Published in final edited form as:

Ann Emerg Med. 2018 June ; 71(6): 679–687.e3. doi:10.1016/j.annemergmed.2017.10.007.

Does Prescription Opioid Shopping Increase Overdose Rates in Medicaid Beneficiaries?

Benjamin C. Sun, MD, MPP¹, Nicoleta Lupulescu-Mann, MS², Christina J. Charlesworth, MPH², Hyunjee Kim, PhD², Daniel M. Hartung, PharmD, MPH³, Richard A. Deyo, MD, MPH⁴, and K. John McConnell, PhD^{1,2}

¹Center for Policy Research-Emergency Medicine, Department of Emergency Medicine, Oregon Health and Science University, Portland, OR

²Center for Health Systems Effectiveness, Oregon Health and Science University, Portland, OR

³College of Pharmacy, Oregon State University/Oregon Health and Science University, Portland, OR

⁴Department of Family Medicine, Department of Medicine and Oregon Institute of Occupational Health Sciences, Oregon Health and Science University, Portland, OR

Abstract

Objective—The link between prescription opioid shopping and overdose events is poorly understood. We tested the hypothesis that a history of prescription opioid shopping is associated with increased risk of overdose events.

Methods—This is a secondary analysis of a linked claims and controlled substance dispense database. We studied adult Medicaid beneficiaries in 2014 with prescription opioid use in the six months prior to an ambulatory care or emergency department visit with a pain related diagnosis. The primary outcome was a non-fatal overdose event within six month of the cohort entry date. The exposure of interest (opioid shopping) was defined as having opioid prescriptions by different prescribers with 1 day overlap and filled at 3 pharmacies in the 6 months prior to cohort entry. We used a propensity score to match shoppers with non-shoppers in a 1:1 ratio. We calculated the absolute difference in outcome rates between shoppers and non-shoppers.

Results—We studied 66,328 patients, including 2,571 (3.9%) opioid shoppers. There were 290 (0.4%) patients in the overall cohort that experienced a non-fatal overdose. In unadjusted analyses, shoppers had higher event rates than non-shoppers (rate difference of 4.4 events per 1000; 95% CI:

Preliminary results will be presented at the American College of Emergency Physicians Research Forum, Washington DC, October 2017

Conflicts of Interest: None

Author Contributions: BCS developed the study question. BCS and KJM obtained funding. NLM and CJC had direct access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. NLM and CJC performed all data management and analysis. BCS prepared the manuscript, and all authors made substantial edits and revisions. BCS has overall responsibility for this study.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

0.8 to 7.9). After propensity score matching, there were no outcome differences between shoppers and non-shoppers (rate difference of 0.4 events per 1000; 95% CI: -4.7 to 5.5). These findings were robust to various definitions of opioid shoppers and look-back periods.

Conclusions—Prescription opioid shopping is not independently associated with increased risk of overdose events.

Introduction

Background

Drug overdoses have exceeded motor vehicle collisions as the leading cause of accidental mortality in the United States, and this epidemic has been fueled by prescription opioid abuse.¹ From 1995 to 2015, more than 183,000 people have died in the U.S. from overdoses related to prescription opioids.² Although North America has been the epicenter of this public health crisis³, increasing rates of opioid prescribing over time have been observed in multiple countries.^{4–8}

There has been specific interest in “shoppers” who obtain prescription opioids from multiple prescribers or pharmacies.^{9–14} Shopping may contribute to overdose events either through risky prescription opioid use (e.g. overlapping prescriptions) or by diversion of legally prescribed opioids to other individuals for illicit use.¹⁵ Shopping may also be a marker for poorly coordinated pain management.¹⁶ Opioid shopping may be particularly prevalent in emergency department settings, where care is delivered on an episodic basis.^{13,17,18}

Prior studies suggest that doctor and pharmacy shopping is associated with increased risk of death. Two of these studies lacked data on patient co-morbidities, so results may have been confounded by unmeasured case-mix.^{9,10} A third report relied on pharmacy claims data¹⁶, which may be an inaccurate measure of opioid dispensing particularly among shoppers who often pay in cash.¹¹ Understanding the relationship between opioid shopping and overdose events is particularly important for Medicaid beneficiaries (typically lower-income individuals in the United States who qualify for state based health benefits), who have a six-fold higher risk of fatal prescription opioid overdose compared to non-Medicaid populations.¹⁹

Importance

Payers and case management programs are increasing efforts to profile patients with prescription opioid shopping behavior.^{20,21} Virtually all state Medicaid programs and many commercial payers have implemented “lock-in” programs, which restrict opioid shoppers to a single prescriber and pharmacy.²² However, the expected mechanism of action is unclear, and improved knowledge may influence program design. If shopping is associated with independent overdose risk to the recipient of the prescriptions, then lock-in programs would be expected to directly reduce overdose events in patients with shopping behavior by restricting prescribers and pharmacies.

Alternatively, if shopping is not associated with overdose risk, then lock-in programs may reduce overdoses through reductions in opioid supply (both to targeted beneficiaries and to

others who receive diverted opioids), rather than through restriction of prescribers and pharmacies. In this scenario, additional resources such as pain treatment specialists may be needed to address independent overdose risk factors (e.g. total quantity of prescription opioids, overlapping opioid and benzodiazepine prescriptions) that are associated with opioid shopping.

Goal of This Investigation

Using data from a large cohort of Medicaid beneficiaries, we analyzed linked claims and Prescription Drug Monitoring Program (PDMP) data to test the following hypothesis: a history of prescription opioid shopping is associated with increased risk of nonfatal overdose events.

Methods

Study Design

We performed a retrospective cohort study of Washington State Medicaid beneficiaries. Washington state provided medical claims and PDMP data linked at the beneficiary level for calendar years 2013–2015. Data from 2014 were used as the intake period during which patients could enter the cohort. Data from 2013 and 2015 were also included to allow assessment of prior history of patient co-morbidities and outcomes, respectively. Claims data used ICD-9 diagnostic codes (i.e. the study time frame preceded nationwide adoption of ICD-10 codes in October 2015). The PDMP is an electronic record of all controlled substances dispensed by Washington state pharmacies. Unlike Medicaid pharmacy claims data, which may miss medications paid by a co-insurer or in cash, the PDMP captures all dispensed opioids regardless of payer.

The Washington state Department of Health links Medicaid and PMP data at the beneficiary level for quality improvement purposes. An external data vendor developed a methodology that uses a combination of deterministic linkage (e.g. on name, date of birth, and address) and a clustering algorithm to combine potentially related PDMP records (e.g. slight variations on linking variables such as ‘John Doe’ and ‘Jon Doe’). Department of Health staff performed validation on a ‘gold standard’ manually reviewed set of 997 linked records pairs and 1,002 non-linked pairs. The matching algorithm has a sensitivity of 67% and specificity of >99%.

The Institutional Review Boards of Washington State and of Oregon Health & Science University approved this study prior to data collection.

Cohort Selection and Rationale

Washington State Medicaid beneficiaries were eligible to enter the cohort between Jan 1, 2014 and Dec 31, 2014. We focused on ambulatory care encounters for which opioid prescribing might be considered. Patients entered the study cohort on the date that the following criteria were met: 1. the patient had an ambulatory care encounter (CPT codes for new office visits [99201-99205], established office visits [99211-99215], or emergency department visit [99281-5, 99291]) for a pain related condition^{25,26} (see eTable 1) that

represented a potential opportunity to prescribe an opioid medication; 2. the encounter did not result in hospitalization or observation care; 3. the patient had a history of prescription for opioid medication in the six months prior to the encounter; and 4. the patient had continuous Medicaid enrollment for the 6 months before and after cohort entry (to allow standardized assessment of pre-existing co-morbidities and outcomes subsequent to cohort entry).

We excluded members with a one year history of cancer.²⁷ We excluded beneficiaries who were dually eligible for Medicare and Medicaid during the study period since linked Medicare utilization and pharmacy data were unavailable. Children under 15 years of age were excluded. Finally, we excluded patients who received hospice or nursing home care at any time during the study period, since opioid analgesics are a widely accepted treatment for hospice patients²⁷, and institutional providers are likely responsible for medication management in nursing facilities.

Outcomes

The primary outcome was the occurrence of a non-fatal overdose event within six-months following cohort entry. We defined non-fatal overdose with an ICD9 code for opioid poisoning or opioid-related adverse events in addition to a diagnosis on the same date that may be related to overdose (see eTable 2).²⁸

Exposure

The independent variable of opioid shopping was defined as opioid prescriptions by different prescribers with 1 day overlap and filled at 3 pharmacies in the 6 months prior to cohort entry.¹¹ We believe that our definition, based on the work of Cepeda et. al¹¹, is highly specific to aberrant use patterns as it requires multiple prescribers, multiple pharmacies, and overlapping prescriptions. We acknowledge that other studies have used a wide range of thresholds and “look-back” time frames to define opioid shopping.^{10,12,16,29–31} We performed sensitivity analyses to assess the impact of varying definitions of opioid shopping (see [Analysis](#) below).

Measures

We included an expansive set of patient-level case-mix measures, evaluated during each calendar quarter, that may be associated with prescription opioid use and overdose events. Demographics included age, sex, race, Hispanic ethnicity, federal poverty level, and disability status. A one-year prior history of 17 physical health condition categories was evaluated using the Chronic Illness and Disability Payment System, which has been validated for use in Medicaid populations.³² Specific mental health and substance abuse diagnoses were identified through medical claims using the previously described Ettner classification system.³³ To control for potential temporal trends, we included dummy variables indicating the calendar-quarter of cohort entry.

We created two measures of high risk prescription opioid use in the six months prior to cohort entry that may be predictors of overdose events and potentially confound the relationship between opioid shopping and outcomes.^{23,27,29,34} We calculated total dispensed

morphine milligram equivalents (MMEs), using the following conversion factors^{35–37}: codeine-0.15; fentanyl citrate-0.13; fentanyl patch-7.2; hydrocodone-1; hydromorphone-4; levorphanol-11; meperidine-0.1; methadone-3; morphine- 1; oxycodone-1.5; oxymorphone-3; and tapentadol- 0.4. We only considered oral/transdermal formulations. We also measured whether there was any prior instance of overlapping opioid and benzodiazepine prescriptions for more than one week.

Analysis

We used a propensity score to match shoppers to non-shoppers; we then calculated the risk difference between the two matched groups (i.e. we did not generate a propensity score adjusted regression model).

We used propensity score matching to control for baseline imbalances in measured covariates.³⁸ A logistic regression model to predict opioid shopping included all covariates described in the previous section.

We used nearest neighbor matching with replacement to identify one non-shopper (control) for each shopper (treated).³⁹ To assess the validity of propensity score matching, we report standardized differences in baseline characteristics before and after matching. A standardized difference with an absolute value <0.1 suggests negligible imbalance in the mean or prevalence of a covariate between the treatment and control groups.⁴⁰ We used methods for paired data to estimate absolute risk differences and 95% confidence intervals for outcomes.⁴¹

Observations that were missing age (0.14%) and gender (0.53%) were dropped from the analysis. A small number of observations that were missing information for federal poverty level (0.0007%) were dropped from the analysis. Observations with missing race and ethnicity were categorized as “unknown” and included in the analysis. After cohort selection, we had no missing MME data. Comorbidities were coded as presence or absence of diagnosis codes, and disability status and expansion were also coded as presence or absence and therefore had no missing values.

We performed multiple sensitivity analyses. We considered the possibility that total MMEs and overlapping opioid and benzodiazepines prescriptions were mediating (i.e. co-linear) rather than confounding factors; in sensitivity analyses, we excluded these variables from the propensity score model. We assessed whether our findings were sensitive to the lookback period (6-months vs 90 days) to define shopping. Finally, we repeated our analyses with alternative definitions of opioid shopping (i.e. 3, 4, and 5 prescribers or pharmacies in prior six months).

All data management and statistical analyses were performed in R version 3.3.2⁴² and STATA MP 14.0.

Results

Of 2,238,568 unique Washington state Medicaid members in 2014, there were 66,328 patients who met study inclusion criteria (Figure 1). Six-month nonfatal overdose occurred

in 290 (0.4%) patients in the overall cohort. We identified 2,571 (3.9%) opioid shoppers who had at opioid prescriptions by different prescribers with 1 day overlap and filled at 3 pharmacies in the 6 months prior to cohort entry.

Baseline characteristics differed on multiple attributes between shoppers and non-shoppers (Table 1). Shoppers were more likely to have risk factors for overdose events, including higher amounts of prescribed MMEs, overlapping opioid and benzodiazepine prescriptions, and pre-existing substance abuse diagnosis. Shoppers were also more likely to have a pain-related ambulatory care visit early in the study year, and to have multiple pre-existing physical and mental health diagnoses. A 1:1 propensity score matching identified a comparison cohort with minimal differences (absolute standardized difference <0.1) between opioid shoppers and matched non-shoppers for all co-variables (Table 1, eTable 3, eFigure).

In unadjusted analyses (Table 2), shoppers had a higher rate of six-month non-fatal overdose events compared to non-shoppers (rate difference of 4.4 events per 1000; 95% CI: 0.8, 7.9). After propensity score matching (Table 2), we found no difference in the primary outcome (rate difference of 0.4 events per 1000; 95% CI: -4.7, 5.5) between opioid shoppers and non-shoppers.

Our findings were robust to multiple sensitivity analyses, including exclusion of prior MMEs and opioid/benzodiazepines as potential mediating factors, a shorter (90-day) look-back period, and alternative definitions of shopping (including 3, 4, and 5 prescribers or pharmacies in prior six months) (Table 3).

Limitations

First, we acknowledge that there are many potential definitions of shopping, and our definition of shopping may potentially triggered by appropriate medical use (e.g. multiple providers at safety net clinic; housing instability resulting in multiple dispensers). However, our findings are robust to alternative definitions and “look-back” time frames. Second, we considered all-cause mortality in a composite outcome with non-fatal overdose. However, we identified only three six-month deaths in the analytic cohort. Our findings did not change when these three fatal events were considered in a composite outcome including non-fatal overdose. Third, we studied Washington state Medicaid beneficiaries because of increased opioid overdose risk in this population¹⁹, and the our requirements for continuous enrollments reduced the potential sample size. The generalizability of our findings should be verified in other populations and states. Fourth, our claims data do not capture overdose events that do not result in death or hospital use (e.g. naloxone administration by a friend or family member). Fifth, the linkage of Medicaid claims and PDMP data demonstrated modest sensitivity. False negative matching with PDMP data likely occur at random due to mismatches in linking elements such as name and data of birth. Therefore, we believe that the modest sensitivity of PDMP linkage may reduce power but not validity of our findings. False negative matches (opioid users without linked PDMP data) are already accounted for in our excluded patients (i.e. no evidence of prior opioid use). The high specificity of matching increases confidence that we correctly identified shoppers. Finally, we analyzed all

available data but did not perform a formal sample size calculation. It is possible that we had insufficient event rates to detect small but clinically importance outcome differences.

Discussion

In this large cohort of Medicaid beneficiaries, a history of prescription opioid shopping behavior was not associated with increased risk of non-fatal overdose events after adjusting for prior opioid use, patient demographics, substance abuse disorders, and other diagnoses. These findings were robust to multiple sensitivity analyses. Our study builds on prior research on shoppers by including extensive co-morbidity data from medical claims, using comprehensive PDMP dispense data, capturing non-fatal overdose events which are much more common than fatal overdoses, and using propensity score methods to mitigate confounding by measurable factors. Our findings suggest that interventions to reduce overdose risk among recipients of prescription opioids should focus on factors other than shopping behavior.

Our results differ from prior reports, which suggested an increased risk of mortality or overdose events associated with shopping behavior. In our cohort, shoppers had increased physical and mental health co-morbidities, as well as riskier patterns of opioid use (e.g. total prescribed MMEs, overlapping prescriptions with benzodiazepines). In unadjusted analyses, shoppers had significantly higher rates of non-fatal overdoses than non-shoppers. However, these differences disappeared after balancing baseline characteristics, suggesting that the link between shopping and adverse events is explained by other associated, high-risk factors.

Two prior case-control studies have used PDMP data to identify risk factors for fatal overdoses. Peirce et. al. studied 698 decedents and 1,049,205 living controls that were prescribed a controlled substance in West Virginia.⁹ Younger age, greater number of prescription dispensed, concurrent opioid and benzodiazepine prescriptions, and doctor and pharmacy shopping were associated with increased odds of death. Using data from Tennessee, Gwira Baumbblatt et. al. compared 932 case patients who died from an opioid related event with 11,840 age and sex matched controls.¹⁰ Risk factors for death include four or more prescribers per year, four or more pharmacies, and >100 daily MMEs per year. Using PDMP and medical examiner data from New Mexico, However, these analyses were restricted to dispensing and demographic data available through the state PDMPs, and neither study included data on patient co-morbidities which may confound the relationship between opioid shopping and outcomes.

A recent study by Yang et. al. of 90,010 Medicaid beneficiaries on long-term opioid therapy explored the link between pharmacy shopping, overlapping prescriptions, and overdose events.¹⁶ In multivariate analyses, a history of pharmacy shopping (4 pharmacies in 90 days) was associated with a hazard ratio of 1.8 for opioid overdose. Overlapping prescriptions were associated with a hazard ratio of 3.0. Our study used a definition of shopping that incorporated both multiple pharmacies and overlapping prescriptions, and our findings differ from the prior work by Yang et. al. There are many methodological similarities between this report and our study (including the use of a Medicaid beneficiary population, the same definition for non-fatal overdose events²⁸, and control of co-

morbidities). However, Yang et. al. used Medicaid pharmacy claims data to identify shopping and control for baseline MMEs, whereas our study used PDMP data that identified the dispensing of opioids regardless of payment source including cash. Tracking the purchase of opioids by cash payments may be critical, since as many as 45% of shoppers may pay with cash for prescription opioids.¹¹ Use of pharmacy claims could potentially introduce differential measurement bias among shoppers vs. non-shoppers, which may explain the discrepancy between our study and the findings by Yang et al. Finally, the Yang et al. study included long-term opioid users, and this population may be different than our inclusion criteria of any opioid medications in the six months prior to enrollment.

Although we did not find a causal link between shopping and outcomes, our study required extensive datasets and complex analytic tools which are unlikely to be available to front line prescribers. We suggest an approach to translating our findings to routine clinical practice. Almost all states operate a PDMP⁴³, which allows prescribers to screen for opioid shopping behavior without the need for prior knowledge of patient characteristics or medication use. Prescribers should strongly consider non-opioid pain management and referral to case management programs for all patients with shopping behavior. Evidence of opioid shopping behavior should alert prescribers to identify and manage associated independent predictors of overdose, including total quantity of prescribed opioids and overlapping prescriptions for opioids and benzodiazepines.^{23,27,29,34} Although physician use of PDMPs has historically been low⁴⁴, initiatives to “push” PDMP data to electronic medical records at the time of patient registration⁴⁵ and embed clinical decision support may overcome logistical barriers to PDMP use.⁴⁶

Our findings provide additional insights into policy approaches to curtailing opioid shopping. Shoppers have been targeted by policies attempting to limit the supply of prescription opioids, reduce health care costs, and prevent overdoses. Virtually all state Medicaid programs and many commercial payers have implemented “lock-in” programs, which restrict opioid shoppers to a single prescriber and pharmacy.²² PDMPs allow prescribers and pharmacies to identify opioid shopping behavior. Despite substantial heterogeneity in lock-in and PDMP programs, both are associated with reduced shopping behavior, health care encounters, and costs.^{22,43} The impact of these policies on overdose events is less clear, although emerging evidence suggests an association between PDMP programs and reduction in overdose events and mortality.⁴³

Lock-in programs may prevent overdoses through two potential and non-exclusive mechanisms: 1. Reduced risk to targeted patients; and 2. Reduced diversion to other individuals. Our findings provide some evidence that restricting patients to a single prescriber or pharmacy may not independently reduce risk, although lock-in programs may have beneficial effects in modifying other risk factors for overdose (e.g. reducing total MMEs). Although we did not specifically study diversion (the second potential mechanism), others have assessed the link between diversion and overdose events. Qualitative research with prescription-drug abusers identified doctor shoppers as a major source of diverted opioids.¹⁵ In a case series of 295 fatal, non-intentional prescription overdose events, doctor shopping (>5 prescribers in the year prior to death) was found in 21%.⁴⁷ Diversion (i.e. death from a prescription drug without evidence of a prescription) was found in 63%,

suggesting that a majority of fatal overdoses may be related to diverted medications rather than to opioids prescribed by physicians. These studies suggest that lock-in programs may reduce overdose in part by limiting diversion, although the direct impact may be difficult to measure.

In summary, prescription opioid shopping is not independently associated with increased risk of overdose events. Screening criteria for interventions to reduce overdose risk should focus on high-risk characteristics associated with shopping.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant Support: This study was supported by National Institutes of Health (NIH) grant R01DA036522. The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. The contents do not necessarily represent the official views of the National Institutes of Health.

References

1. NCHS Data Brief. [Accessed October 10, 2012] Drug Poisoning Deaths in the United States, 1980–2008. 2011. p. 81 <http://www.cdc.gov/nchs/data/databriefs/db81.htm>
2. CDC. [Accessed Apr 20, 2017] Prescription opioid overdose data. 2016. <https://www.cdc.gov/drugoverdose/data/overdose.html>
3. Fischer B, Keates A, Buhringer G, Reimer J, Rehm J. Non-medical use of prescription opioids and prescription opioid-related harms: why so markedly higher in North America compared to the rest of the world? *Addiction*. Feb; 2014 109(2):177–181. [PubMed: 23692335]
4. Casati A, Sedefov R, Pfeiffer-Gerschel T. Misuse of medicines in the European Union: a systematic review of the literature. *European addiction research*. 2012; 18(5):228–245. [PubMed: 22572594]
5. Leong M, Murnion B, Haber PS. Examination of opioid prescribing in Australia from 1992 to 2007. *Internal medicine journal*. Oct; 2009 39(10):676–681. [PubMed: 19460051]
6. Myers B, Siegfried N, Parry CD. Over-the-counter and prescription medicine misuse in Cape Town--findings from specialist treatment centres. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. May; 2003 93(5):367–370. [PubMed: 12830601]
7. Iravani FS, Akhgari M, Jokar F, Bahmanabadi L. Current trends in tramadol-related fatalities, Tehran, Iran 2005–2008. *Substance use & misuse*. Nov; 2010 45(13):2162–2171. [PubMed: 20394504]
8. Rintoul AC, Dobbin MD, Drummer OH, Ozanne-Smith J. Increasing deaths involving oxycodone, Victoria, Australia, 2000–09. *Injury prevention: journal of the International Society for Child and Adolescent Injury Prevention*. Aug; 2011 17(4):254–259. [PubMed: 21164159]
9. Peirce GL, Smith MJ, Abate MA, Halverson J. Doctor and pharmacy shopping for controlled substances. *Medical care*. Jun; 2012 50(6):494–500. [PubMed: 22410408]
10. Gwira Baumblatt JA, Wiedeman C, Dunn JR, Schaffner W, Paulozzi LJ, Jones TF. High-risk use by patients prescribed opioids for pain and its role in overdose deaths. *JAMA internal medicine*. May; 2014 174(5):796–801. [PubMed: 24589873]
11. Cepeda MS, Fife D, Chow W, Mastrogianni G, Henderson SC. Opioid shopping behavior: how often, how soon, which drugs, and what payment method. *Journal of clinical pharmacology*. Jan; 2013 53(1):112–117. [PubMed: 23400751]
12. Pradel V, Frauger E, Thirion X, et al. Impact of a prescription monitoring program on doctor-shopping for high dosage buprenorphine. *Pharmacoepidemiology and drug safety*. Jan; 2009 18(1):36–43. [PubMed: 19040199]

13. Shaffer EG, Moss AH. Physicians' perceptions of doctor shopping in West Virginia. *The West Virginia medical journal*. 2010; 106(4 Spec):10–14.
14. Worley J. Prescription drug monitoring programs, a response to doctor shopping: purpose, effectiveness, and directions for future research. *Issues in mental health nursing*. May; 2012 33(5): 319–328. [PubMed: 22545639]
15. Inciardi JA, Surratt HL, Cicero TJ, Beard RA. Prescription opioid abuse and diversion in an urban community: the results of an ultrarapid assessment. *Pain Med*. Apr; 2009 10(3):537–548. [PubMed: 19416440]
16. Yang Z, Wilsey B, Bohm M, et al. Defining risk of prescription opioid overdose: pharmacy shopping and overlapping prescriptions among long-term opioid users in medicaid. *The journal of pain: official journal of the American Pain Society*. May; 2015 16(5):445–453. [PubMed: 25681095]
17. Hansen GR. The drug-seeking patient in the emergency room. *Emergency medicine clinics of North America*. May; 2005 23(2):349–365. [PubMed: 15829387]
18. Cantrill SV, Brown MD, Carlisle RJ, et al. Clinical policy: critical issues in the prescribing of opioids for adult patients in the emergency department. *Annals of emergency medicine*. Oct; 2012 60(4):499–525. [PubMed: 23010181]
19. CDC. Overdose deaths involving prescription opioids among medicaid enrollees - Washington, 2004–2007. *MMWR Weekly*. 2009; 58(42):1171–1175. [Accessed March 7, 2016] <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5842a1.htm>.
20. Franklin G, Sabel J, Jones CM, et al. A comprehensive approach to address the prescription opioid epidemic in Washington State: milestones and lessons learned. *American journal of public health*. Mar; 2015 105(3):463–469. [PubMed: 25602880]
21. Garcia MC, Dodek AB, Kowalski T, et al. Declines in Opioid Prescribing After a Private Insurer Policy Change - Massachusetts, 2011–2015. *MMWR. Morbidity and mortality weekly report*. Oct 21; 2016 65(41):1125–1131. [PubMed: 27764082]
22. Roberts AW, Skinner AC. Assessing the present state and potential of Medicaid controlled substance lock-in programs. *Journal of managed care & specialty pharmacy*. May; 2014 20(5): 439–446c. [PubMed: 24761815]
23. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA: the journal of the American Medical Association*. Apr 6; 2011 305(13):1315–1321. [PubMed: 21467284]
24. Kim H, Hartung DM, Jacob RL, McCarty D, McConnell KJ. The Concentration of Opioid Prescriptions by Providers and Among Patients in the Oregon Medicaid Program. *Psychiatr Serv*. Apr 01; 2016 67(4):397–404. [PubMed: 26766755]
25. Sullivan MJ, Adams H, Tripp D, Stanish WD. Stage of chronicity and treatment response in patients with musculoskeletal injuries and concurrent symptoms of depression. *Pain*. Mar; 2008 135(1–2):151–159. [PubMed: 17646052]
26. Logan J, Liu Y, Paulozzi L, Zhang K, Jones C. Opioid prescribing in emergency departments: the prevalence of potentially inappropriate prescribing and misuse. *Medical care*. Aug; 2013 51(8): 646–653. [PubMed: 23632597]
27. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. *JAMA: the journal of the American Medical Association*. Mar 15.2016
28. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Annals of internal medicine*. Jan 19; 2010 152(2):85–92. [PubMed: 20083827]
29. Federal Register. Apr 14.2010 75(71)
30. Katz N, Panas L, Kim M, et al. Usefulness of prescription monitoring programs for surveillance--analysis of Schedule II opioid prescription data in Massachusetts, 1996–2006. *Pharmacoepidemiology and drug safety*. Feb; 2010 19(2):115–123. [PubMed: 20014166]
31. Weiner SG, Griggs CA, Langlois BK, et al. Characteristics of emergency department “doctor shoppers”. *J Emerg Med*. Apr; 2015 48(4):424–431. e421. [PubMed: 25638051]
32. Kronick R, Gilmer T, Dreyfus T, Lee L. Improving health-based payment for Medicaid beneficiaries: CDPS. *Health care financing review*. Spring;2000 21(3):29–64. [PubMed: 11481767]

33. Ettner SL, Frank RG, McGuire TG, Hermann RC. Risk adjustment alternatives in paying for behavioral health care under Medicaid. *Health services research*. Aug; 2001 36(4):793–811. [PubMed: 11508640]
34. Leider HL, Dhaliwal J, Davis EJ, Kulakodlu M, Buikema AR. Healthcare costs and nonadherence among chronic opioid users. *The American journal of managed care*. Jan; 2011 17(1):32–40. [PubMed: 21348566]
35. Paulozzi LJ, Kilbourne EM, Desai HA. Prescription drug monitoring programs and death rates from drug overdose. *Pain Med*. May; 2011 12(5):747–754. [PubMed: 21332934]
36. Oregon Health & Science University. [Accessed March 16, 2016] Guideline for Safe Chronic Opioid Therapy Prescribing For Patients with Chronic Non-cancer Pain. 2014. http://www.ohsu.edu/gim/epiclinks/opioidresources/OHSU_Opioid%20Guideline_1%2014.pdf
37. Centers for Medicare and Medicaid Services. [Accessed March 8, 2016] Opioid Morphine Equivalent Conversion Factors. 2015. <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-March-2015.pdf>
38. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. Nov 10; 2009 28(25):3083–3107. [PubMed: 19757444]
39. Austin PC, Mamdani MM. A comparison of propensity score methods: a case-study estimating the effectiveness of post-AMI statin use. *Stat Med*. Jun 30; 2006 25(12):2084–2106. [PubMed: 16220490]
40. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate behavioral research*. May; 2011 46(3):399–424. [PubMed: 21818162]
41. Abadie A, Imbens GW. Matching on the estimated propensity score. *Econometrica*. 2016; 84(2): 781–807.
42. [Accessed July 9, 2016] R: A language and environment for statistical computing. 2015. <https://www.r-project.org/>
43. [Accessed Jan 25, 2017] Briefing on PDMP Effectiveness. 2014. http://www.pdmpassist.org/pdf/COE_documents/Add_to_TTAC/Briefing%20on%20PDMP%20Effectiveness%203rd%20revision.pdf
44. Feldman L, Williams KS, Coates J, Knox M. Awareness and utilization of a prescription monitoring program among physicians. *Journal of pain & palliative care pharmacotherapy*. 2011; 25(4):313–317. [PubMed: 21936637]
45. Greenwood-Ericksen MB, Poon SJ, Nelson LS, Weiner SG, Schuur JD. Best Practices for Prescription Drug Monitoring Programs in the Emergency Department Setting: Results of an Expert Panel. *Annals of emergency medicine*. Jun; 2016 67(6):755–764. e754. [PubMed: 26619757]
46. Poon SJ, Greenwood-Ericksen MB, Gish RE, et al. Usability of the Massachusetts Prescription Drug Monitoring Program in the Emergency Department: A Mixed-methods Study. *Academic emergency medicine: official journal of the Society for Academic Emergency Medicine*. Apr; 2016 23(4):406–414. [PubMed: 26806310]
47. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA: the journal of the American Medical Association*. Dec 10; 2008 300(22):2613–2620. [PubMed: 19066381]

Figure 1.
Cohort Selection

Table 1

Characteristics of Shoppers and Non-Shoppers, Before and After Matching

	Shoppers (N= 2,571)						Non - Shoppers					
	All - before matching (N= 63,757)			Std. Diff Shoppers vs all Non-shoppers			Matched only (N= 2,571)			Std. Diff Shoppers vs matched Non-Shoppers		
	Est.	SD	Est.	SD	Est.	SD	Est.	SD	Est.	SD	Est.	SD
Six Month History of Morphine Milligram Equivalents	8,897	12,118	2,288	7,117	0.67		8,151	15,158			0.05	
Six Month History of Overlapping Opioid & Benzodiazepine prescriptions – %	0.29	0.45	0.08	0.28	0.55		0.28	0.45			0.02	
Age (years) – mean	40.10	11.24	38.55	13.51	0.12		40.78	12.23			–0.06	
Male Sex – %	0.30	0.46	0.32	0.47	–0.04		0.30	0.46			0.01	
Race – %												
White	0.71	0.46	0.69	0.46	0.03		0.71	0.45			–0.01	
Black	0.11	0.32	0.08	0.27	0.11		0.13	0.33			–0.04	
Asian	0.00	0.07	0.02	0.13	–0.12		0.00	0.05			0.03	
American Indian/Alaska Native	0.05	0.22	0.04	0.18	0.07		0.05	0.21			0.01	
Hawaiian/Pacific Islander	0.01	0.08	0.01	0.10	–0.04		0.01	0.07			0.02	
Other (including mixed race)	0.10	0.30	0.14	0.34	–0.12		0.09	0.28			0.03	
Unknown	0.02	0.15	0.03	0.17	–0.04		0.02	0.14			0.01	
Ethnicity – %												
Not Hispanic	0.85	0.36	0.79	0.41	0.14		0.85	0.36			–0.01	
Hispanic	0.07	0.25	0.10	0.30	–0.11		0.07	0.25			0.00	
Unknown	0.09	0.28	0.11	0.31	–0.08		0.08	0.28			0.01	
Time Period of Cohort Entry – %												
Jan – Mar 2014	0.68	0.47	0.36	0.48	0.68		0.70	0.46			–0.05	
Apr – June 2014	0.14	0.35	0.21	0.41	–0.18		0.13	0.34			0.02	
Jul – Sept 2014	0.10	0.30	0.23	0.42	–0.35		0.10	0.29			0.02	
Oct – Dec 2014	0.08	0.27	0.20	0.40	–0.37		0.07	0.26			0.03	
Any Disability – %	0.54	0.50	0.40	0.49	0.28		0.56	0.50			–0.04	
Enrolled under Medicaid Expansion – %	0.29	0.46	0.34	0.47	–0.10		0.29	0.45			0.02	
Percent of Federal Poverty Level – %												
< 10	0.91	0.29	0.76	0.43	0.41		0.91	0.28			–0.03	

	Shoppers (N= 2,571)						Non - Shoppers					
	All - before matching (N= 63,757)			Std. Diff Shoppers vs all Non-shoppers			Matched only (N= 2,571)			Std. Diff Shoppers vs matched Non-Shoppers		
	Est.	SD	Est.	SD	Est.	SD	Est.	SD	Est.	SD	Est.	SD
10-50	0.04	0.20	0.07	0.26	0.04	0.19	0.04	0.19	0.04	0.19	0.01	
50-100	0.04	0.18	0.10	0.31	0.03	0.18	0.03	0.18	0.03	0.18	0.02	
> 100	0.02	0.13	0.07	0.25	0.01	0.12	0.01	0.12	0.01	0.12	0.03	
Physical Health Conditions – %												
Cardiovascular	0.45	0.50	0.33	0.47	0.26		0.47	0.50	0.47	0.50	–0.04	
Skeletal & connective	0.60	0.49	0.41	0.49	0.40		0.62	0.49	0.62	0.49	–0.04	
Nervous system	0.21	0.40	0.14	0.34	0.18		0.21	0.41	0.21	0.41	–0.00	
Pulmonary	0.37	0.48	0.27	0.44	0.23		0.40	0.49	0.40	0.49	–0.06	
Gastrointestinal	0.39	0.49	0.25	0.43	0.29		0.39	0.49	0.39	0.49	–0.02	
Diabetes	0.15	0.35	0.13	0.34	0.04		0.15	0.36	0.15	0.36	–0.01	
Skin	0.26	0.44	0.16	0.37	0.24		0.26	0.44	0.26	0.44	–0.02	
Renal	0.12	0.32	0.07	0.26	0.15		0.12	0.32	0.12	0.32	0.00	
Developmental disability	0.00	0.04	0.00	0.06	–0.05		0.00	0.04	0.00	0.04	–0.01	
Genital	0.14	0.35	0.08	0.27	0.19		0.14	0.35	0.14	0.35	0.01	
Metabolic	0.15	0.35	0.09	0.29	0.17		0.15	0.36	0.15	0.36	–0.02	
Pregnancy	0.11	0.31	0.11	0.32	–0.02		0.11	0.31	0.11	0.31	0.00	
Eye	0.04	0.19	0.04	0.19	–0.01		0.04	0.21	0.04	0.21	–0.03	
Cerebrovascular	0.03	0.16	0.01	0.11	0.10		0.03	0.17	0.03	0.17	–0.03	
HIV/AIDs	0.01	0.11	0.01	0.09	0.03		0.02	0.13	0.02	0.13	–0.04	
Other infectious disease	0.13	0.34	0.08	0.27	0.18		0.14	0.35	0.14	0.35	–0.03	
Henatological	0.06	0.23	0.03	0.17	0.14		0.05	0.22	0.05	0.22	0.02	
Behavioral Health Conditions – %												
Adjustment disorders	0.02	0.15	0.02	0.14	0.02		0.02	0.14	0.02	0.14	0.01	
Alcohol disorder	0.13	0.34	0.09	0.28	0.14		0.13	0.34	0.13	0.34	–0.01	
Anxiety disorders	0.53	0.50	0.33	0.47	0.41		0.53	0.50	0.53	0.50	–0.02	
Bipolar disorder	0.13	0.34	0.09	0.29	0.12		0.13	0.34	0.13	0.34	–0.00	
Disorders originating in childhood	0.07	0.25	0.06	0.23	0.04		0.06	0.23	0.06	0.23	0.04	
Dysthymia or other depressive disorder	0.42	0.49	0.28	0.45	0.30		0.42	0.49	0.42	0.49	0.00	
Major depression	0.23	0.42	0.16	0.37	0.17		0.23	0.42	0.23	0.42	0.01	

	Shoppers (N= 2,571)						Non - Shoppers					
	All - before matching (N= 63,757)			Std. Diff Shoppers vs all Non-shoppers			Matched only (N= 2,571)			Std. Diff Shoppers vs matched Non-Shoppers		
	Est.	SD		Est.	SD		Est.	SD		Est.	SD	
Personality disorder	0.03	0.17		0.02	0.13		0.03	0.17		0.03	0.17	
Schizophrenia & other non-mood Disorders	0.05	0.22		0.04	0.20		0.05	0.22		0.05	0.22	
Substance disorders	0.67	0.47		0.42	0.49		0.68	0.47		0.68	0.47	
Other	0.42	0.49		0.31	0.46		0.40	0.49		0.40	0.49	

Notes: Est = estimate; SD= standard deviation; Std Diff = standardized difference

Table 2
Association Between Shopping and Outcomes, in Un-matched and Matched Cohorts

	Rates per 1,000		Difference	Confidence interval	P-value
	Shoppers	Non-Shoppers			
<i>Primary Outcome: Nonfatal overdose</i>					
Un-matched cohorts	8.6	4.2	4.4	(0.8, 7.9)	<0.001
Propensity score matched cohort	8.6	8.2	0.4	(-4.7, 5.5)	0.881

Table 3

Sensitivity Analyses

	Rates per 1,000		Difference	Confidence Interval	P-value
	Shoppers	Non-Shoppers			
Shopper w/out morphine milligram equivalents and no opioid/benzo overlap covariates (n=2,571 [3.9%])	8.6	7.0	1.6	(-3.4, 6.5)	0.54
Shopper 90 day lookback (n=1,004 [1.8%])	5.0	5.0	0.0	(-6.3, 6.3)	1.00
Shoppers with 3 prescribers or pharmacies (n=9,652 [14.6%])	5.7	7.7	-2.0	(-4.6, 0.6)	0.14
Shoppers with 4 prescribers or pharmacies (n=4,150 [6.3%])	6.5	9.2	-2.7	(-6.7, 1.4)	0.20
Shoppers with 5 prescribers or pharmacies (n=1,952 [2.9%])	6.7	9.7	-3.0	(-8.9, 2.8)	0.30

Notes:

1. In the Shopper no morphine milligram equivalents and no opioid/benzo overlap covariates model, the Shopper is defined based on Cepeda study¹¹ with a 6 month look back for history of opioid use. The morphine milligram equivalents and opioid/benzo overlap covariates were not included in the propensity score models.
2. In the Shopper 90 day lookback, the Shopper is defined based on Cepeda study¹¹ with a 90 day look back for history of opioid use. The morphine milligram equivalents and no opioid/benzo overlap covariates are included in the propensity score model.
3. In the Shoppers with 3 prescribers or pharmacies, the shopper is defined as an individual with at least 3 pharmacies or 3 prescribers in the past 6 months from cohort entry date.
4. In the Shoppers with 4 prescribers or pharmacies, the shopper is defined as an individual with at least 4 pharmacies or 4 prescribers in the past 6 months from cohort entry date.
5. In the Shoppers with 5 prescribers or pharmacies, the shopper is defined as an individual with at least 5 pharmacies or 5 prescribers in the past 6 months from cohort entry date.