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Naloxone dispensing among the commercially insured population in the United States from 2015 to 2018

Christopher Dunphy[*], **Kun Zhang**, **Gery P. Guy Jr**, **Christopher M. Jones**

Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Overdose Prevention, 4770 Buford Hwy NE, Atlanta, GA 30341, USA

Abstract

The Centers for Disease Control and Prevention's (CDC) *Guideline for Prescribing Opioids for Chronic Pain* recommends that providers consider co-prescribing naloxone when factors that increase the risk of overdose are present. Naloxone is an opioid receptor antagonist that counteracts the effects of an opioid overdose. This paper explores trends in naloxone dispensing and out-of-pocket costs among commercially insured individuals in the United States. Administrative claims data from the IBM Watson Health MarketScan database are analyzed to assess trends in naloxone dispensing from 2015 to 2018. Descriptive statistics on concurrent dispensing of naloxone with opioid analgesics are performed among several at-risk populations. The rate of commercially insured individuals being co-dispensed naloxone increased between 2015 and 2018 across all population subgroups. In 2018, 16.2 individuals were co-dispensed naloxone for every 1000 receiving an opioid dosage ≥ 90 MME/day compared to 0.9 in 2015, 27.6 individuals were co-dispensed naloxone for every 1000 concurrently dispensed benzodiazepines and an opioid dosage ≥ 90 MME/day compared to 7.6 in 2015, and 43.7 individuals were co-dispensed naloxone for every 1000 receiving an opioid dosage ≥90 MME/day with a past overdose compared to 17.6 in 2015. Median out-of-pocket cost for naloxone increased from $12 in 2015 to $25 in 2018. Despite increases in naloxone dispensing from 2015 to 2018, the provision of naloxone to the commercially insured population remains low. Opportunities remain to increase the supply of naloxone to at-risk populations. Considering ways to reduce out-of-pocket costs associated with naloxone may be a potential strategy to increase access to this life-saving drug.

[*]Corresponding author. Ppz1@cdc.gov (C. Dunphy).

Credit author statement

Christopher Dunphy: Lead author. Responsible for project conceptualization and methodology, data analysis, interpreting results, and manuscript drafting and editing.

Kun Zhang: Responsible for conceptualization and methodology, interpreting results, manuscript editing.

Gery P. Guy Jr.: Responsible for conceptualization and methodology, interpreting results, manuscript editing, and supervision.

Christopher M. Jones: Responsible for conceptualization and methodology, interpreting results, manuscript editing, and supervision.

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Declaration of Competing Interest

The authors have no conflicts of interest to report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2021.106820.

Keywords

Naloxone; Opioids; Co-prescribing; MarketScan; Overdose; Benzodiazepine

1. Introduction

Opioid-involved overdose deaths remain at high levels in the United States. In 2018, 46,802 overdose deaths in the United States involved opioids, an age-adjusted rate of 14.6 deaths per 100,000 population (Wilson et al., 2020). Naloxone is an opioid receptor antagonist that counteracts the potentially life-threatening respiratory depressant effects of an opioid overdose, providing life-saving capability (Boyer, 2012). For several decades, naloxone has been administered by emergency medical service providers, first responders, and emergency department clinicians to individuals experiencing an opioid overdose. Recent policy efforts at the national, state, and local levels aim to expand the provision of naloxone to individuals at risk of opioid overdose through clinician prescribing and pharmacy dispensing (U.S. Department of Health and Human Services, 2018a, b).

As of 2017, every state has passed some form of policy, including naloxone access laws (NALs), to encourage naloxone prescribing and dispensing (PDAPS, 2019). Variations in these laws include third party prescribing (to patients seeking naloxone and individuals who may be in position to assist in an overdose reversal), Good Samaritan laws and immunity provisions for prescribers and dispensers of naloxone, standing orders for naloxone distribution from pharmacies and other community-based organizations, and community-based and peer distribution (Davis and Carr, 2015). The implementation of NALs are associated with increases in naloxone dispensing (Abouk et al., 2019; Gertner et al., 2018; Xu et al., 2018). In addition to a supportive legal framework in states, guidance about when to consider prescribing or dispensing naloxone has been developed in order to facilitate increased access to naloxone (Dowell et al., 2016; U.S. HHS, 2018a, b). The Centers for Disease Control and Prevention's (CDC's) 2016 *Guideline for Prescribing Opioids for Chronic Pain* recommends that providers consider co-prescribing naloxone when factors that increase the risk for overdose are present (Dowell et al., 2016). Risk factors include a history of overdose or substance use disorder, prescribed opioid dosages ≥50 morphine milligram equivalents (MME) per day (high-dose), and concurrent use of opioids and benzodiazepines. Since 2017, nine states have passed legislation mandating that clinicians co-prescribe naloxone with opioid analgesics to patients at high-risk for an opioid overdose (ASTHO, 2019), with evidence suggesting these laws may be associated with increased naloxone dispensing within those states (Sohn et al., 2019).

Despite these supply side efforts, naloxone dispensing remains low across the country. Nationally, in 2018, one naloxone prescription was dispensed for every 69 high-dose opioid prescriptions (Guy Jr. et al., 2019). Around 1.5% of high-risk individuals among the commercially insured population were prescribed naloxone in 2016 (Follman et al., 2019). Estimates from 2017 suggest that only 1.1% of Medicare patients prescribed high-dose opioids were co-prescribed naloxone (Jones et al., 2019). From the perspective of the prescriber, low self-efficacy, lack of appropriate training, and fear of liability are all

documented barriers for clinicians prescribing naloxone (Wilson et al., 2016). Demand side barriers such as out-of-pocket costs may also be contributing to low rates of filling and dispensing naloxone prescriptions (Gupta et al., 2016). In a non-emergency setting, such as outpatient naloxone co-prescribing to patients receiving opioid analgesics, the benefits of filling the prescriptions only accrue when the drug is administered (i.e. after an opioid overdose). This may not occur, and therefore the demand for naloxone may be more likely to be affected by costs to the consumer. In 2018, approximately one-half of naloxone prescriptions received by patients with commercial insurance or Medicaid and over two-thirds of naloxone prescriptions received by Medicare recipients required out-of-pocket costs (Guy Jr. et al., 2019), suggesting that cost sharing may be an important consideration when implementing policies to expand naloxone access.

Given the life-saving potential of naloxone, increasing access to individuals at high-risk of opioid overdose is an important public health issue. Previous research has demonstrated substantial variation in naloxone dispensing by county-level sociodemographic characteristics (Guy Jr. et al., 2019), Understanding the population gaps and barriers to naloxone dispensing, including the role that co-prescribing and cost sharing may play in filling prescriptions, is critical when developing and implementing public health interventions to expand naloxone access. In this study, we examine trends in naloxone dispensing, co-dispensing of naloxone with opioid analgesics, and out-of-pocket costs for naloxone among the commercially insured population from 2015 to 2018. This study builds upon previous work by examining a longer time horizon, analyzing patient-level variation in naloxone dispensing, and studying the trends in these variables over time. Additionally, this study is one of the first to explore trends in naloxone out-of-pocket costs over time, providing a baseline for future studies that analyze costs associated with naloxone.

2. Methods

We used the 2015–2018 IBM® MarketScan® commercial claims and encounters database for this retrospective analysis (IBM, 2019) The database is one of the largest administrative databases of the commercially insured population in the United States. It includes de-identified healthcare claims from health plans and self-insured employers across the United States for the full continuum of care (e.g., inpatient, outpatients, outpatient pharmacy, enrollment). The database reflects real-world treatment patterns, corresponding drug prescriptions, and costs by tracking millions of commercially insured patients as they navigate through the healthcare system and service delivery. This study utilizes only the commercial versions of the dataset (i.e. does not use Medicare on Medicaid supplements). Dispensed pharmaceutical products are observed in the dataset as long as a commercial insurance claim was filed for the product.

Descriptive statistics of naloxone dispensing were generated by age, sex, and U.S. census region for each year from 2015 to 2018 among enrollees with both medical and pharmacy benefits who were continuously enrolled for the given year. Trends in naloxone co-dispensing with opioids were assessed among the following high-risk populations: dispensed high-dose opioids (≥50 morphine milligram equivalents [MME] per day and ≥ 90 MME per day), concurrent use of opioids and benzodiazepines, recent documented opioid overdose,

and recent diagnosis of opioid use disorder. All co-dispensing rates were reported per 1000 individuals dispensed an opioid in the given high-risk category. In addition, we examined naloxone dispensing rates for all individuals with substance use disorder (SUD), opioid use disorder (OUD), or a recent opioid overdose. Rates were reported per 1000 individuals in the given category. *t*-Tests were used to assess statistically significant differences in rates between 2015 and 2018 and by enrollee sex within a given year. Chi-square tests were used to assess statistically significant associations between naloxone co-dispensing and both the region and age group of the enrollee. Following recent studies using claims data, statistical significance was defined as $p < 0.001$ to account for the large number of observations present in claims data (Follman et al., 2019).

Age, sex, U.S. census region, and enrollment status were obtained from enrollment files. Dispensed naloxone, opioids, and benzodiazepines were identified from the outpatient pharmacy file by using National Drug Code (NDC). Dosage of dispensed opioids were converted into MME (National Center for Injury Prevention and Control, 2018). Dispensed buprenorphine used in the treatment of OUD were excluded from the analysis; Butrans and Belbuca, buprenorphine products used in the treatment of pain, were also excluded from the analysis due to unavailable MME conversion rates. Dispensed methadone prescriptions were included in the analysis because MarketScan outpatient pharmaceutical claims only include methadone prescriptions used in the treatment of pain as opposed to treatment of OUD. Following previous literature, naloxone co-dispensing was defined as a naloxone claim within seven days of an opioid claim (Jones et al., 2019). While this may appear arbitrary, expanding this definition to naloxone receipt within 365 days of an opioid has produced similar estimates (Guy et al., 2021). Naloxone co-dispensing within a high-risk subgroup was defined as a naloxone claim within seven days of an opioid claim that associated with the given high-risk use category (e.g. dispensed naloxone within seven days of receiving an opioid and benzodiazepine). Thus, claim level observations were used to create individual level samples for each year. A dispensed opioid was flagged as concurrent with a dispensed benzodiazepine if there was at least a one day overlap between days covered by the two prescriptions. Similar to naloxone co-dispensing, the benzodiazepine claim can be up to 7 days after the opioid claim.

Individuals with a recent SUD diagnosis were identified with the *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* codes F10 – F19 from the outpatient and inpatient claims files. This includes use disorders for alcohol, opioids, cannabis, sedatives, cocaine, other stimulants, hallucinogens, nicotine, inhalants, and other psychoactive substances. Individuals with OUD were identified with the ICD-10-CM codes F11.1 and F11.2. Individuals with a recent opioid overdose were identified with the ICD-10-CM codes T40.0 × 1–4, T40.1, T40.2 × 1–4, T40.3 × 1–4, T40.4 × 1–4, T40.601–4 from the outpatient and inpatient claims files. Naloxone dispensing to individuals with a recent SUD, OUD, or opioid overdose diagnosis were defined as a naloxone claim within 90 days of a corresponding SUD, OUD, or overdose diagnosis. For this analysis, we expanded our continuous enrollment criteria for a given year to include the last 90 days of the prior year (i.e., 2018 continuous enrollment included all of 2018 and the last 90 days of 2017). Ninety days was chosen so as not to exclude a large portion of observations that were not continuously enrolled across multiple years of the data. SUD, OUD, and overdose subgroups

were analyzed only for the years 2016, 2017, and 2018 to avoid inconsistencies in reported numbers arising from the change from ICD-9-CM codes to ICD-10-CM codes in October of 2015 (Heslin et al., 2017).

Out-of-pocket costs associated with dispensed naloxone were examined by product type and census region over the study period. Out-of-pocket costs were defined as the sum of the co-pay, deductible, and coinsurance paid by the beneficiary to fill their prescription. Aspects of the distribution and regional breakdown of out-of-pocket costs were analyzed in addition to summarizing the median out-of-pocket costs by year.

All estimates were weighted using population weights provided within the MarketScan database and analyses were performed using the Statistical Analysis System (SAS) version 9.4. This research was deemed exempt from IRB approval by CDC as the study involved secondary data analysis.

3. Results

Table 1 reports the number of patients dispensed naloxone, stratified by whether or not they were co-dispensed naloxone with an opioid. In 2018, an estimated 78,339 commercially insured individuals were dispensed naloxone compared to an estimated 5866 in 2015 (Table 1), and 66% of them received their naloxone with a corresponding opioid analgesic. There were significant differences in the underlying demographics of individuals co-dispensed naloxone compared to those who received naloxone without an opioid prescription. In 2018, individuals in the co-dispensed group were more likely to be female (56%) ($p < 0.001$), age 45–54 years (33%) ($p < 0.001$), age 55–64 years (41%) ($p < 0.001$), residing in the West (25%) ($p < 0.001$), and from the South (49%) ($p < 0.001$) compared to individuals in the non-co-dispensed group. In addition, individuals in the co-dispensed group were less likely to be male (44%) ($p < 0.001$), age 18–34 years (8%) ($p < 0.001$), and in the Northeast (9%) ($p < 0.001$).

To provide clarity in viewing the results of Table 2–4, primary sample sizes were omitted and reported in Supplemental Table 1. The rate of commercially insured individuals being co-dispensed naloxone with opioid analgesics increased ($p < 0.001$) from 0.2 individuals for every 1000 dispensed opioids in 2015 to 3.8 per 1000 in 2018 (Table 2). This increase occurred across age, sex, and U.S. census region. In 2018, 5.4 individuals were co-dispensed naloxone for every 1000 individuals receiving an opioid dosage between 50 and 89 MME/day and 16.2 per 1000 receiving an opioid dosage ≥90 MME/day. Among individuals receiving an opioid dosage ≥90 MME/day in 2018, a significant association (p-value <0.001) was found between naloxone co-dispensing and both age and region.

Naloxone co-dispensing rates for individuals concurrently dispensed opioids and benzodiazepines also increased over the study period. In 2018, among this subgroup, 12.7 were co-dispensed naloxone per 1000 receiving benzodiazepines and an opioid dosage between 50 and 89 MME/day and 27.6 per 1000 receiving benzodiazepines and an opioid dosage ≥90 MME/day, up from 0.7 ($p < 0.001$) and 1.7 ($p < 0.001$) per 1000 in 2015, respectively (Table 3). Naloxone co-dispensing among this high-risk group was higher for

males (31.9) compared ($p < 0.001$) to females (24.9), and a significant association was found between co-dispensing and both age and region, with rates of 33.0 in the South, 26.3 in the West, 23.8 in the Northeast, and 20.9 in the Midwest.

In 2018, among individuals with an OUD diagnosis within the past 90 days receiving an opioid, 27.4 per 1000 were co-dispensed naloxone, up from 11.0 per 1000 in 2016, $p < 0.001$ (Supplemental Table 2). Among individuals with a history of OUD receiving an opioid dosage between 50 and 89 MME/day 27.4 per 1000 were co-dispensed naloxone and 42.9 per 1000 receiving an opioid dosage ≥90 MME/day received were co-dispensed naloxone. Naloxone co-dispensing rates among individuals with a recent OUD diagnosis and dispensed an opioid dosage ≥90 MME/day varied by census region, with rates of 42.3 in the South, 51.6 in the West, 33.4 in the Northeast, and 38.9 in the Midwest. In 2018, 33.8 individuals were co-dispensed naloxone per 1000 receiving an opioid and having an overdose in the past 90 days compared to 8.9 per 1000 in 2016, $p = 0.001$ (Supplemental Table 3). Additionally, among this subgroup receiving an opioid and having an overdose in the past 90 days, rates of naloxone co-dispensing were 34.7 per 1000 for those receiving an opioid dosage between 50 and 89 MME/day and 43.7 per 1000 for those receiving an opioid dosage ≥90 MME/day, insignificantly up from 13.8 ($p = 0.10$) and 17.6 ($p = 0.07$) per 1000 in 2016, respectively.

More broadly, naloxone dispensing increased among individuals with a SUD, OUD, or overdose diagnosis in the last 90 days (Table 4). In 2018, 4.1 individuals per 1000 with a SUD and 24.7 per 1000 with OUD were dispensed naloxone, up from 2.1 ($p < 0.001$) and 14.5 ($p < 0.001$) per 1000 in 2016, respectively. Additionally, naloxone dispensing to individuals with a recent overdose increased over the study period across all demographic groups. Despite these trends, naloxone dispensing remains low among individuals with a recent diagnosis of SUD, OUD, or opioid overdose.

Median out-of-pocket costs for naloxone increased from $12.00 in 2015 to $24.88 in 2018 (Table 5). Twenty-four percent of dispensed naloxone required no out-of-pocket costs in 2015, and 32% required no out-of-pocket costs in 2018; however, the percentage of naloxone requiring out-of-pocket costs greater than $100 decreased from 13% in 2015 to 5% by 2018. Out-of-pocket costs varied substantially by naloxone formulation. The median out-of-pocket cost of EVZIO, an auto injector form of naloxone (discontinued in 2020), was higher than any other formulation and increased over the study period (from $40 in 2015 to $70 in 2018). In addition, the percent of EVZIO prescriptions with out-of-pocket costs greater than $100 increased from 19% in 2015 to 35% in 2018. The median out-of-pocket cost of Narcan Nasal Spray decreased from about $30 in 2016 (first year available) to $25 in 2018, with only 4% of prescriptions resulting in out-of-pocket costs greater than $100. The introduction of Narcan Nasal Spray in the market led to a substantial shift in EVZIO's market share over the study period. In 2016, 67.0% of the dispensed naloxone were EVZIO compared to 19.4% Narcan. In 2018, Narcan represented 89.5% of all dispensed naloxone in our data, while EVZIO's share fell to 5.0%. This shift in market structure is likely due to EVZIO's high price (over $4000 in 2018) compared to Narcan ($130 in 2018) and is one explanation for the sharp decrease in the total percent of individuals with out-of-pocket costs greater than $100 from 2016 to 2018 (CBSNews, 2018; Time, 2018). The median

out-of-pocket cost of Naloxone Hydrochloride (HCL) injection, older generic formulations of naloxone, remained at $10 over the study period, with very few dispensed prescriptions resulting in out-of-pocket costs greater than $100. The market share of Naloxone HCL injection decreased from 28% in 2015 to 5.5% in 2018. Additionally, there is a significant association between product market share and US census region (Supplemental Table 4).

4. Discussion

The amount of naloxone dispensed to individuals with commercial insurance increased 13-fold between 2015 and 2018, with dispensing rates increasing across all demographic groups examined in this analysis. However, despite these positive trends, the overall provision of naloxone to the commercially insured population at increased risk for an opioid overdose remains low. This finding holds even when examining patients who are at the highest risk for overdose – those with OUD or history of overdose, as naloxone was only prescribed to 2.5% and 4.5% of patients with a history of OUD or past overdose, respectively. Naloxone co-dispensing rates were significantly associated with age and region of residence from 2015 to 2018. Additionally, the way that naloxone was received differed by demographics in 2018, as females, individuals aged 45–64, and individuals residing in the South and West census regions were more likely to receive naloxone that was co-dispensed with an opioid; while males, individuals aged 18–34, and individuals residing in the Northeast census region were more likely to receive naloxone outside of our defined 7-day co-dispensing window. The expanded use of standard procedures, such as electronic health records, may be one approach to providing more equitable access to naloxone via co-prescribing.

Opportunities remain to increase the provision of naloxone via both supply-side and demand-side interventions. Additional efforts to implement the recommendations set forth by the 2016 CDC *Guideline for Prescribing Opioids for Chronic Pain* (Dowell et al., 2016) and the HHS Naloxone Guidance (U.S. Department of Health and Human Services, 2018a) have the potential to improve access to naloxone among high-risk patients. State policies mandating that clinicians co-prescribe naloxone with opioids may play a role in expanding access to naloxone and have been shown to lead to increases in naloxone prescribing (Sohn et al., 2019). State naloxone co-prescribing laws generally apply when certain risk factors are present, such as concurrent opioid and benzodiazepine use, high daily opioid MME dosages, or a history of SUD. States that currently have such a law in place include Arizona, California, Florida, New Mexico, Ohio, Rhode Island, Vermont, Virginia, and Washington (ASTHO, 2019). Given the success in expanding naloxone dispensing in some of the early adopting states (Jones et al., 2019), continued effort to expand implementation of these policies may be a viable strategy to increase the supply of naloxone.

Strategies such as the implementation of virtual mentoring among clinicians, electronic health record (EHR) prompts, and academic detailing can further educate clinicians about naloxone prescribing, provide organizational clarity about which patients should be counseled on naloxone and may mitigate time-related barriers frequently noted by clinicians (Wilson et al., 2016). Academic detailing has been associated with increases in naloxone prescribing in various settings, including the U.S. Veterans' Health Administration (Bounthavong et al., 2020), among primary care providers (Behar et al., 2017), and

among community pharmacies (Evoy et al., 2020). In addition, virtual mentoring programs, such as innovative tele-education interventions, and EHR prompts have been shown to increase naloxone prescribing and administration (Furlan et al., 2018; Marino et al., 2019). Availability of over-the-counter naloxone, which would allow naloxone to be freely bought and sold at non-pharmacy locations, is another strategy that may help expand access to individuals at high-risk for an overdose (Davis and Carr, 2020). One caveat for this strategy is there is uncertainty as to how patient demand may respond to such measures, as some patient barriers, such as the perceived stigma of purchasing naloxone, would remain. Nevertheless, these public health strategies are an important part of the overall comprehensive effort to expand naloxone access.

Opportunities also exist to address potential demand-side barriers present in the market for naloxone. In 2018, 68% of naloxone prescriptions resulted in out-of-pocket costs and 1-in-20 prescriptions resulted in out-of-pocket costs greater than $100. Even if substantial increases in naloxone prescribing occur, out-of-pocket costs of this frequency and magnitude may deter patients from filling these prescriptions. A recent survey of pharmacists in Tennessee found that naloxone cost was the most commonly cited barrier to naloxone dispensing (Spivey et al., 2020). Other researchers have also identified naloxone cost as an important barrier to access (Darracq et al., 2019; Graves et al., 2019). State and federal laws that require insurers to cover naloxone without copayments, coinsurance, and/or deductibles could help reduce demand side barriers to naloxone among high-risk populations. Early adopters of such policies include The United Sates Department of Veterans Affairs, which eliminated copayments for naloxone and education on naloxone in 2016 in response to the Comprehensive Addiction and Recovery Act of 2016. Additionally, the Centers for Medicare and Medicaid Services (CMS) is strongly encouraging Part D sponsors to provide lower cost sharing for opioid-reversal agents, such as naloxone, by taking advantage of new flexibilities that provide cost sharing reductions for patients with chronic pain or undergoing substance use disorder treatment (CMS, 2019). Future research opportunities could include exploring the extent to which addressing out-of-pocket costs of prescription naloxone can increase its provision to high-risk populations.

The findings of this study are subject to limitations. First, our definition of naloxone co-dispensing utilizes a fixed window of time for individuals to receive naloxone after being dispensed an opioid analgesic. While we do increase this window to examine naloxone receipt among patients diagnosed with OUD, SUD, or past overdose (e.g. 90 days), some patients identified as high-risk through outreach efforts outside the 7-day window may be missed in our analysis. Furthermore, there are several barriers in addition to cost, such as stigma associated with naloxone, that may lead patients to not fill prescribed naloxone, which are unobservable in these data. Second our results may not generalize to populations without commercial insurance such as individuals with Medicaid. Third, the use of claims data only allows us to observe dispensed prescriptions and diagnoses (e.g. opioid overdose) if a claim was filed; overdose events that occurred outside of medical settings are not captured in our data. Thus, individuals prescribed naloxone are not observed if they paid with cash or received naloxone outside of their commercial insurance through other distribution channels [such as give away programs and harm reduction programs, which have been expanded in recent years (Clark et al., 2014)]. Fourth, we are unable to observe

both individuals that were prescribed naloxone but did not fill their prescription order and those that had an unexpired naloxone script from a previous (unobserved) clinical encounter.

Addressing the opioid overdose epidemic requires a multifaceted approach, including efforts to improve the social determinants of health (such as reducing poverty, improving employment opportunities, reducing racial/ethnic inequities, etc.), improve opioid prescribing and the safety and effectiveness of pain treatment, establish linkages to care, expand access to medication-assisted treatment for opioid use disorder, and enhance public health and safety partnerships. The community distribution of naloxone is an important component of this public health response. Opportunities remain to expand access to naloxone through clinician co-prescribing and pharmacy dispensing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Abouk R, Pacula RL, Powell D, 2019. Association between state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose. JAMA Intern. Med 179 (6), 805–811. [PubMed: 31058922]

Association of State and Territorial Health Officials, 2019. Increasing Number of States Require Naloxone to be Co-prescribed With Opioids. Retrieved from: https://www.astho.org/StatePublicHealth/Increasing-Number-of-States-Require-Naloxone-Co-Prescribed-with-Opioids/08-15-19/ (accessed on 1/5/2020).

Behar E, Rowe C, Santos GM, Santos N, Coffin PO, 2017. Academic detailing pilot for naloxone prescribing among primary care providers in San Francisco. Fam. Med 49, 122–126. [PubMed: 28218937]

Bounthavong M, Harvey MA, Kay CL, Lau MK, Wells DL, Himstreet JE, Popish SJ, Oliva EM, Christopher MLD, 2020. Comparison of naloxone prescribing patterns due to educational outreach conducted by full-time and part-time academic detailers at the U.S. Veterans Health Administration. J. AM. Pharm. Assoc 60 (4), 639–646.

Boyer EW, 2012. Management of opioid analgesic overdose. N. Engl. J. Med 367 (2), 146–155. [PubMed: 22784117]

CBSNews, 2018. Evzio: The Overdose-reversal Drug With a $4000+ Price Tag. Retrieved from: https://www.cbsnews.com/news/evzio-the-opioid-overdose-reversal-drug-naloxone-with-a-4000price-tag-60-minutes/ (accessed on 7/16/2021).

Centers for Medicare and Medicaid Services, 2019. 2020 Medicare Advantage and Part D Rate Announcement and Final Call Letter Fact Sheet. Retrieved from: https://www.cms.gov/newsroom/fact-sheets/2020-medicare-advantage-and-part-d-rateannouncement-and-final-call-letter-fact-sheet (accessed on 2/10/2020).

Clark AK, Wilder CM, Winstanley EL, 2014. A systematic review of community opioid overdose prevention and naloxone distribution programs. J. Addict. Med 8 (3), 153–163. [PubMed: 24874759]

Darracq MA, Lee J, Wilson T, Lasoff D, Armenian P, 2019. Pharmacist dispensed naloxone: knowledge, availability, participation, and cost in selected California counties. Int. J. Drug Policy 71, 113–117. [PubMed: 31301549]

Davis CS, Carr D, 2015. Legal changes to increase access to naloxone for opioid overdose reversal in the United States. Drug Alcohol Depend. 157, 112–120. [PubMed: 26507172]

Davis CS, Carr D, 2020. Over the counter naloxone needed to save lives in the United States. Prev. Med 130, 105932. [PubMed: 31770540]

Dowell D, Haegerich TM, Chou R, 2016. CDC guideline for prescribing opioids for chronic pain United States, 2016. JAMA 315 (15), 1624–1625. [PubMed: 26977696]

Evoy KE, Groff L, Hill LG, Godinez W, Gandhi R, Reveles KR, 2020. Impact of student pharmacist-led naloxone academic detailing at community pharmacies in Texas. J. Am. Pharm. Assoc 60 (1), 81–86.

Follman S, Arora VM, Lyttle C, Moore PQ, Pho M, 2019. Naloxone prescriptions among commercially insured individuals at high risk of opioid overdose. JAMA Netw. Open 2 (5), e193209. [PubMed: 31050777]

Furlan AD, Zhao J, Voth J, Hassan S, Dubin R, Stinson JN, Jaglal S, Fabico R, Smith AJ, Taenzer P, Flannery JF, 2018. Evaluation of an innovative tele-education intervention in chronic pain management for primary care clinicians practicing in underserved areas. J. Telemed. Telecare 25 (8), 484–492. [PubMed: 29991316]

Gertner AK, Domino ME, Davis CS, 2018. Do naloxone access laws increase outpatient naloxone prescriptions? Evid. Med. Drug Alcohol Depend 190, 37–41.

Graves RL, Andreyeva E, Perrone J, Shofer F, Merchant RM, Meisel ZF, 2019. Naloxone availability and pharmacy staff knowledge of standing order for naloxone in Pennsylvania pharmacies. J. Addict. Med 13 (4), 272–278. [PubMed: 30585876]

Gupta R, Shah ND, Ross JS, 2016. The rising price of naloxone – risks to efforts to stem overdose deaths. N. Engl. J. Med 375 (23), 2213–2215. [PubMed: 27959694]

Guy GP Jr., Haegerich TM, Evans ME, Losby JL, Young R, Jones CM, 2019. Vital signs: pharmacy-based naloxone dispensing – United States, 2012–2018. MMWR Morb. Mortal. Wkly Rep 68 (31), 679–686. [PubMed: 31393863]

Guy GP, Strahan AE, Haegerich T, Losby JL, Ragan K, Evans ME, Jones CM, 2021. Concurrent naloxone dispensing among individuals with high-risk opioid prescriptions, USA, 2015–2019. J. Gen. Intern. Med 1–3.

Heslin KC, Owens PL, Karaca Z, Barrett ML, Moore BJ, Elixhauser A, 2017. Trends in opioid related inpatient stays shifted after the US transitioned to ICD-10-CM diagnosis coding in 2015. Med. Care 55 (11), 918–923. [PubMed: 28930890]

IBM Watson Health, 2019. IBM MarketScan Research Databases for Health Services Researchers, 2019. Available at. https://www.ibm.com/downloads/cas/6KNYVVQ2 (Accessed January 2020).

Jones CM, Compton W, Vythilingam M, Giroir B, 2019. Naloxone co-prescribing to patients receiving prescription opioids in the Medicare Part D Program, United States, 2016–2017. JAMA 322 (5), 462–464. [PubMed: 31386124]

Marino R, Landau A, Lynch M, Callaway C, Suffoletto B, 2019. Do electronic health record prompts increase take-home naloxone administration for emergency department patients after an opioid overdose? Addiction 114 (9), 1575–1581. [PubMed: 31013394]

National Center for Injury Prevention and Control, 2018. CDC Compilation of Benzodiazepines, Muscle Relaxants, Stimulants, Zolpidem, and Opioid Analgesics With Oral Morphine Milligram Equivalent Conversion Factors, 2018 Version. Centers for Disease Control and Prevention, Atlanta, GA. Available at. https://www.cdc.gov/drugoverdose/resources/data.html (Accessed on 1/5/2020).

Prescription Drug Abuse Policy System, 2019. Retrieved from: http://pdaps.org/ (Accessed on 12/1/2019).

Sohn M, Talbert JC, Huang Z, Lofwall MR, Freeman PR, 2019. Association of naloxone coprescription laws with naloxone prescription dispensing in the United States. JAMA Netw. Open 2 (6), e196215. [PubMed: 31225895]

Spivey CA, Wilder A, Chisholm-Burns MA, Stallworth S, Wheeler J, 2020. Evaluation in naloxone access, pricing, and barriers to dispensing in Tennessee retail community pharmacies. J. Am. Pharm. Assoc 60 (5), 694–701.

Time, 2018. The Surgeon General Says More People Should Carry Naloxone, the Opioid Antidote. Here's Where to Get It and How Much It Costs. Retrieved from: https://time.com/5229870/naloxonesurgeon-general-cost-where-buy/ (Accessed on 7/24/2021).

U.S. Department of Health and Human Services, 2018a. Naloxone: The Opioid Reversal Drug That Saves Lives. Retrieved from: https://www.hhs.gov/opioids/sites/default/files/2018-12/naloxonecoprescribing-guidance.pdf (Accessed on 12/10/2019).

U.S. Department of Health and Human Services, 2018b. Strategy to Combat Opioid Abuse, Misuse, and Overdose. Retrieved from: https://www.hhs.gov/opioids/sites/default/files/2018-09/opioidfivepoint-strategy-20180917-508compliant.pdf (Accessed on 12/10/2019).

Wilson JD, Spicyn N, Matson P, Alvanzo A, Feldman L, 2016. Internal medicine resident knowledge, attitudes, and barriers to naloxone prescription in hospital and clinic settings. Subst. Abus 37 (3), 480–487. [PubMed: 26820604]

Wilson N, Kariisa M, Seth P, Smith H IV, Davis NL, 2020. Drug and opioid-involved overdose deaths - United States, 2017–2018. MMWR Morb. Mortal. Wkly Rep 69 (11), 290–297. [PubMed: 32191688]

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 Alcohol Depend. 189, 37–41. [PubMed: 29860058]

Table 1

Differences in demographics by type of naloxone receipt, 2015–2018.

	2015		2016		2017		2018	
Naloxone co-dispensed with opioid?	Yes	No	Yes	No	Yes	No	Yes	No
Number of enrollees dispensed naloxone	3317	2549	15,781	11,206	24,196	14,093	51,538	26,801
% male	41	57*	46	51	45	52*	44	49*
Female	59	43*	54	49	55	48*	56	51*
Age: 0–17	1	1	0	1*	1	1	1	1
Age: 18–34	10	35*	9	36*	8	35*	8	26*
Age: 35–44	18	13	21	16*	19	15*	17	17
Age: 45–54	34	22*	35	23*	34	23*	33	26*
Age: 55–64	36	29	35	23*	39	26*	41	30*
Northeast	14	30*	13	31*	9	26*	9	24*
Midwest	16	13	11	14	14	18*	16	18
South	45	38	47	37*	54	37*	49	37*
West	25	19	28	17*	23	20*	25	22*

Notes: All estimates (% and totals) are weighted to be nationally representative for the commercially insured population with continuous enrollment. Individuals were considered to have been co-dispensed naloxone if an opioid claim and naloxone claim were within 7 days of each other. *t*-Tests were conducted to test for statistical significance.

*indicates $p < 0.001$.

Table 2

Co-dispensing of naloxone with opioid analgesics among the commercially insured population: rates by demographic groups 2015–2018.

	Naloxone w/ any opioid				**Naloxone w/ <50 MME opioid**				**Naloxone w/ 50–89 MME/day opioid**				**Naloxone w/ ≥90 MME/day opioid**			
Demographic-group	2015	2016	2017	2018	2015	2016	2017	2018	2015	2016	2017	2018	2015	2016	2017	2018
All	0.2	0.9	1.5	3.8*	0.1	0.5	1.0	2.6*	0.2	1.1	1.9	5.4*	0.9	4.0	6.6	16.2*
Male	0.2	1.0	1.6	3.9*	0.1	0.5	0.9	2.5*	0.1	1.1	1.9	5.6*	0.9	4.2	6.7	17.1*
Female	0.2	0.9	1.5	3.8*	0.1	0.5	1.0	2.7*	0.2	1.2	2.0	5.3*	0.9	3.8	6.5	15.4*
p-value (*t*-Test)	0.27	0.06	0.40	0.26	0.29	0.65	0.19	0.003	0.01	0.34	0.56	0.11	0.94	0.05	0.61	0.004
Age: 0–17	0.02	0.01	0.1	0.4*	0.01	0.02	0.1	0.3*	0.1	0.0	0.2	1.1*	0.2	0.0	0.6	1.2*
Age: 18–34	0.1	0.4	0.5	1.4*	0.04	0.2	0.4	0.9*	0.1	0.4	0.7	2.4*	0.8	1.9	2.9	7.5*
Age: 35–44	0.2	1.0	1.5	3.4*	0.1	0.6	0.9	2.3*	0.2	1.2	1.7	4.4*	0.9	4.4	6.5	15.7*
Age: 45–54	0.2	1.3	2.0	5.1*	0.1	0.7	1.3	3.4*	0.2	1.6	2.5	7.4*	1.1	4.9	7.7	18.9*
Age: 55–64	0.2	1.2	2.2	5.6*	0.1	0.7	1.4	3.9*	0.2	1.4	2.8	7.0*	1.0	4.4	8.1	19.7*
p-Value (chi-square)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Northeast	0.2	0.9	1.0	2.6*	0.1	0.4	0.6	1.7*	0.2	1.2	1.1	3.4*	1.1	5.3	6.2	16.9*
Midwest	0.1	0.4	0.9	2.6*	0.1	0.2	0.6	1.8*	0.1	0.5	1.2	3.8*	0.7	2.0	4.1	11.7*
South	0.2	1.1	2.0	4.5*	0.1	0.7	1.3	3.2*	0.2	1.4	2.6	6.7*	0.9	4.8	7.8	18.6*
West	0.2	1.2	1.7	4.5*	0.1	0.7	1.0	2.9*	0.2	1.3	2.0	5.9*	1.1	3.9	6.9	16.1*
p-value (chi-square)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Source: IBM® MarketScan® commercial claims and encounters database notes: Estimates are the number of individuals co-dispensed naloxone per 1000 individuals that have received an opioid prescription within the given category. All estimates are weighted to be nationally representative for the commercially insured population. Individuals were considered to have been co-dispensed naloxone if an opioid claim and naloxone claim were within 7 days of each other. Estimates are obtained from individuals who were continuously enrolled for the year. *t*-Tests were conducted to examine statistical differences in co-dispensing rates between 2015 and 2018 for each demographic group/morphine milligram equivalent category combination. Chi-square tests were conducted to examine statistical differences among categorical groups.

*represents that co-dispensing rates were statistically different in 2018 compared to 2015 ($p < 0.001$).

Table 3

Co-dispensing of naloxone with opioid analgesics while concurrently dispensed benzodiazepines among commercially insured individuals: rates 2015–2018.

	Naloxone w/ any opioid				**Naloxone w/ <50 MME/day opioid**				**Naloxone w/ 50–89 MME/day opioid**				**Naloxone w/ ≥90 MME/day opioid**			
Demographic-group	2015	2016	2017	2018	2015	2016	2017	2018	2015	2016	2017	2018	2015	2016	2017	2018
All	0.5	2.5	4.2	10.3*	0.3	1.3	2.7	7.1*	0.7	2.7	5.1	12.7*	1.7	7.9	11.3	27.6*
Male	0.5	2.7	4.3	11.3*	0.2	1.3	2.8	7.1*	0.6	2.7	5.1	14.4*	1.7	7.9	11.2	31.9*
Female	0.6	2.4	4.1	9.8*	0.3	1.3	2.6	7.1*	0.7	2.7	5.2	11.7*	1.7	7.9	11.5	24.9*
p-Value (*t*-Test)	0.44	0.15	0.28	<0.001	0.11	0.88	0.50	0.99	0.59	0.93	0.93	0.01	0.93	0.98	0.78	<0.001
Age: 0–17	0.0	0.0	1.4	6.3*	0.0	0.0	1.5	5.6*	0.0	0.0	2.0	11.0*	0.0	0.0	0.0	6.0*
Age: 18–34	0.4	1.4	2.6	6.6*	0.2	0.9	1.7	4.2*	0.5	0.8	3.5	7.8*	1.8	6.1	10.3	25.4*
Age: 35–44	0.5	2.5	3.3	8.5*	0.3	1.1	2.3	5.6*	0.6	2.8	4.5	10.5*	1.8	9.0	8.4	25.4*
Age: 45–54	0.6	3.0	4.7	11.4*	0.3	1.7	2.9	7.9*	0.6	3.2	5.5	14.1*	2.0	9.0	12.1	27.5*
Age: 55–64	0.6	2.6	5.0	11.9*	0.3	1.4	3.1	8.4*	0.8	3.1	5.9	14.3*	1.4	7.2	12.7	29.7*
p-value (chi-square)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Northeast	0.6	2.5	2.7	7.5*	0.3	1.0	1.9	4.7*	0.6	2.3	3.1	8.0*	1.9	9.0	8.4	23.8*
Midwest	0.4	1.5	2.2	8.1*	0.2	0.8	1.3	5.8*	0.2	1.8	3.5	10.6*	1.8	4.9	6.4	20.9*
South	0.6	2.9	5.5	11.9*	0.3	1.5	3.7	8.5*	1.0	3.4	6.5	14.9*	1.7	9.5	14.3	33.0*
West	0.5	2.9	4.3	11.2*	0.2	1.6	2.4	7.1*	0.7	2.8	5.3	13.2*	1.4	7.6	12.3	26.3*
p-Value (chi-square)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.07	<0.001	<0.001	<0.001

Source: IBM® MarketScan® commercial claims and encounters database Notes: Estimates are the number of individuals co-dispensed naloxone per 1000 individuals that have received an opioid prescription while concurrently holding a benzodiazepine prescription for at least one day at the time the opioid was dispensed within the given opioid dosage category. All estimates are weighted to be nationally representative for the Commercially Insured Population. Individuals were considered to have been co-dispensed naloxone if an opioid claim and naloxone claim were within 7 days of each other. Estimates are obtained from individuals who were continuously enrolled for the year, *t*-Tests were conducted to examine statistical differences in co-dispensing rates between 2015 and 2018 for each demographic group/morphine milligram equivalent category combination. Chi-square tests were conducted to examine statistical differences among categorical groups.

* represents that co-dispensing rates were statistically different in 2018 compared to 2015 ($p < 0.001$).

Table 4

Naloxone dispensing rates to commercially insured individuals with a substance use disorder, opioid use disorder, or recent opioid overdose 2016–2018.

	Any substance use disorder			**Opioid use disorder**			**Past opioid overdose**		
Demographic-group	2016	2017	2018	2016	2017	2018	2016	2017	2018
All	2.1	2.4	4.1*	14.5	15.7	24.7*	18.1	26.2	45.2*
Male	2.2	2.4	3.8*	15.1	17.1	23.2*	22.9	29.1	49.5*
Female	2.1	2.3	4.4*	13.8	13.7	26.6*	12.1	22.8	40.0*
p-Value (*t*-Test)	0.29	0.58	<0.01	0.22	<0.01	0.03	0.02	0.28	0.24
Age: 0–17	0.8	0.9	1.4	13.5	8.7	17.3	0.0	6.4	0.0
Age: 18–34	3.2	3.6	4.5*	19.9	22.6	29.4*	25.3	29.1	56.8*
Age: 35–44	1.9	2.0	3.3*	10.9	12.1	17.0*	2.3	15.9	26.9*
Age: 45–54	1.7	2.1	4.2*	11.8	12.8	22.9*	14.2	28.1	55.3*
Age: 55–64	1.7	1.8	4.3*	12.4	12.4	28.5*	18.4	34.1	42.9*
p-value (chi-square)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Northeast	3.5	2.3	3.5	24.0	14.6	21.7	39.6	30.5	64.9*
Midwest	0.9	1.6	2.6*	8.2	14.8	20.4*	14.2	21.2	35.8*
South	2.4	2.6	4.7*	14.2	14.1	24.8*	12.6	24.4	37.2*
West	1.8	3.3	5.6*	10.6	21.2	32.5*	6.1	33.0	52.7*
p-Value (chi-square)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Source: IBM® MarketScan® commercial claims and encounters database notes: Estimates are the number of individuals dispensed naloxone per 1000 individuals within the given category that had the corresponding diagnosis less than 90 days before the naloxone rx. All estimates are weighted to be nationally representative for the commercially insured population. Estimates are obtained from individuals who were continuously enrolled for the year and the last 90 days of the previous year. *t*-Tests were conducted to examine statistical differences in dispensing rates between 2016 and 2018 for each demographic group/diagnosis category combination. Chi-square tests were conducted to examine statistical differences among categorical groups.

* represents that naloxone dispensing rates were statistically different in 2018 compared to 2016 ($p < 0.001$).

Table 5

Out of pocket costs for dispensed naloxone among the commercially insured population 2015–2018.

Product	Year	N	25th Pctl ($)	50th Pctl ($)	75th Pctl ($)	% $0 OOP	% > $100 OOP
All	2015	7229	3.09	12.00	60.00	24	13
	2016	36,671	10.00	35.00	75.00	20	16
	2017	49,117	8.00	25.00	40.00	21	8
	2018	99,917	0.00	24.88	35.69	32	5
EVZIO auto injector	2015	5206	0.00	40.00	100.00	29	19
	2016	24,577	25.00	50.00	100.00	18	23
	2017	8963	40.00	70.00	130.00	14	29
	2018	4990	30.00	70.00	150.00	18	35
Naloxone hydrochloride injection	2015	2023	5.00	10.00	10.00	15	0
	2016	4983	5.00	10.00	10.00	20	0
	2017	5102	5.00	10.00	10.00	20	0
	2018	5459	5.00	10.00	10.00	15	0
Narcan nasal spray	2015	0	–	–	–	–	–
	2016	7111	0.00	29.80	40.00	26	4
	2017	35,052	12.00	25.00	37.34	23	4
	2018	89,468	0.00	25.00	35.00	34	4

Notes: Median is reported in dollars, % $0 OOP is the percent of dispensed naloxone in the given category that required zero out of pocket costs, and % > $100 OOP is the percent of dispensed naloxone that required out of pocket costs greater than $100. N is the nationally weighted number of naloxone prescriptions dispensed.