

Doctor Shopping Behavior and the Diversion of Prescription Opioids

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ABSTRACT

OBJECTIVES: “Doctor shopping” as a means of prescription opioid diversion is examined. The number and percentage of prescriptions and morphine-equivalent milligrams diverted in this manner are estimated by state and molecule for the period 2008–2012.

METHODS: Eleven billion prescriptions with unique patient, doctor, and pharmacy identifiers were used to construct diversion “events” that involved between 1 and 6 unique doctors and between 1 and 6 unique pharmacies. Diversion thresholds were established based on the probability of each contingency.

RESULTS: A geographically widespread decline occurred between 2008 and 2012. The number of prescriptions diverted fell from approximately 4.30 million (1.75% of all prescriptions) in 2008 to approximately 3.37 million (1.27% of all prescriptions) in 2012, and the number of morphine-equivalent milligrams fell from approximately 6.55 metric tons (2.95% of total metric tons) in 2008 to approximately 4.87 metric tons (2.19% of total metric tons) in 2012.

CONCLUSIONS: Diversion control efforts have likely been effective. But given increases in opioid-related deaths, opioid-related drug treatment admissions, and the more specific resurgence of heroin-related events, it is clear that additional public health measures are required.

KEYWORDS: Doctor shopping, prescription opioids, prescription diversion, prescription opioid diversion

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Introduction

The Substance Abuse and Mental Health Services Administration (SAMHSA) has reported that rates of initiation, past month prevalence, and past year prevalence of nonmedical prescription opioid use among those aged 12 and over have remained generally constant over much of the past decade. Rates of initiation, past month prevalence, and past year prevalence actually declined during this same period of time among members of subpopulations aged 12 to 17 and 18 to 25.^{1,2} Although this is encouraging, other statistics reveal the untoward consequences of nonmedical prescription opioid use as those who were once initiated continue to use and progress toward a diagnosable substance use disorder (SUD), often requiring health, mental health, and other drug treatment services.

Between 2005 and 2011, emergency department (ED) visits involving prescription opioids increased by 146% according to data provided by the Drug Abuse Warning Network (DAWN).³ Findings from the Treatment Episode Data Set (TEDS) indicate that in the decade ending 2013, admissions with prescription opioids (nonprescription methadone and “other opiates” excluding heroin) as the primary drug of abuse increased 10-fold, rising from about 3% in 2003 to about 30% in 2013.^{4,5} But perhaps the most alarming findings are those reported by the Centers for Disease Control and Prevention (CDC);

between 1999 and 2014, there was a 5-fold increase in prescription opioid-related deaths and a concomitant increase in heroin-related deaths.⁶ Drug-related unintentional poisonings, driven largely by prescription opioids, now exceed deaths attributable to motor vehicle accidents or handguns in the United States.⁶

In response to what has been perceived as a public health problem of greatest importance, the President of the United States has proposed a strategy that calls for increased education of parents, children, patients, and health care providers regarding the dangers of prescription opioids; continued implementation of Prescription Drug Monitoring Programs (PDMPs); introduction of measures designed to ensure proper disposal of unused prescription opioids; and increased law enforcement efforts intended to deter the illicit prescribing and dispensing of such drugs.⁷

For these efforts to succeed, it is important that policy-makers and health care professionals understand more about the progression toward regular nonmedical use of prescription opioids, the means by which regular users obtain their drugs, and the additional measures that must be taken to decrease non-medical use and its sequelae.⁸

Nonmedical users require a source of supply. The most common is the social environment itself. Examining data provided



by IMS Health, the National Institute of Health (NIH) reports that prescriptions for opioid analgesics increased more than 167% between 1991 and 2013.⁹

The use of opioid analgesics in treating pain had been a common practice in medicine for many years. Over time, these drugs gained acceptance for long-term use in dealing with patients with cancer. A marked acceleration in the rates of prescription for opioid analgesics occurred when the pharmaceutical industry implemented aggressive marketing campaigns encouraging physicians to regard these drugs as safe and effective for treating pain unrelated to cancer. The behavior of the pharmaceutical industry in this regard has been characterized as both predatory and opportunistic.^{10,11} Their efforts culminated in what one professional organization characterized as “a perfect storm” that allowed the nonmedical use of prescription opioids to become increasingly prevalent in American society.¹²

The vast majority of prescription opioids that find their way into the possession of nonmedical users originate from legitimate sources. This may occur when a physician “overprescribes” in response to a presenting problem or simply when prescriptions that, for whatever reason, are not taken as indicated make their way into the hands of other users.^{1,2} But this finding may not be representative for those engaged in chronic nonmedical use and where a reliable source capable of providing drugs in sufficient quantity is needed.

There is a growing body of literature suggesting that although large-scale population studies, such as the National Survey on Drug Use and Health (NSDUH), indicate only a very small proportion of nonmedical prescription opioid users obtain their drugs from more than 1 physician or actually purchase the product from a dealer, friend, or acquaintance, these sources of supply are much more common among those who make contact with health care systems or who seek treatment for an SUD.²

Examining data from a national sample of about 100 treatment centers, known as the Survey of Key Informants’ Patients (SKIP), researchers found that more than 60% of prescription opioid users reported dealers as their primary source. Other less common sources included doctors and theft.¹³ This evidence begs the question, “Where and how do dealers acquire prescription opioids for distribution?”

Research has elaborated on the mechanisms by which dealers acquire prescription opioids and in so doing casts light on the interrelationships that exist among doctors, pharmacies, and patients.^{14,15} Doctors become a source of supply whenever they write a prescription for an opioid analgesic that provides the basis for nonmedical use. The relatively liberal burden of proof required by some pain clinics may be indicative of criminal intent on the part of a prescribing physician. Any physical place that maintains a store of prescription opioids is a target for theft. Pharmacies are therefore vulnerable in this regard, and often to their own employees. Pain clinics, which sometimes maintain an inventory of drugs

on site, may be particularly susceptible to such behavior. Patients who engage in doctor shopping behavior are another principal source of supply. Such patients may deliberately engage in transactions with doctors and pharmacies that are most likely to be complicit in their endeavors. They are sometimes sponsored by a dealer who pays for medical costs with the ultimate objective of accumulating inventory.

This work focuses narrowly on doctor shopping. Such behavior normally becomes observable when prescriptions of a similar class overlap in time and are written by multiple doctors and filled by multiple pharmacies.^{16–18}

Data

The data used to support these analyses were provided by IMS Government Solutions (IMS-GS), a subsidiary of IMS Health. They are unique in a number of ways. The objective of this work is to measure doctor shopping as a mechanism of diversion over the period 2008–2012, and during this time, IMS Health gathered information on more than 11 billion prescription records. Each doctor, pharmacy, patient, and prescription in their data warehouse is associated with a unique identifier that is consistent across geographic locations. And this, in principle, allows differences in doctor, pharmacy, and patient behavior to be examined over time and across geography.

Although the sample is extraordinarily large, the data collection process is opportunistic. The sample has no formal statistical properties, and this may limit the extent to which findings can be generalized to all doctors, pharmacies, patients, and prescriptions in the United States. It is possible that selection bias may exist in the data because pharmacies engaged in illicit behavior are not likely to report on their transactions. IMS does not release information on pharmacy identifiers which mitigates this as a potential problem. But selection bias may exist nonetheless, and it is not addressed here. Bias may also be attributable to other characteristics of the data, and these are discussed in the sections that follow.

IMS Health has a sophisticated (and proprietary) system for weighting its data at the pharmacy outlet level. A roster is established for any given year for all known outlets, and agreements are made between it and *some of these outlets* to provide prescription records. In cases where such agreements cannot be made, values for numbers of prescriptions by drug are imputed using information derived from pharmacies of a similar size and type, and within some arbitrarily circumscribed radius, with which agreements *have* been made. This allows projection to any level of geographic aggregation based on the known and imputed numbers. But this system cannot of its own accord yield valid estimates of diversion. In the simplest case, the rate of diversion is just the number of suspect prescriptions divided by the total number of prescriptions dispensed. Projections made in the manner described above do not alter the ratio of diverted to total prescriptions. They only increase the numbers in the numerator and the denominator by a constant. The ratio

itself remains a function of detection, and detection remains a function of sample coverage.

IMS Health receives information on the prescribing and dispensing behavior of hundreds of thousands of pharmacies on a continuous basis. This information is consolidated via “feeds” that comprise groups of pharmacies. Pharmacies have certain characteristics related to size, type, and geographic location. Feeds change over time. Some begin contributing to the pool of pharmacies that provide prescription records, whereas others cease entirely. As this occurs, the characteristics of the sample change, systematically, and in a manner that is correlated with the behavior of doctors, pharmacies, and patients.

The effects of this churning can be quite dramatic because any one feed may be associated with tens of millions of prescriptions. This presents a challenge because it would be desirable to examine doctor shopping behavior over time, and some method of stabilization must be introduced to ensure comparability among doctors, pharmacies, and patients over time.

The solution to these problems involves the use of 2 pharmacy panels, one intended to maximize sample coverage (and therefore the ability to detect doctor shopping events) and another intended to hold the participation of pharmacies constant over time (thereby allowing the estimation of change in the rate of doctor shopping behavior to be observed).

The first is referred to as a “base year panel,” and it includes all pharmacies that reported on at least 95% of their claims during calendar 2012. This selection criterion yields 35 311 sites. At the state level, these pharmacies are associated with 60 732 837 unweighted prescriptions and with 265 644 177 weighted prescriptions. Mean state-level pharmacy coverage for the base year panel represents approximately 30% of the pharmacy universe.

The second is referred to as a “5-year stability panel,” and it includes all pharmacies that reported on at least 95% of their claims over the entire 2008–2012 period. This selection criterion yields 8 954 sites. At the state level, these pharmacies are associated with an average of 35 589 553 unweighted prescriptions per year and with an average of 257 483 435 weighted prescriptions per year. Mean state-level coverage for the 5-year stability panel represents approximately 12% of the pharmacy universe.

The ability to detect prescriptions that overlap in time, which are written for the same patient by multiple doctors and filled for this patient by multiple pharmacies, will of necessity increase as the proportion of all pharmacies represented in a sample increases, and so estimates of diversion derived from the 5-year stability panel will be biased downward relative to those derived from the base year panel as mean coverage is approximately 12% in the 5-year stability panel and 30% in the base year panel.

In the analysis that follows, an assumption is made that the *percent change* in diversion which occurs from year to year in the

5-year stability panel may be regarded as unbiased even though the estimate of diversion itself is known to be biased downward. For this to be true, variability in the rate of coverage in the 5-year stability panel must be uncorrelated with the percent change in diversion that occurs from one year to the next. Having examined the data in some detail, this assumption is found to be tenable.

The downward bias in estimates of diversion derived from the 5-year stability panel is corrected by using information from the base year panel to rescale these estimates. A hypothetical example might be in order at this point. If we knew from the 5-year stability panel that the rate of diversion was 5% in 2011 and 10% in 2012, then we would also know that the *rate of change* between 2011 and 2012 was 100%. But these estimates of diversion would rest on a sample coverage rate of approximately 12%. If the base year sample were examined, then we might find a rate of diversion of 20% for 2012. We would regard this as more believable because the coverage rate for the base year sample is 30%. And this would imply that the rate of diversion for 2011 was actually 10% (because $5 \times (20/10) = 10$).

Analysis

Measurement of doctor shopping begins with the construction of one record for each unique individual. This record includes data on each opioid analgesic prescription filled for the individual during the period beginning January 1, 2008, and ending December 31, 2012. The prescription data include the date on which the prescription was filled, the prescriber responsible for the prescription, the pharmacy at which the prescription was filled, the opioid molecule associated with the prescription, and the number of morphine-equivalent milligrams associated with the prescription.^{19–28} The conversion factors that are used here were provided by the Food and Drug Administration (FDA) and current as of October 2013.

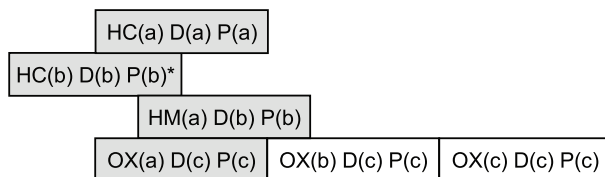
Doctor shopping may occur whenever 2 or more prescriptions for the individual overlap in time by at least 1 day. Any such overlap is defined as a potential diversion “event.” Data on these events are accumulated in a 6×6 matrix (number of unique doctors involved \times number of unique pharmacies involved). These dimensions exhaust more than 99% of all diversion events detected in the data.

A matrix of this kind is constructed, for the base year panel and the 5-year stability panel, for prescriptions written during each study year, within each state, for each molecule. The molecules include alfentanil, buprenorphine, butorphanol tartrate, codeine, dihydrocodeine, fentanyl, hydrocodone (HC), hydro-morphone (HM), levomethadyl acetate, levomethadyl tartrate, meperidine, methadone hydrochloride, morphine, oxycodone (OX), oxymorphone hydrochloride, pentazocine, propoxyphene, remifentanyl hydrochloride, sufentanyl citrate, tapentadol hydrochloride, and tramadol hydrochloride.

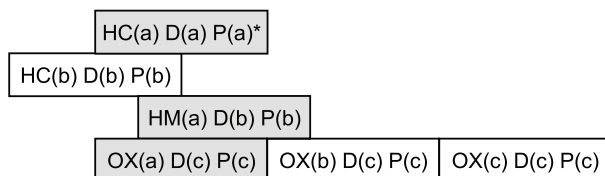
Figure 1 demonstrates the manner in which the 6×6 matrix is populated. The example begins with data on all prescriptions

Patient A1342

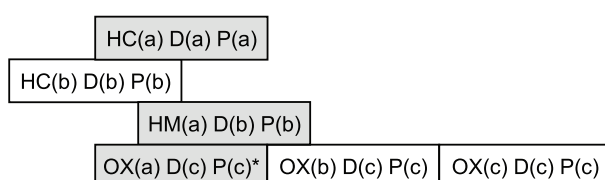
Event 1



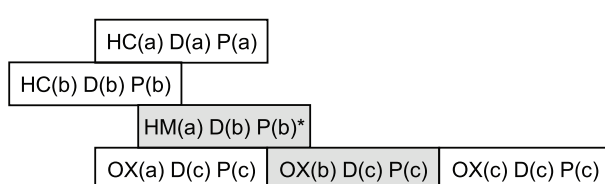
Event 2



Event 3



Event 4



*Denotes index prescription.

Time →

Figure 1. Event generation.

dispensed over some arbitrarily defined period of time for a hypothetical patient known only as “A1342.” Three opioid analgesics are considered in Figure 1: HC, HM, and OX. In practice, all opioid analgesics relevant to the study are represented in the matrix.

The prescriptions that appear in Figure 1 are identified as HC(a) and HC(b); HM(a); and OX(a), OX(b), and OX(c). The illustration includes 3 doctors, denoted D(a), D(b), and D(c), and 3 pharmacies, denoted P(a), P(b), and P(c). Thus, HC(a) D(a) P(a) indicates that prescription (a) for HC was written by doctor (a) and filled by pharmacy (a). A forward-searching algorithm is used to identify overlapping prescriptions, and in this example, the procedure generates 4 diversion events:

- (1) When HC(b) D(b) P(b) is taken as the “index prescription,” it generates event 1 comprising prescriptions {HC(b) D(b) P(b); HC(a) D(a) P(a); HM(a)

D(b) P(b); OX(a) D(c) P(c)} and attributes information associated with this event (molecule name, number of milligrams, cash payment amount, third party payment amount, and location filled for each prescription) to cell 3,3. This is because 3 doctors, D(a), D(b), and D(c), and 3 pharmacies, P(a), P(b), and P(c), are involved. Prescriptions OX(b) D(c) P(c) and OX(c) D(c) P(c) are not included in event 1 because they do not overlap with the index prescription.

- (2) When HC(a) D(a) P(a) is taken as the index prescription, it generates event 2 comprising {HC(a) D(a) P(a); HM(a) D(b) P(b); OX(a) D(c) P(c)} and attributes information associated with this event to cell 3,3. As before, 3 doctors, D(a), D(b), and D(c), and 3 pharmacies, P(a), P(b), and P(c), are involved. Prescription HC(b) D(b) P(b) is not included in event 2 because it begins prior to the index prescription. Prescriptions OX(b) D(c) P(c) and OX(c) D(c) P(c) are not included

in event 2 because they do not overlap with the index prescription.

- (3) When OX(a) D(c) P(c) is taken as the index prescription, it generates event 3 comprising {OX(a) D(c) P(c); HC(a) D(a) P(a); HM(a) D(b) P(b)} and attributes information associated with the event to cell 3,3. Three doctors, D(a), D(b), and D(c), and 3 pharmacies, P(a), P(b), and P(c), are involved. Prescription HC(b) D(b) P(b) is not included in event 3 because it begins prior to the index prescription. Prescriptions OX(b) D(c) P(c) and OX(c) D(c) P(c) are not included in event 3 because they do not overlap with the index prescription.
- (4) When HM(a) D(b) P(b) is taken as the index prescription, it generates event 4 comprising {HM(a) D(b) P(b); OX(b) D(c) P(c)} and attributes information associated with the event to cell 2,2. Two doctors, D(b) and D(c), and 2 pharmacies, P(b) and P(c), are involved. Prescriptions {HC(a) D(a) P(a); HC(b) D(b) P(b); OX(a) D(c) P(c)} are not included in event 4 because they begin prior to the index prescription. Prescription OX(c) D(c) P(c) is not included in event 4 because it does not overlap with the index prescription.

It is possible, although unlikely, for an event to be generated which exceeds the range of the 6×6 matrix. When this occurs, it is assigned to the row and column in which the maximum has been surpassed. Thus, an event involving 3 doctors and 7 pharmacies would be assigned to cell 3,6 and an event involving 8 doctors and 5 pharmacies would be assigned to cell 6,5.

Prescriptions may be represented more than once in the matrix. For example, prescriptions associated with an event involving 2 unique doctors and 2 unique pharmacies may also be represented in an event involving 3 unique doctors and 3 unique pharmacies. This is by design. The possibility of duplication is retained so that areas of discontinuity (or inflection) in the matrix can be identified. Any such inflection may constitute a “threshold” that serves to operationally define diversion.

Thresholds are therefore not defined based up a “criterion standard” or external point of validation. It is not ordinarily possible to conduct confirmatory case investigations. Instead they are defined based on their statistical improbability and the extent to which prescriptions associated with these thresholds appear suspicious for other reasons, perhaps because they involve cash payments rather than payments by a third party. Large numbers of cash transactions are often indicative of efforts to conceal illicit activity.

Results

Table 1 provides information derived in the manner described above for the 2012 base year panel. Referring to cell 2,3 in Table 1 (i.e. 2 doctors and 3 pharmacies), the measures may be read thus: 0.1732% of all prescriptions for opioid analgesics

involved 2 doctors and 3 pharmacies; 0.3146% of all milligrams associated with all prescriptions for opioid analgesics involved 2 doctors and 3 pharmacies; and 0.6268% of all cash expended on prescriptions for opioid analgesics involved 2 doctors and 3 pharmacies.

Within this cell, 13.4774% of the total payment amount was made in cash. The fact that the value of this measure (Cash/Total | Contingency) increases along the major diagonal lends credence to the notion that prescriptions associated with increasing numbers of doctors and increasing numbers of pharmacies may be viewed with increasing suspicion.

Arbitrary but reasonable thresholds are used to define doctor shopping. In this case, a zero in the first place to the left of the decimal for percent prescriptions in Table 1 is treated as a threshold for the upper bound of diversion (a number less than 1% is indicated by the yellow and orange areas there), and a zero in the first place to the right of the decimal for percent prescriptions in Table 1 is treated as a threshold for the lower bound of diversion (a number less than one-tenth of 1% as indicated by the orange area there). These definitions are justified by their statistical improbability, observed increase in percent cash on the major diagonal, and conventions adopted elsewhere.^{16–18} Note that the terms “upper bound” and “lower bound” are not used here as would be the case if one were describing a confidence interval.

Estimation of the prevalence of diversion requires that the prescriptions in the 6×6 matrix become unduplicated. To accomplish this, we create unduplicated sets of observations involving what is depicted as the orange area in Table 1 (this provides the basis for a lower bound estimate), the yellow area depicted in Table 1 (which subsumes the orange area and provides the basis for an upper bound estimate), and the white area depicted in Table 1 (in which case “All” observations in the matrix become unduplicated). The results of this exercise are presented in Table 2. They indicate an estimate of 0.0834% (involving 221 665 prescriptions) as a lower bound and an estimate of 1.2685% (involving 3 369 660 prescriptions) as an upper bound for the base year. It is also possible to produce total cost estimates based on the material presented in Table 2. Referring to that table, \$26 497 104 was expended in cash (using the upper bound estimate as our indicator). If this constitutes 10.0123% of the total cost, then the total cost is given by $\$26\,497\,104/0.100123 = \$264\,645\,526$.

Variability over time

Estimates made using the base year and stability panels as described above appear in Figure 2. The findings presented indicate sustained downward trends in the proportion and number of prescriptions diverted over the period 2008–2012. The upper bound estimate is approximately 1.75% (4.30 million prescriptions) in 2008 and approximately 1.27% (3.37 million prescriptions) in 2012. The lower bound estimate is

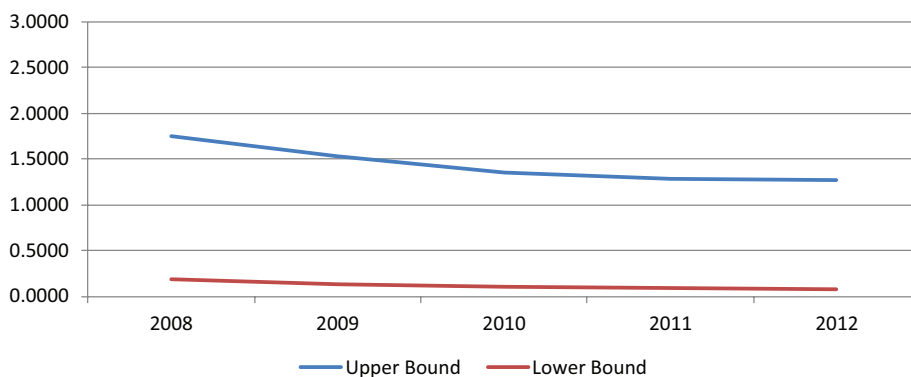
Table 1. Event matrix percent (base year panel, duplicated prescriptions).

PHARMACIES		1	2	3	4	5	6
DOCTORS							
Prescriptions	1	35.6299%	3.4808%	0.1678%	0.0088%	0.0009%	0.0001%
Milligrams		57.4543%	7.2671%	0.4861%	0.0285%	0.0025%	0.0004%
Cash		56.1081%	6.7304%	0.5224%	0.0506%	0.0098%	0.0023%
Cash/Total Contingency		6.8246%	6.5808%	7.1465%	11.8680%	31.9071%	40.6688%
Prescriptions	2	10.5696%	2.9625%	0.1732%	0.0105%	0.0009%	0.0002%
Milligrams		12.3341%	3.6239%	0.3146%	0.0222%	0.0020%	0.0006%
Cash		9.7258%	5.9662%	0.6268%	0.0600%	0.0087%	0.0044%
Cash/Total Contingency		5.5213%	11.7571%	13.4774%	17.4453%	31.8414%	71.1948%
Prescriptions	3	0.5629%	0.2934%	0.0990%	0.0095%	0.0009%	0.0002%
Milligrams		0.6558%	0.3569%	0.1237%	0.0149%	0.0017%	0.0003%
Cash		0.7040%	0.6469%	0.4496%	0.0590%	0.0087%	0.0017%
Cash/Total Contingency		6.6738%	12.1341%	25.4383%	27.4920%	34.7532%	40.0214%
Prescriptions	4	0.0222%	0.0180%	0.0108%	0.0061%	0.0012%	0.0002%
Milligrams		0.0285%	0.0235%	0.0132%	0.0075%	0.0018%	0.0003%
Cash		0.0379%	0.0724%	0.0474%	0.0459%	0.0086%	0.0043%
Cash/Total Contingency		7.7119%	19.3462%	24.3492%	32.7986%	29.7655%	51.4998%
Prescriptions	5	0.0009%	0.0008%	0.0009%	0.0009%	0.0009%	0.0003%
Milligrams		0.0026%	0.0013%	0.0010%	0.0009%	0.0012%	0.0004%
Cash		0.0027%	0.0033%	0.0019%	0.0072%	0.0079%	0.0024%
Cash/Total Contingency		8.8174%	16.2750%	17.9575%	38.8045%	29.2235%	31.0807%
Prescriptions	6	0.0001%	0.0000%	0.0001%	0.0001%	0.0002%	0.0002%
Milligrams		0.0008%	0.0000%	0.0001%	0.0001%	0.0002%	0.0002%
Cash		0.0006%	0.0000%	0.0001%	0.0006%	0.0017%	0.0024%
Cash/Total Contingency		18.5197%	0.0000%	25.0238%	51.2582%	35.7184%	42.5517%

Table 2. Event matrix percent (base year panel, unduplicated prescriptions).

MEASURE	PERCENT		
	LOWER	UPPER	ALL
Prescriptions	0.0834%	1.2685%	48.3508%
Milligrams	0.1343%	1.8781%	72.2978%
Cash	0.3651%	2.8757%	72.2960%
Cash/Total Contingency	17.2676%	10.0123%	7.0352%
MEASURE	NUMBER		
Prescriptions	221 665	3 369 660	128 441 156
Milligrams	348 246 842	4 871 138 710	187 519 579 271
Cash	\$3 364 138	\$26 497 104	\$666 136 384
Cash/Prescriptions	\$15	\$8	\$5

	Upper Bound Prescriptions (%)	Lower Bound Prescriptions (%)	Upper Bound Prescriptions (n)	Lower Bound Prescriptions (n)
2008	1.7512	0.1927	4 295 445	472 782
2009	1.5368	0.1368	3 882 450	345 561
2010	1.3530	0.1071	3 532 179	279 637
2011	1.2795	0.0945	3 362 412	248 451
2012	1.2685	0.0834	3 369 660	221 665



	Upper Bound Milligrams (%)	Lower Bound Milligrams (%)	Upper Bound Milligrams (n)	Lower Bound Milligrams (n)
2008	2.9492	0.3825	6 551 225 405	849 599 352
2009	2.7431	0.2865	6 093 491 236	636 360 172
2010	2.4804	0.2299	5 509 900 609	510 609 476
2011	2.3393	0.2000	5 196 533 648	444 249 460
2012	2.1928	0.1568	4 871 138 710	348 246 842

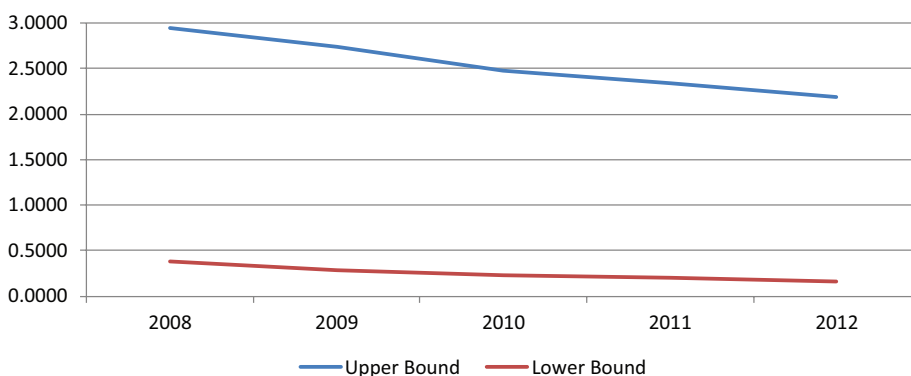


Figure 2. Projected Trends (Prescriptions and Milligrams per Year).

approximately 0.19% (473 000 prescriptions) in 2008 and approximately 0.08% (222 000 prescriptions) in 2012.

The findings presented in Figure 2 also indicate sustained downward trends in the proportion and number of milligrams diverted. The upper bound estimate is approximately 2.95% (6.55 billion morphine-equivalent milligrams) in 2008 and approximately 2.19% (4.87 billion morphine-equivalent milligrams) in 2012. These numbers equate to 6.55 and 4.87 morphine-equivalent metric tons, respectively. The lower bound estimate is approximately 0.38% (849.60 million morphine-equivalent milligrams) in 2008 and approximately 0.16% (348.25 morphine-equivalent million milligrams) in 2012. These numbers equate to approximately 0.85 and 0.35 morphine-equivalent metric tons, respectively.

The findings for the upper bound estimate are used in more detailed analyses that appear in subsequent sections of this

article. This is because findings associated with the lower bound are based on extraordinarily restrictive criteria (only the most active of the most active doctor shoppers qualify for inclusion there). They remain informative because state-level PDMPs often establish thresholds at higher levels (5 doctors and 5 pharmacies), and this may serve to underestimate the magnitude of the problem.

The drugs that figure prominently when doctor shopping is defined using criteria for the upper bound estimate are those most commonly prescribed: OX (marketed under the brand name OxyContin) and HC (marketed under the brand names Vicodin and Lortab). In 2008 OX-based products constituted 33.90% of all prescriptions diverted and 56.33% of all morphine-equivalent milligrams diverted. In 2012, these numbers were about the same: 32.56% and 49.46%, respectively. In 2008, HC-based products constituted 37.90%

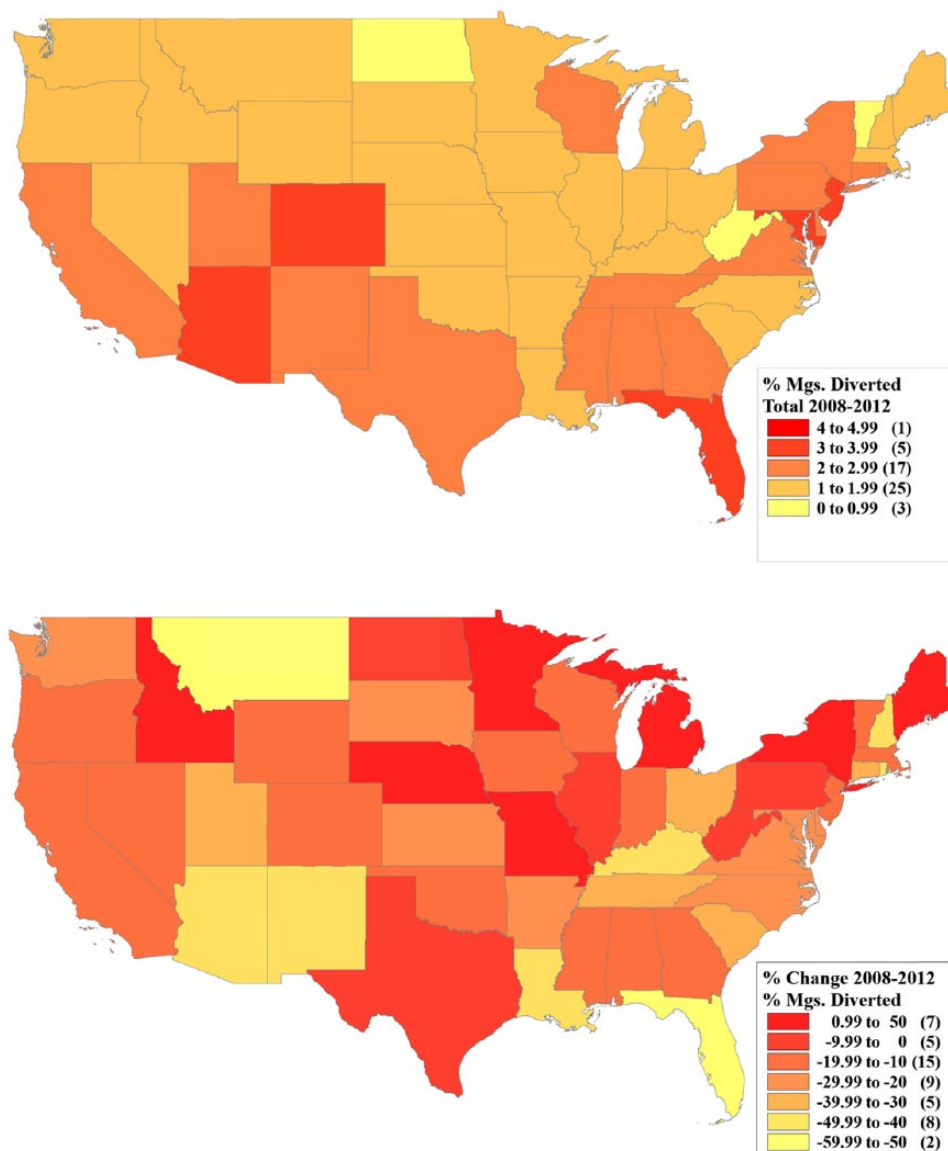


Figure 3. Percent total morphine-equivalent milligrams diverted by state and percent change in percent morphine-equivalent milligrams diverted by state over the period 2008-2012.

of all prescriptions diverted and 15.26% of all morphine-equivalent milligrams diverted. In 2012 these numbers were about the same: 32.70% and 14.21%, respectively. The ratio of percent prescriptions diverted to morphine-equivalent milligrams diverted is higher for OX than for HC, and this reflects in part the difference in their morphine-equivalent conversion factors. Milligram for milligram OX is a more potent drug than HC.

Variability across geography

Upper bound estimates for percent prescriptions diverted, and for percent change in percent morphine-equivalent milligrams diverted, are presented by state for the period 2008-2012 in Figure 3. Over the entire period, rates of prescription diversion were highest in Florida, the Delaware-Maryland-Virginia area, and the Southwest, findings generally consistent with

public perceptions of the problem as it existed during that period of time. Marked reductions in percent morphine-equivalent milligrams diverted can be noted between 2008 and 2012, particularly in Florida where a great deal of attention was focused on pain clinics and their operations.

Discussion

Sustained declines in the percent and number of prescriptions diverted via doctor shopping and in the percent and number of morphine-equivalent milligrams diverted via doctor shopping have been described in preceding sections. When this information is examined not only over time but also across geography, the declines appear to be pervasive and widespread. The results suggest that the efforts of government to stem the tide of prescription opioid diversion may have been effective—at least when diversion is operationally defined as doctor shopping.

But these findings must be reconciled with those reported in the introduction to this article. Notably, that NSDUH data indicate relative stability in both past year and past month non-medical use of prescription opioids over the past decade; that DAWN data indicate marked increases in ED visits involving prescription opioids over the period 2004-2011; that TEDS data indicate continuing and marked increases in prescription opioids as the primary drug of abuse; and that CDC data indicate marked and sustained increases in opioid-related deaths.¹⁻⁶

There are at least 2 explanations for why indicators measuring the consequences of nonmedical prescription opioid use trend upward even as diversion of these drugs attributable to doctor shopping behavior trends downward. The first is related to the process normally associated with drug use epidemics, in which incidence rises rapidly, reaches a plateau, and then declines, and where prevalence eventually becomes the residual product of long-term use, resulting ultimately in contact with health care and drug treatment systems, as well as death.²⁹⁻³² This would confirm, not surprisingly, the importance of early detection and intervention in minimizing the consequences of drug-using behavior.²⁹⁻³⁰ The second is related to the apparent success that has been achieved in reducing the diversion of prescription opioids attributable to doctor shopping. Substitution of illicit opioids for licit opioids may have occurred as a function of availability. The increase in deaths attributable to opioid poisoning observed over the past decade has been driven largely by prescription opioids. But in the more recent past, this trend has been perpetuated by deaths attributable to heroin poisoning.⁶ Deaths attributable to prescription opioids grew from 16 908 in 2010 to 19 159 in 2014, an increase of about 12%, whereas deaths attributable to heroin grew from 3 058 to 10 650, an increase of about 249%, during this same period of time.⁶ This explanation seems tenable but should be regarded as speculative pending rigorous empirical examination of individual-level drug-using behavior over time.

Policy Implications

As noted above, the results suggest that the efforts of government to reduce prescription opioid diversion may have been successful. But methods of detection such as those used here can be defeated by an enterprising dealer who simply uses more individuals to serve as prescription collection agents. So, greater attention must be focused on forms of criminal activity that may be more highly organized. In addition, the findings presented above suggest that substitution may have occurred across drugs but within drug class and that the preference of chronic nonmedical opioid users may have shifted from licit to illicit drugs as a function of relative availability. This is cause for serious concern. Steps have already been taken to deal with this probable phenomenon, including education initiatives, use of opioid substitution, and use of opioid antagonists.^{33,34} Given that drug-related unintentional poisonings, driven largely by opioids, now exceed deaths attributable to motor

vehicles or handguns in the United States, interventions of this kind should be as broadly implemented as possible.

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Author Contributions

RS reviewed and approved the final manuscript.

REFERENCES

1. Substance Abuse and Mental Health Services Administration. Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings (Detailed Tables). Rockville, MD: Department of Health and Human Services; 2015. HHS Publication No. (SMA) 13-4795, NSDUH Series H-46.
2. Substance Abuse and Mental Health Services Administration. *Behavioral Health Trends in the United States: Results from the 2014 National Survey on Drug Use and Health*. Rockville, MD: Department of Health and Human Services; 2015. HHS Publication No. (SMA) 15-4927, NSDUH Series H-50.
3. Substance Abuse and Mental Health Services Administration. *Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits*. Rockville, MD: Department of Health and Human Services; 2013. HHS Publication No. (SMA) 13-4760, DAWN Series D-39.
4. Substance Abuse and Mental Health Services Administration. *Treatment Episode Data Set—Admissions (TEDS-A)—Concatenated, 1992 to 2012*. Ann Arbor, MI: Inter-University Consortium for Political and Social Research; 2015. ICPSR 25221.
5. Substance Abuse and Mental Health Services Administration. *National Admissions to Substance Abuse Treatment Services*. Rockville, MD: Department of Health and Human Services; 2015. HHS Publication No. (SMA) XX-XXXX, BHSIS Series X-XX.
6. National Center for Health Statistics. *Multiple Cause of Death 1999-2014 on CDC WONDER Online Database*. Atlanta, GA: Centers for Disease Control and Prevention; 2015.
7. Executive Office of the President of the United States. *Epidemic: Responding to America's Prescription Drug Abuse Crisis*. https://obamawhitehouse.archives.gov/sites/default/files/ondcp/policy-and-research/rx_abuse_plan.pdf. Published 2011.
8. Martins SS, Sampson L, Cerdá M, Galea S. Worldwide prevalence and trends in unintentional drug overdose: a systematic review of the literature. *Am J Public Health*. 2015;105:e29-e49.
9. Volkow ND. America's addiction to Opioids: heroin and prescription drug abuse. Paper presented at: Senate Caucus on International Narcotics Control; Washington DC; May 14, 2014.
10. United States General Accounting Office. *Prescription Drugs: Oxycontin Abuse and Diversion and Efforts to Address the Problem*. Washington, DC: United States General Accounting Office; 2003. GAO-04-110.
11. Ryan H, Girion L, Glover S. OxyContin goes global—"We're only just getting started." *Los Angeles Times*. December 18, 2016. <http://www.latimes.com/projects/la-me-oxycontin-part3/>
12. Coalition against Insurance Fraud. *Prescription for Peril: How Insurance Finances Theft and Abuse of Addictive Prescription Drugs*. Washington, DC: Coalition against Insurance Fraud; 2007.
13. Cicero TJ, Kurtz SP, Surratt HL, et al. Multiple determinants of specific modes of prescription opioid diversion. *J Drug Issues*. 2011;41:283-304.
14. Rigg KK, March SJ, Inciardi JA. Prescription drug abuse & diversion: role of the pain clinic. *J Drug Issues*. 2010;40:681-702.
15. Rigg KK, Kurtz SP, Surratt HL. Patterns of prescription medication diversion among drug dealers. *Drugs (Abingdon Engl)*. 2012;19:144-155.
16. Cepeda MS, Fife D, Chow W, Mastrogiorganni G, Henderson SC. Assessing opioid shopping behavior: a large cohort study from a medication dispensing database. *Drug Saf*. 2012;35:325-334.

17. Cepeda MS, Fife D, Chow W, Mastrogiovanni G, Henderson SC. Opioid shopping behavior: how often, how soon, which drugs, and what payment method. *J Clin Pharmacol*. 2012;53:112–117.
18. Pradel V, Frauger E, Thirion X, et al. Impact of a prescription monitoring program on doctor-shopping for high dosage buprenorphine. *Pharmacoepidemiol Drug Saf*. 2009;18:36–43.
19. Anderson R, Saiers JH, Abram S, Schlic C. Accuracy in equianalgesic dosing: conversion dilemmas. *J Pain Symptom Manage*. 2001;21:397–406.
20. Beaver WT, Wallerstein SL, Rogers A, Houde RW. Analgesic studies of codeine and oxycodone in patients with cancer. II. Comparisons of intramuscular oxycodone with intramuscular morphine and codeine. *J Pharmacol Exp Ther*. 1978;207:101–108.
21. Bruera E, Belzile M, Pitushkin E, et al. Randomized, double-blind, cross-over trial comparing safety and efficacy of oral controlled-release oxycodone with controlled-release morphine in patients with cancer pain. *J Clin Oncol*. 1998;16:3222–3229.
22. Bruera E, Pereira J, Watanabe S, Belzile M, Kuehn N, Hanson J. Opioid rotation in patients with cancer pain. *Cancer*. 1996;78:852–857.
23. Dunbar PJ, Chapman CR, Buckley FP, Garvin JR. Clinical analgesic equivalence for morphine and hydromorphone with prolonged PCA. *Pain*. 1996;68:265–270.
24. Hunt R, Fazekas B, Thorne D, Brooksbank M. A comparison of subcutaneous morphine and fentanyl in hospice cancer patients. *J Pain Symptom Manage*. 1999;18:111–119.
25. Inturrisi CE. Clinical pharmacology of opioids for pain. *Clin J Pain*. 2002;18:S1–S11.
26. Kalso E, Vainio A. Morphine and oxycodone hydrochloride in the management of cancer pain. *J Clin Pharm Ther*. 1990;47:639–646.
27. Pereira J, Lawlor P, Vigano A, Dorgan M, Bruera E. Equianalgesic dose ratios for opioids: a critical review and proposals for long-term dosing. *J Pain Symptom Manage*. 2001;22:672–687.
28. Ripamonti C, Groff L, Brunelli C, Polastri D, Stravakis A, DeConno F. Switching from morphine to oral methadone in treating cancer pain: what is the equianalgesic dose ratio. *J Clin Oncol*. 1998;16:3216–3221.
29. Caulkins JP. Models pertaining to how drug policy should vary over the course of an epidemic cycle. In: Lindgren B, Grossman M, eds. *Substance Use: Individual Behavior, Social Interactions, Markets, and Politics, Advances in Health Economics and Health Services Research*. Vol 16: 407–439. Amsterdam, The Netherlands: Elsevier; 2005.
30. Caulkins JP. The Need for Dynamic Drug Policy. Heinz Research Paper; 2006:23. <https://pdfs.semanticscholar.org/2b7c/83e274d94e1f0668797719fc1e55877d1996.pdf>
31. Golub A, Brownstein H, Dunlap E. *Monitoring Drug Epidemics and the Markets That Sustain Them, Arrestee Drug Abuse Monitoring (ADAM) and ADAM II Data, 2000–2003 and 2007–2010*. Ann Arbor, MI: Inter-University Consortium for Political and Social Research; 2012. ICPSR33201.v1.
32. Simeone R, Holland L, Viveros-Aguelara R. Estimating the size of an illicit drug-using population. *Stat Med*. 2003;22:2969–2993.
33. Sherman SG, Han J, Welsh C, Chaulk P, Serio-Chapman C. Efforts to reduce overdose deaths. *Am J Public Health*. 2013;103:e1–e2.
34. Schwartz RP, Gryczynski J, O'Grady KE, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995–2009. *Am J Public Health*. 2013;10:917–922.