disease Control and Prevention, 2017, 2018). Opioid-related deaths were five times higher in 2016 than 1999 (Centers for Disease Control and Prevention, 2017). In response, the Centers for Disease Control and Prevention (CDC) issued guidelines in 2013 encouraging the replacement of opioid medications with non-opioid alternatives to treat chronic pain (Dowell, Haegerich, & Chou, 2016). Despite such efforts, fentanyl prescribing and its related harms have been rising nationwide. Fentanyl, a schedule II opioid, is approximately 100 times more potent than morphine, acts rapidly, and has a high potential for addiction (Jumbelic, 2010; Roxburgh et al., 2013). Deaths from fentanyl (both prescription and illicit) and other non-methadone synthetic opioids (with the exception of methadone) climbed from 8% in 2010 to 18% in 2015 (Hedegaard, Warner, & Miniño, 2017). Another study reported that the number of illicit fentanyl-related deaths increased from 2,128 in 2014 to 15,646 in 2016, indicating a surge of illicit fentanyl use (Lilly, 2018).

1.1 Importance

While a study of nationwide opioid prescriptions from 2002–2013 suggested that opioid prescriptions began to decline prior to the 2013 CDC guideline announcement (Richard C Dart et al., 2015), the response to these guidelines has not been very well studied. Furthermore, while the substantial recent increase in fentanyl-associated deaths suggests an increasing rate of fentanyl distribution (Seth, Rudd, Noonan, & Haegerich, 2018; Whalen, 2017), it remains unknown whether the source of this increased availability is from clinician prescriptions or from illicit distribution (e.g., black markets). A recent set of CDC reports show that in states with the highest burden of fentanyl-related deaths, the increase in deaths has no correlation with changes in fentanyl prescription (Gladden, 2016; O'Donnell, Halpin,

Mattson, Goldberger, & Gladden, 2017); Instead, they are likely an effect of illicit fentanyl distribution (Lilly, 2018). However, these technical reports are limited as they investigated fentanyl prescribing at the state level only, and did not differentiate between different prescriber settings (e.g., outpatient care versus emergency department). Examining these two different prescriber settings is important as the acuity of care is very different, which impacts the appropriateness of pain medication prescribing (e.g., opioid therapy may be indicated for acute pain and not for most causes of chronic pain).

1.2 Goals of this Investigation

Our objective was to investigate and compare current prescribing rates of opioid medications, including fentanyl, and of non-opioid medications in the outpatient and emergency department settings using a nationally-representative sample.

2. Methods

2.1 Study design and setting and selection of participants

We used 2006–2015 data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS), which provide nationally representative samples of office-based outpatient visits and emergency department visits, respectively (National Center for Health Statistics, 2017b). NAMCS and NHAMCS both sample non-federally employed physicians who are primarily engaged in direct patient care. The data provide an analytic base that serves as an important tracking tool on ambulatory and emergency care utilization regarding national trends, medication use, and practice patterns in the US (National Center for Health Statistics, 2017a). Both NAMCS and NHAMCS utilize a complex survey design and sampling weights (i.e., unequal probability of selection, clustering, and stratification), where physicians are selected in the first stage and visits in the second stage. Samples included 390,538 visits in NAMCS and 305,570 visits in NHAMCS. Additional information regarding descriptions, questionnaires, sampling methodology and datasets is publicly available on the NAMCS and NHAMCS website (https://www.cdc.gov/nchs/ahcd/about_ahcd.htm).

2.2 Measures

2.2.1 Pain medications—To characterize pain medication prescribing, we examined the first eight medications listed for all outpatient and ED visits, ensuring consistency across all survey years. We constructed three indicator variables using generic names of medications: fentanyl and its analogue products (i.e., fentanyl droperidol-fentanyl, alfentanil, sufentanil, and remifentanil), all opioid products other than fentanyl (including their analogues), and all other non-opioid pain medications. Opioid products other than fentanyl consisted of the following medications: codeine, meperidine, methadone, alfentanil, hydromorphone, morphine, oxycodone, pentazocine, propoxyphene, sufentanil, opium, levorphanol, oxymorphone, butorphanol, nalbuphine, buprenorphine, hydrocodone, dihydrocodeine, remifentanil, tapentadol, tramadol, and their combined products. Other non-opioid pain medications are nonsteroidal anti-inflammatory drugs (NSAIDs), non-analgesics, and other drugs (i.e., acetaminophen, aspirin, diclofenac, ibuprofen,

indomethacin, ketoprofen, ketorolac, naproxen, phenylbutazone, piroxicam, tolmetin, gabapentin, and pregabalin).

2.2.2 Demographic and clinical covariates—We included a number of patient demographic and clinical covariates provided during visits. Demographic variables included: age (<19, 19–44, 45–64, or ≥65), gender, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, or other), primary source of payment (private, Medicare, Medicaid, or other). Medicare is a federal program that provides health insurance coverage for US adults aged 65 or older, and Medicaid is a state and federal program that provides health insurance coverage for low-income individuals and families (U.S. Department of Health & Human Services, 2015). Clinical variables included visit diagnosis and physician specialty. Both NAMCS and NHAMCS collect up to three visit diagnoses for each sampled visit using the *International Classification of Diseases, 9th edition, Clinical Modification* (ICD-9-CM) diagnostic codes. We categorized visit diagnosis into three groups: cancer-related pain diagnoses (i.e., 140–239 or 338.3X), non-cancer related pain diagnoses (i.e., 338.XX, 350.1X–350.2X, 354.4X, 355.71, 379.91, 388.7X, 719.4X, 724.1X–724.2X, 729.1X, 780.96, 786.5X, or 789.XX), and no pain-related diagnosis. For physician specialty, we distinguished between generalists (i.e., general/family practice, internal medicine, pediatrics, and obstetrics and gynecology) vs. other in NAMCS. In NHAMCS, we distinguished clinical specialty by clinical degree (i.e., MD vs. other). We also reported number of visits in the past 12 months (0, 1–2, 3–5, or ≥6), number of chronic conditions (0–1 or ≥2), and number of concomitant medications (0–5 or ≥6) prescribed in NAMCS datasets.

2.3 Ethics and Data Availability

As we used publicly available de-identified data, our study was deemed the Institutional Review Board exempt by Yale School of Medicine (#2000021850). The datasets generated and/or analysed during the current study are available in the NAMCS/NHAMCS repository (https://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm).

2.4 Statistical Analysis

We determined the proportion of visits for which any pain medication was prescribed and examined associations with selected characteristics (e.g., age, sex, race/ethnicity, clinical comorbidities, concomitant medication use, and physician specialty), using Bonferroni-adjusted bivariate analyses. Next, we determined the proportion of visits for which any pain medication was prescribed across survey years, overall and for each pain medication class, also stratifying overall analyses by selected patient and visit characteristics. We used Chi-Square analysis to compare rates in 2006–2007 and 2014–2015. All analyses were conducted using Stata MP/6-Core version 15.1 (College Station, TX), accounting for the complex survey design and sampling weights.

3. Results

3.1 Selected characteristics of the study subjects

Between 2006 and 2015, 66,987 (17.4%) of 390,538 office-based outpatient visits (nationally-representative of 961 million visits) and 134,953 (45.0%) of 305,570 ED visits

(nationally-representative of 130 million visits) listed a pain medication prescription (Table 1). 56.3% of office-based outpatient visits were to primary care physicians, and of these visits, 18.3% involved a prescription for a pain medication. Among office-based outpatient visits, pain medication prescription was highest among patients aged 45–64, non-Hispanic Black patients, patients with Medicare coverage, patients receiving care from primary care physicians, and patients receiving care for a pain-related diagnosis (all p -values < 0.001). Furthermore, visits involved with two or more chronic conditions and six or more medications concomitantly prescribed were also associated with receiving pain medications (all p -values < 0.001). Among ED visits, pain medication prescription was highest among patients aged 19–44, males, Hispanic patients, patients with private insurance, patients receiving care from MDs, and patients receiving care for a pain-related diagnosis (all p -values < 0.001).

3.2 National prescribing trends of opioids, fentanyl and other pain medications

The proportion of all outpatient visits in which any pain medication was prescribed increased significantly from 15.0% in 2006–2007 to 20.5% in 2014–2015 ($p < 0.001$). Among ED visits, the proportion did not change significantly, ranging from 44.2% in 2006–2007 to 44.5% in 2014–2015 ($p = 0.72$) (Table 2).

The proportion of all outpatient visits in which any fentanyl product was prescribed remained stable at 0.3% in 2006–2007 and 0.4% in 2014–2015 ($p = 0.32$), but prescribing of fentanyl product increased significantly among ED visits from 0.5% in 2006–2007 to 1.1% in 2014–2015 ($p = 0.006$). In contrast, the proportion of all outpatient visits in which any nonfentanyl opioid product was prescribed increased significantly from 6.6% in 2006–2007 to 9.7% in 2014–2015 ($p < 0.001$), but remained relatively stable among ED visits from 26.2% in 2006–2007 to 24.4% in 2014–2015 ($p = 0.07$). Non-opioid pain medication prescription increased in both settings, from 9.7% to 13.7% ($p < 0.001$) in the outpatient setting and from 25.6% to 27.6% ($p = 0.02$) in the ED setting in 2006–2007 and 2014–2015, respectively.

3.3 Factors of prescribing any pain medication

There were several patient factors predictive of higher rates of prescribing of any pain medication among both outpatient and ED visits (Table 3). Among outpatient visits, pain medication prescription was highest among visits by patients aged 45–64 years, increasing significantly over time to 25.6% in 2014–2015 ($p < 0.001$), and among visits by patients with Medicare, increasing significantly over time to 24.2% in 2014–2015 ($p < 0.001$). In contrast, among ED visits, pain medication prescription was lowest among visits by patients with Medicare insurance, but increased significantly over time to 36.4% in 2014–2015 ($p = 0.003$).

4. Discussion

In this study of pain medication prescribing in a nationally-representative sample of outpatient and ED visits from 2006–2015, overall rates of pain medication prescribing were high, with a prescription provided among approximately one in five outpatient visits and nearly one in two ED visits. Over this period, we found increased opioid pain medication

prescribing in the outpatient setting, rising to nearly one in twelve visits, and a small but significant increase in fentanyl prescribing in the ED, peaking at a rate of prescribing of 1.1% of all ED visits in 2014–2015. Finally, reassuringly, there was an increase in non-opioid pain medication prescribing in both the outpatient and ED settings, which has not been previously reported or well-investigated.

The prescription of opioid medications increased in the outpatient setting. Chronic non-cancer-related pain is a common presentation in primary care, and the difficulties of determining when to prescribe opioids, and for how long, has been acknowledged in multiple studies (Harle et al., 2015; Jamison, Kerry Anne Sheehan, Elizabeth Scanlan, & Ross, 2014). Our results suggest the need to implement several interventions in order to reduce opioid prescribing for chronic pain in the primary care setting. For instance, there have been numerous efforts to encourage appropriate opioid prescribing, including targeted physician education (Leece et al., 2017). Requiring patients to have a structured care system comprising of periodic visits dedicated to monitoring and discussion of their current opioid medications has been shown to reduce opioid prescriptions (McCann et al., 2018). Ongoing education for patients who are currently struggling with opioid dependence is especially important. Patients with opioid dependence are more likely to experience an opioid overdose event (Substance Abuse and Mental Health Services Administration, 2018) and a recent study has shown that patients who have experienced a non-fatal overdose are at high risk of fatal opioid overdose throughout this period (Olfson, Wall, Wang, Crystal, & Blanco, 2018). A multicomponent system involving a nurse care manager, electronic registry, data-driven academic detailing (i.e., face-to-face education of prescribers by trained healthcare professionals in order to improve evidence-based prescribing of targeted drugs), and clinical decision support (such as care reminders, up-to-date guidelines, recommendations, and databases that can provide information relevant to particular patients) have also shown to improve adherence to opioid-prescribing guidelines (Cushman, 2017; Liebschutz et al., 2017).

There was a small but significant increase in fentanyl prescribing which is important to acknowledge. This was particularly notable in the ED setting, where patients often have a short stay and are discharged without monitoring or follow-up care, inherently leading to increased risk of abuse potential (Compton & Volkow, 2006). Strategies for preventing subsequent fentanyl diversion after ED prescription are three-fold: ED providers could dispense a small amount of fentanyl with no or minimal refills; they could then schedule primary care follow-up for further pain management, with instructions that therapy be non-opioid in nature; and/or they could utilize alternative, non-opioid analgesic treatments within the ED setting before patients are discharged.

Conversely, it is promising to see that despite the small increase in fentanyl-specific prescribing, opioid prescribing in the ED decreased from 2010 to 2015, with the most notable decline between 2010 and 2013. These results are consistent with previous studies both at the state-level (O'Donnell et al., 2017; Peterson et al., 2016; Somerville et al., 2017) and nationally (Cicero, Ellis, & Kasper, 2017), suggesting that, regardless of prescriber setting, the recent increase in fentanyl-related deaths is less likely attributable to physician prescribing and more likely represents non-prescription distribution. This may actually be

the effect of efforts to reduce opioid prescribing and limit utilization of opioids by pain specialists, which some have raised concerns about having unintended downstream consequences, including opening up a market for illicit opioid distribution (Cicero, Ellis, Surratt, & Kurtz, 2014).

Given that many of the fentanyl-related deaths are likely attributable to illicitly manufactured fentanyl, targeted efforts towards monitoring illicit fentanyl production and distribution are needed in addition to monitoring prescription fentanyl diversion. Multiple strategies can be implemented, such as increased access to rapid-acting potent naloxone for high-risk individuals and their close contacts, adding fentanyl to point-of-care screening tests, targeting illicit drug production into safer formulations that do not involve fentanyl, and revision of current legal penalties involving illicit opioid drug distribution (Frank & Pollack, 2017; Suzuki & El-Haddad, 2017; Xu, Davis, Cruz, & Lurie, 2018).

In addition, enhancing public health measures to identify populations at increased risk and upscaling availability of treatment for opioid dependence is critical moving forward. Enrollment in both methadone and buprenorphine treatment programs has been shown to be protective against opioid overdose (Bruneau et al., 2018; Davoli et al., 2007; Esteban et al., 2003). A recent study estimates that in the United States, there are less than 20 opioid therapy recipients per 100 injection drug users – this leaves much room for expansion and increased availability of opioid treatment programs (Larney et al., 2017). This strategy will target opioid use disorders stemming from both over-prescription and illicit opioid distribution.

The increase in non-opioid pain medication prescribing in both outpatient and emergency room settings is reassuring. Previous reports on pain medication, specifically in the ED, reported an increase in opioid prescribing and no change in non-opioid prescribing from 2001–2010 (Mazer-Amirshahi, Mullins, Rasooly, van den Anker, & Pines, 2014). Our results showed the opposite, with an increase in non-opioid prescription. Our results suggests a response by ED providers to replace opioid treatments with non-opioid NSAIDs for patients presenting with pain disorder starting in 2010 (Dowell et al., 2016). Likewise, multiple studies in the primary care setting have shown the benefit of choosing non-opioid therapies for chronic pain – our results show that outpatient physicians are starting to use evidence-based guidelines for managing chronic pain (Renthal, 2016; Schneiderhan, Clauw, & Schwenk, 2017). Furthermore, WHO guidelines on pain prescribing have been updated to include greater specificity of pain type and recommend use of NSAIDs and non-opioids as well as non-pharmacologic treatments such as physiotherapy and occupational therapy before an initial prescription of a weak opioid (Vargas-Schaffer & Cogan, 2014). These strategies enable physicians to make clinical decisions that reduce long-term opioid dependence for their patients.

There are important limitations to this study. First, both NAMCS and NHAMCS limit the number of medications that are listed as prescribed during each visit. For patient visits where more than eight medications were prescribed, fentanyl or other opioid prescriptions, and especially NSAIDs (which are not consistently prescribed as they are available over the counter), may have not been captured, potentially underestimating pain medication

prescribing. Second, NHAMCS only captures ED visits and does not include visits to hospital-based outpatient clinics, which limits the generalizability of our findings. Third, NAMCS and NHAMCS are representative of visits to physicians in the US, but they are likely to underestimate physician prescriptions as they excluded any prescription orders made by phone and do not capture physicians working in other settings (e.g., veterans' health affairs or long-term care facilities). Fourth, we did not explicitly test whether patterns of prescribing changed after the CDC guideline was issued or evaluate appropriateness of fentanyl prescribing; rather, our analysis is primarily descriptive, characterizing pain medication prescribing before and afterwards. Of note, change in clinical practice often occurs slowly and the 2013 release of the CDC guideline may not yet have been fully considered and implemented across health systems to observe its full effect in our study period of 2006–2015.

5. Conclusion

In summary, in this study of pain medication prescribing in a nationally-representative sample of outpatient and ED visits from 2006–2015, we found increased opioid pain medication prescribing in the outpatient setting, decreased opioid prescribing in the ED and an increased rate of fentanyl prescribing in the ED. These findings, consistent with state-level findings, suggest an illicit, non-prescription source of the fentanyl epidemic, rather than prescriptions by health care practitioners. To address current opioid crisis, both clinical and public health interventions are needed, such as targeted education outreach on evidence-based opioid prescribing and nonopioid alternatives, a multicomponent database system for prescription opioid monitoring and to foster guideline recommended care, and increased nationwide access to opioid dependence treatment programs.

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Conflict of Interest Statement

All research procedures performed in this study are in accordance with the ethical standards of the Institutional Review Board at Yale University School of Medicine (#2000021850). In the past 36 months, Dr. Rhee received funding support from the National Institutes of Health (NIH) (#T32AG019134); Dr. Ross received research support through Yale University from Johnson and Johnson to develop methods of clinical trial data sharing, from Medtronic, Inc. and the Food and Drug Administration (FDA) to develop methods for post-market surveillance of medical devices (U01FD004585), from the Food and Drug Administration to establish Yale-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI) program (U01FD005938), from the Blue Cross Blue Shield Association to better understand medical technology evaluation, from the Centers of Medicare and Medicaid Services (CMS) to develop and maintain performance measures that are used for public reporting (HHSM-500-2013-13018I), from the Agency for Healthcare Research and Quality (R01HS022882), from the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH) (R01HS025164), and from the Laura and John Arnold Foundation to establish the Good Pharma Scorecard at Bioethics International and the Collaboration on Research Integrity and Transparency (CRIT) at Yale.

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References

- Bohnert AS, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, & Blow FC (2011). Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*, 305(13), 1315–1321. doi:10.1001/jama.2011.370 [PubMed: 21467284]
- Bruneau J, Ahamad K, Goyer M-È, Poulin G, Selby P, Fischer B, ... Wood E (2018). Management of opioid use disorders: a national clinical practice guideline. *Canadian Medical Association Journal*, 190(9), E247–E257. [PubMed: 29507156]
- Centers for Disease Control and Prevention. (2017). Drug Overdose Death Data. Retrieved from <https://www.cdc.gov/drugoverdose/data/statedeaths.html>
- Centers for Disease Control and Prevention. (2018). Opioid Overdoses Treated in Emergency Departments. Retrieved from <https://www.cdc.gov/vitalsigns/opioid-overdoses/>
- Cicero TJ, Ellis MS, & Kasper ZA (2017). Increases in self-reported fentanyl use among a population entering drug treatment: The need for systematic surveillance of illicitly manufactured opioids. *Drug and Alcohol Dependence*, 177, 101–103. [PubMed: 28582697]
- 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(7), 821–826. [PubMed: 24871348]
- Compton WM, & Volkow ND (2006). Major increases in opioid analgesic abuse in the United States: concerns and strategies. *Drug and Alcohol Dependence*, 81(2), 103–107. [PubMed: 16023304]
- Cushman PA (2017). The primary care provider experience in an intervention to improve adherence to opioid prescribing guidelines. Retrieved from <https://hdl.handle.net/2144/27086>
- Dart RC, Severtson SG, & Bucher-Bartelson B (2015). Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med*, 372(16), 1573–1574. doi:10.1056/NEJMc1501822
- Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, & Green JL (2015). Trends in opioid analgesic abuse and mortality in the United States. *New England Journal of Medicine*, 372(3), 241–248. [PubMed: 25587948]
- Davoli M, Bargagli AM, Perucci CA, Schifano P, Belleudi V, Hickman M, ... Faggiano F (2007). Risk of fatal overdose during and after specialist drug treatment: the VEdette study, a national multi-site prospective cohort study. *Addiction*, 102(12), 1954–1959. [PubMed: 18031430]
- Dowell D, Haegerich TM, & Chou R (2016). CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. *JAMA*, 315(15), 1624–1645. doi:10.1001/jama.2016.1464 [PubMed: 26977696]
- Esteban J, Gimeno C, Barril J, Aragonés A, Climent J. M. a., & de la Cruz Pelli M. a. (2003). Survival study of opioid addicts in relation to its adherence to methadone maintenance treatment. *Drug and Alcohol Dependence*, 70(2), 193–200. [PubMed: 12732413]
- Frank RG, & Pollack HA (2017). Addressing the fentanyl threat to public health. *New England Journal of Medicine*, 376(7), 605–607. [PubMed: 28199808]
- Gladden RM (2016). Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths—27 states, 2013–2014. *MMWR. Morbidity and mortality weekly report*, 65.
- Harle CA, Bauer SE, Hoang HQ, Cook RL, Hurley RW, & Fillingim RB (2015). Decision support for chronic pain care: how do primary care physicians decide when to prescribe opioids? a qualitative study. *BMC Family Practice*, 16(1), 48. [PubMed: 25884340]
- Hedegaard H, Warner M, & Miniño AM (2017). Drug overdose deaths in the United States, 1999–2015. *NCHS data brief*(273), 1–8.
- Jamison RN, Kerry Anne Sheehan B, Elizabeth Scanlan N, & Ross EL (2014). Beliefs and attitudes about opioid prescribing and chronic pain management: survey of primary care providers. *Journal of opioid management*, 10(6), 375–382. [PubMed: 25531955]
- Jumbelic MI (2010). Deaths with transdermal fentanyl patches. *The American journal of forensic medicine and pathology*, 31(1), 18–21. [PubMed: 19918162]
- Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, & Alexander GC (2015). The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annu*

Rev Public Health, 36, 559–574. doi:10.1146/annurevpublhealth-031914-122957 [PubMed: 25581144]

Larney S, Peacock A, Leung J, Colledge S, Hickman M, Vickerman P, ... Hines L (2017). Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: a systematic review. *The Lancet Global Health*, 5(12), e1208–e1220. [PubMed: 29074410]

Leece P, Buchman DZ, Hamilton M, Timmings C, Shantharam Y, Moore J, & Furlan AD (2017). Improving opioid safety practices in primary care: protocol for the development and evaluation of a multifaceted, theory-informed pilot intervention for healthcare providers. *BMJ open*, 7(4), e013244.

Liebschutz JM, Xuan Z, Shanahan CW, LaRochelle M, Keosaian J, Beers D, ... Parker V (2017). Improving adherence to long-term opioid therapy guidelines to reduce opioid misuse in primary care: a cluster-randomized clinical trial. *JAMA internal medicine*, 177(9), 1265–1272. [PubMed: 28715535]

Lilly JL (2018). Estimating the actual death rate caused by prescription opioid medication and illicit fentanyl. *Journal of American Physicians and Surgeons*, 23(1), 20–22.

Mazer-Amirshahi M, Mullins PM, Rasooly I, van den Anker J, & Pines JM (2014). Rising opioid prescribing in adult U.S. emergency department visits: 2001–2010. *Acad Emerg Med*, 21(3), 236–243. doi:10.1111/acem.12328 [PubMed: 24628748]

McCann KS, Barker S, Cousins R, Franks A, McDaniel C, Petrany S, & Riley E (2018). Structured Management of Chronic Nonmalignant Pain with Opioids in a Rural Primary Care Office. *The Journal of the American Board of Family Medicine*, 31(1), 57–63. [PubMed: 29330240]

National Center for Health Statistics. (2017a, 2017). Ambulatory Health Care Data. Retrieved from <https://www.cdc.gov/nchs/ahcd/index.htm>

National Center for Health Statistics. (2017b, 2017). Ambulatory Health Care Data: Questionnaires, Datasets, and Related Documentation. Retrieved from https://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm

O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, & Gladden RM (2017). Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 – 10 States, July–December 2016. *MMWR Morb Mortal Wkly Rep*, 66(43), 1197–1202. doi:10.15585/mmwr.mm6643e1 [PubMed: 29095804]

Olfson M, Wall M, Wang S, Crystal S, & Blanco C (2018). Risks of fatal opioid overdose during the first year following nonfatal overdose. *Drug and Alcohol Dependence*, 190, 112–119. [PubMed: 30005310]

Peterson AB, Gladden RM, Delcher C, Spies E, Garcia-Williams A, Wang Y, ... Goldberger BA (2016). Increases in Fentanyl-Related Overdose Deaths - Florida and Ohio, 2013–2015. *MMWR Morb Mortal Wkly Rep*, 65(33), 844–849. doi:10.15585/mmwr.mm6533a3 [PubMed: 27560948]

Renthal W (2016). Seeking Balance Between Pain Relief and Safety: CDC Issues New Opioid-Prescribing Guidelines. *JAMA Neurol*, 73(5), 513–514. doi:10.1001/jamaneurol.2016.0535 [PubMed: 26978030]

Roxburgh A, Burns L, Drummer OH, Pilgrim J, Farrell M, & Degenhardt L (2013). Trends in fentanyl prescriptions and fentanyl-related mortality in Australia. *Drug and alcohol review*, 32(3), 269–275. [PubMed: 23442164]

Schneiderhan J, Clauw D, & Schwenk TL (2017). Primary Care of Patients With Chronic Pain. *JAMA*, 317(23), 2367–2368. doi:10.1001/jama.2017.5787 [PubMed: 28520835]

Seth P, Rudd RA, Noonan RK, & Haegerich TM (2018). Quantifying the Epidemic of Prescription Opioid Overdose Deaths. *American Journal of Public Health*, 108(4), 500–502. doi:10.2105/AJPH.2017.304265 [PubMed: 29513577]

Somerville NJ, O'Donnell J, Gladden RM, Zibbell JE, Green TC, Younkin M, ... Walley AY (2017). Characteristics of Fentanyl Overdose - Massachusetts, 2014–2016. *MMWR Morb Mortal Wkly Rep*, 66(14), 382–386. doi:10.15585/mmwr.mm6614a2 [PubMed: 28406883]

Substance Abuse and Mental Health Services Administration. (2018). Locating data on risk factors for opioid overdose. Retrieved from https://www.samhsa.gov/capt/sites/default/files/capt_resource/risk-factor-mapping-tool.pdf

- Suzuki J, & El-Haddad S (2017). A review: fentanyl and non-pharmaceutical fentanyls. *Drug and Alcohol Dependence*, 171, 107–116. [PubMed: 28068563]
- U.S. Department of Health & Human Services. (2015). What is the difference between Medicare and Medicaid? Retrieved from <https://www.hhs.gov/answers/medicare-and-medicaid/what-is-the-difference-between-medicare-medicaid/index.html>
- Vargas-Schaffer G, & Cogan J (2014). Patient therapeutic education: placing the patient at the centre of the WHO analgesic ladder. *Canadian Family Physician*, 60(3), 235–241. [PubMed: 24627377]
- Whalen J (2017). Fentanyl Fueled 21% Jump in Total Drug-Overdose Deaths in Year. Available at: <https://www.wsj.com/articles/fentanyl-fueled-21-jump-in-total-drug-overdose-deaths-in-year-1509048073>. Accessed August 26, 2018 Wall Street Journal.
- Xu J, Davis CS, Cruz M, & Lurie P (2018). State naloxone access laws are associated with an increase in the number of naloxone prescriptions dispensed in retail pharmacies. *Drug and Alcohol Dependence*.

Highlights

- Prescribing rates of opioid, fentanyl and other pain medications were examined.
- In 2006–2015, opioid prescribing increased in the outpatient visits, but decreased in ED visits.
- The prescribing rate of fentanyl were low (<2%) but increased modestly among ED visits.
- Illicit, non-prescription sources may explain the fentanyl epidemic.
- Clinical and public health interventions are needed to address current opioid crisis.

Table 1.

Selected characteristics (weighted %) of visits in which pain medications were prescribed, 2006–2015
NAMCS and NHAMCS.

	NAMCS			NHAMCS		
	Total (column %)	Pain medication prescription (row %)	<i>P</i> -value [†]	Total (column %)	Pain medication prescription (row %)	<i>P</i> -value [†]
Sample size						
Unweighted sample	390,538	66,987		305,570	134,953	
	961,261,3	167,349,60		130,155,3	58,568,338	
Weighted visits	67	6		21		
Age						
<19	18.9	9.6		24.1	40.0	
19–44	24.1	17.3	<0.001	39.0	51.9	<0.001
45–64	29.7	21.8		21.7	47.8	
65	27.3	18.1		15.2	31.1	
Gender						
Female	58.5	17.6	0.045	54.9	43.6	<0.001
Male	41.5	17.1		45.1	46.1	
Race/ethnicity						
Non-Hispanic White	71.8	17.5		59.7	44.9	
Non-Hispanic Black	10.3	19.0	<0.001	22.5	44.8	0.001
Hispanic	12.5	16.9		14.6	46.3	
Other ^{a)}	5.3	14.1		3.2	43.3	
Primary source of payment						
Private	53.7	15.3		32.6	47.8	
Medicare	25.9	20.1	<0.001	18.7	35.5	<0.001
Medicaid	12.5	17.7		28.8	45.3	
Other	7.9	21.6		19.9	50.0	
Physician specialty						
Generalists ^{b)}	56.3	18.3	<0.001	-	-	-
Other ^{c)}	43.7	16.3		-	-	
Clinician specialty						
MDs	-	-		90.1	45.8	
Other ^{d)}	-	-	-	9.9	39.6	<0.001
Repeat of visits in the past 12 months						
0 visit	6.9	12.4		-	-	
1–2 visits	36.4	15.7	<0.001	-	-	-
3–5 visits	31.2	18.3		-	-	
6+ visits	25.4	21.2		-	-	
Chronic conditions ^{e)}				-	-	-

	NAMCS			NHAMCS		
	Total (column %)	Pain medication prescription (row %)	P-value [†]	Total (column %)	Pain medication prescription (row %)	P-value [†]
<2	68.2	14.7	<0.001			
2	31.8	23.8				
Concomitant medications prescribed				-	-	-
<6	83.9	13.0	<0.001			
6	16.1	37.7				
Visit diagnosis						
Cancer-related ^{f)}	4.7	14.9		0.6	46.5	
Other pain-related ^{g)}	5.0	43.8	<0.001	13.0	60.6	<0.001
No indication	90.3	16.1		86.5	42.7	

Note:

[†] compares proportion differences by any pain prescription using a weight-corrected, Bonferroni-adjusted chi-squared statistic.

^{a)} includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), or 2+ reported racial/ethnic groups;

^{b)} includes general/family practice, internal medicine, pediatrics, and obstetrics and gynecology;

^{c)} includes psychiatry, general surgery, orthopedic surgery, cardiovascular diseases, dermatology, urology, neurology, ophthalmology, otolaryngology, and others;

^{d)} includes physician assistants (PAs) and nurse practitioners (NPs);

^{e)} was based 14 chronic conditions (yes/no) collected by the NAMCS (e.g., arthritis, congestive heart failure, and diabetes);

^{f)} was based on ICD-9-CM diagnostic codes 140–239, 338.3X; and

^{g)} was based on ICD-9-CM codes 338.XX, 350.1X–350.2X, 354.4X, 355.71, 379.91, 388.7X, 719.4X, 724.1X–724.2X, 729.1X, 780.96, 786.5X, 789.XX.

Table 2.

Pain medication prescribing trends, 2006–2015 NAMCS and NHAMCS.

	Years (%)					2006-2007 vs. 2014-2015, <i>P</i> -value ^a
	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	
NAMCS						
Visits in which any pain medication prescribed	15.0%	16.4%	17.4%	18.0%	20.5%	<0.001
Visits in which any pain medication from the specific class prescribed						
Fentanyl and analogues [*]	0.3%	0.3%	0.2%	0.3%	0.4%	0.318
Opioid and combined products [‡]	6.6%	7.7%	8.1%	9.0%	9.7%	<0.001
Non-analgesics, NSAIDs, tylenol, and non-opioid combined products [‡]	9.7%	10.5%	11.2%	11.8%	13.7%	<0.001
NHAMCS						
Visits in which any pain medication prescribed	44.2%	45.6%	46.8%	44.0%	44.5%	0.719
Visits in which any pain medication from the specific class prescribed						
Fentanyl and analogues [*]	0.5%	0.5%	0.9%	0.7%	1.1%	0.006
Opioid and combined products [‡]	26.2%	27.0%	28.7%	26.0%	24.4%	0.072
Non-analgesics, NSAIDs, tylenol, and non-opioid combined products [‡]	25.6%	26.6%	26.8%	25.7%	27.6%	0.016

Note:

^a compares proportion (%) differences between 2006–2007 and 2014–2015, using a weight-corrected, Bonferroni-adjusted chi-squared statistic.^{*} includes fentanyl and droperidol-fentanyl, alfentanil, sufentanil, and remifentanyl;[‡] codeine, meperidine, methadone, hydromorphone, morphine, oxycodone, pentazocine, propoxyphene, opium, levorphanol, oxycodone, butorphanol, nalbuphine, buprenorphine, hydrocodone, dihydrocodeine, tapentadol, tramadol, and their combined products;[‡] includes gabapentin and pregabalin for non-analgesics, and NSAIDs include acetaminophen, aspirin, diclofenac, ibuprofen, indomethacin, ketoprofen, ketorolac, naproxen, phenylbutazone, piroxicam, and tolmetin.

Table 3.

Stratified analysis of pain medication prescribing trends by key patient and visit characteristics, 2006–2015 NAMCS and NHAMCS.

	Years (%)					2006–2007 vs. 2014–2015, <i>P</i> -value ^a
	2006–2007	2008–2009	2010–2011	2012–2013	2014–2015	
NAMCS						
Visit diagnosis						
Cancer-related [*]	11.9%	14.3%	16.0%	15.2%	16.4%	0.037
Other pain-related [†]	43.4%	43.6%	43.3%	44.2%	44.1%	0.846
No indication	13.9%	15.1%	16.0%	16.5%	19.1%	<0.001
Physician specialty						
Generalist [‡]	16.3%	17.7%	17.8%	18.4%	21.6%	<0.001
Other [§]	13.1%	14.4%	16.8%	17.6%	19.2%	<0.001
Age						
<19	9.4%	10.1%	10.1%	8.4%	10.0%	0.504
19–44	15.7%	15.5%	17.6%	18.7%	19.5%	0.001
45–64	18.8%	20.3%	21.7%	22.5%	25.6%	<0.001
65	14.6%	17.0%	18.2%	19.0%	21.4%	<0.001
Gender						
Female	15.0%	16.9%	17.6%	18.1%	20.6%	<0.001
Male	14.9%	15.5%	17.1%	18.0%	20.2%	<0.001
Race/ethnicity						
Non-Hispanic White	15.1%	16.7%	17.5%	17.9%	20.8%	<0.001
Non-Hispanic Black	15.6%	16.7%	19.8%	19.6%	22.9%	<0.001
Hispanic	14.5%	15.1%	16.6%	18.9%	19.5%	0.003
Other ^{//}	13.4%	14.1%	12.7%	15.0%	15.3%	0.331
Primary source of payment						
Private	13.5%	14.8%	15.2%	15.7%	17.8%	<0.001
Medicare	15.8%	19.1%	19.8%	20.9%	24.2%	<0.001
Medicaid	16.6%	15.9%	19.0%	17.3%	19.5%	0.055
Other	19.1%	19.5%	22.6%	23.9%	22.8%	0.168
NHAMCS						
Visit diagnosis						
Cancer-related [*]	41.0%	46.2%	46.8%	47.8%	49.3%	0.074
Other pain-related [†]	57.9%	62.2%	63.2%	60.0%	59.3%	0.262
No indication	42.5%	43.3%	44.3%	41.3%	41.9%	0.548
Clinician specialty						
MDs	45.4%	46.8%	47.5%	44.7%	44.8%	0.580
Other [¶]	35.5%	36.5%	43.5%	37.7%	42.5%	<0.001
Age						

	Years (%)					2006–2007 vs. 2014–2015, <i>P</i> -value ^a
	2006–2007	2008–2009	2010–2011	2012–2013	2014–2015	
<19	39.6%	41.9%	41.2%	39.0%	38.2%	0.350
19–44	51.4%	52.9%	54.2%	50.0%	51.1%	0.785
45–64	45.5%	47.5%	49.9%	47.4%	48.6%	0.024
65	30.1%	30.1%	31.9%	31.1%	32.1%	0.118
Gender						
Female	45.2%	46.7%	48.0%	44.9%	45.8%	0.570
Male	42.9%	44.2%	45.4%	42.6%	42.9%	0.955
Race/ethnicity						
Non-Hispanic White	44.6%	45.3%	46.5%	43.6%	44.2%	0.646
Non-Hispanic Black	43.1%	46.1%	46.8%	43.7%	44.1%	0.561
Hispanic	44.2%	46.4%	48.5%	45.8%	46.2%	0.157
Other ^{//}	42.4%	43.5%	45.6%	40.3%	44.6%	0.395
Primary source of payment						
Private	48.2%	48.2%	49.5%	46.1%	46.8%	0.253
Medicare	32.6%	35.1%	37.0%	35.3%	36.4%	0.003
Medicaid	43.0%	46.8%	46.7%	44.7%	45.3%	0.067
Other	48.5%	51.0%	52.1%	49.3%	48.3%	0.839

Note:

^a compares proportion (%) differences between 2006–2007 and 2014–2015, using a weight-corrected, Bonferroni-adjusted chi-squared statistic.

* was based on ICD-9-CM diagnostic codes 140–239, 338.3X;

[†] was based on ICD-9-CM codes 338.XX, 350.1X–350.2X, 354.4X, 355.71, 379.91, 388.7X, 719.4X, 724.1X–724.2X, 729.1X, 780.96, 786.5X, 789.XX;

[‡] includes general/family practice, internal medicine, pediatrics, and obstetrics and gynecology;

[§] includes psychiatry, general surgery, orthopedic surgery, cardiovascular diseases, dermatology, urology, neurology, ophthalmology, otolaryngology, and others;

^{//} includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), or 2+ reported racial/ethnic groups; and

[¶] includes physician assistants (PAs) and nurse practitioners (NPs).