An Analysis of the Number of Multiple Prescribers for Opioids Utilizing Data from the California Prescription Monitoring Program

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INTRODUCTION

Non-medical use and diversion of prescription drugs are the reasons that most states monitor controlled substances using prescription monitoring programs (PMPs). These administrative databases can be a valuable investigative tool for law enforcement, as well as a potential source of important information for health care professionals. In many states, clinicians can receive reports listing prescriptions for all monitored medications that a patient obtains over a specified time period, with one vital statistic being the number of prescribers.

Unfortunately, the number of multiple prescribers that a patient utilizes for controlled substances has received limited appraisal. The number of prescribers per patient has, in the past, often been used as a proxy measure for doctor shopping. [1] Many state PMPs have adopted thresholds that trigger notifications to providers and dispensers. As no empirical data currently exists for this metric, individual states have considerable latitude in selecting a cut-off point. [2] In a study by Parente [3] examining administrative health insurance claims to identify potentially aberrant behaviors involving controlled substances, "multiple prescribers" was defined as the utilization of six or more prescribers by one patient over a one-year period. This quantification was derived by an expert panel comprised of individuals from the medical profession and the pharmaceutical diversion investigation community, relying on "a combination of evidence and professional consensus." [3] Their operationalization of multiple providers derived from a scenario whereby patients visit several practitioners in a given year, obtaining controlled substance prescriptions from a primary care physician, nurse practitioner, dentist, and several medical specialists (personal communication with an author of the above study, J. David Haddox, Purdue Pharma, February 2009). In essence, this expert panel dichotomized patients with multiple providers into doctor shoppers and those who utilized an acceptable number of practitioners.

As PMPs are being increasingly used in the context of patient care, it is important that the use of multiple providers be interpreted correctly as this activity may or may not be associated with substance abuse and diversion. At present, only anecdotal and survey data support the efficacy of these programs, and there are concerns about the "chilling effect" that they may have on the prescribing of pain medications. [4] Although only a very small percentage of individuals have dubious intent, prescriptions associated with questionable activity represented millions of opioid dosage units. [5] It is, therefore, important that practitioners and regulatory agencies receive some guidance on how to construe information gleaned from PMP administrative databases.

This study examined data from the California PMP, the Controlled Substance Utilization Review and Evaluation System (CURES), to identify the characteristics of patients who had two to five prescribers compared to those using only one prescriber. This was structured to empirically validate the classification developed by professional consensus discussed above. [3] It is hypothesized that patients who used two to five providers in a single year, compared to patients who utilized a single provider, have similar (1) utilization of opioid prescriptions and (2) demographic characteristics.

METHODS

Administrative Approvals

The Institutional Review Board of the UC Davis Medical Center (UCDMC) and the Northern California Veterans Administration Research and Development Committee granted approval with waivers of consent and authorization to conduct this research. The Office of the Attorney General of California (overseer of the California Department of Justice (DOJ) and CURES) required security checks on members of the investigative team

who were granted access to the original source electronic information by means of a memorandum of understanding (MOU). The MOU was a legal document devised jointly by UCDMC and the California DOJ; its purpose was to operationalize administrative, physical, and technical safeguards to assure the confidentiality, integrity, and availability of the electronic health information in CURES. To satisfy requirements of anonymity, an algorithm was devised using SQL Server™ to generate de-identified codes for patients, prescribers, and pharmacies to permit identification of sequential prescriptions.

Data Acquisition—The CURES database contained patient demographics, drug name, dose, refills, administration route, quantity supplied, date of prescription, and prescriber Drug Enforcement Administration (DEA) registration number. Because unique identifiers for individual patients were not provided in the CURES database, a methodology was employed to permit identification of sequential prescriptions for each individual using an algorithm consisting of the first seven characters of the first and last names, gender and age to identify individual patients. [6] Using SQL Server, these four variables were replaced with a unique numerical identifier permitting longitudinal assessment of prescribing to the same individual over time. Prescriber information was de-identified substituting a computer-generated code for their DEA registration number and/or their Pharmacy License. In this manner, no individual-level information either left the California DOJ or was entered into the statistical analysis.

Study Design

Study Sample: CURES Prescriptions: Schedule II prescription data over a 96-month period (January 1, 1999 to December 31, 2007) were evaluated. Only 36 months of prescription data (January 1, 2005 to December 31, 2007) were available for Schedule III medications, corresponding to the period when CURES began requiring reporting of these medications. Individual records were excluded for either: (a) missing or incomplete controlled substance data and/or patient pharmacy, or prescriber identification, (b) implausible prescriptions (i.e., duplicate formulations recorded for the same time interval and commercial transactions), and (c) use of opioid medications not suggestive of practicality or suitability in chronic pain (e.g., rectal suppositories, intravenous preparations, syrups, solutions, etc.).

Regression Analysis of Number of Prescribers

Dependent Variable: The database was searched in a manner to simulate the operationalized multiple prescriber definition in the Parente study. [3] A dichotomized dependent variable was devised using the following types of patients:

> Category 1: Putative Acceptable Use of Multiple Prescribers – the same patient had a prescription for the same opioid issued by two to five prescribers in any 365-day period, and

> Category 2: No Use of Multiple Prescribers – patients for which the use of multiple prescribers was not identified.

Types of Opioids: Patients using two to five prescribers and those using only a single prescriber in a one year period were compared with respect to their utilization of individual opioids. In justifying the potential utility of this covariate in the present study, our previous work [7] demonstrated differences in multiple provider episodes for the same opioids.

Demographic Variables (Age, Gender, and Geographic Location): As the prevalence in national surveys of prescription abuse and dependence decreases with age [8, 9] and is higher in males than females, [8] our analysis included age and gender. Geographic location was also integrated as an explanatory variable because of its relationship with doctor shopping;

relative to metropolitan areas with greater than one million people, smaller populated counties appear to be associated with a decreased likelihood of doctor shopping for opioids. [7] Geographic location was stratified into six ordinal categories by separating California counties into groups, based upon published population estimates, [10] so that rurality could be defined in terms of the Office of Management and Budget's definition of metropolitan and nonmetropolitan populations. [11, 12]

Statistical analyses

Descriptive statistics examined the variety of opioids and patients in the CURES database. Logistic regression was used to study the association between the binary dependent variable, the number of providers prescribing opioids to patients during a one-year period, and the above four covariates. All analyses were performed with SAS V9.2 (SAS Institute, Inc., Cary, NC).

RESULTS

Descriptive Statistics

There were 56,723,021 prescriptions collated in the CURES database between 1999 and 2007 distributed to 2,849,464 patients in the Putative Acceptable Use of Multiple Prescribers Category (i.e., patients who received prescriptions from two to five prescribers in the same year), and 10,021,367 patients in the No Use of Multiple Providers Category. Table 1 provides the frequency distributions for each independent variable in these two categories.

Regression Analysis

Statistical comparisons of the frequencies of prescribed opioids in the CURES database, with respect to differences between the two multiple prescriber categories, yielded significant results but did not confirm our hypothesis (Table 2). Patients with a prescription for the same opioid issued by two to five prescribers in any 365-day period were more likely to use long-acting opioids than hydrocodone, ranging from 7.8% (for the fentanyl patch) to 38.8% (for methadone) depending on the opioid. Conversely, those same patients were less likely to use short-acting opioids (e.g., meperidine, codeine, hydromorphone, immediate-release morphine, and immediate-release oxycodone). The differences for levorphanol and buccal fentanyl were not statistically significant, probably as a result of the small sample sizes for these opioids.

Demographic covariates (Table 2) refuted our other hypothesis. Regarding age, the odds of having two to five providers increased by 1.2% (95% CI, 1.012, 1.012) for each additional year. In the case of gender, patients with two to five providers were 2.7% to 4.4% (95% CI, 0.956, 0.973) more likely to be female. In addition, patients with two to five providers were more likely to arise from smaller geographic areas.

DISCUSSION

The major finding of this study was that utilization of opioid prescriptions and demographic characteristics differed between the groups of patients who used two to five prescribers and those who only used one provider over a one-year period. Although the divergence was not consistent with our initial hypothesis, the differences were in the opposite direction to those consistent with the assumption that the patients who used more than one provider were manipulating the system. The basis for this inference is discussed below.

Patients with a prescription for the same opioid issued by two to five prescribers in any 365-day period were more likely to avoid short-acting Schedule II opioids and instead used long-acting Schedule II opioids. The explanation for why the group that used two to five providers were prescribed long-acting opioids is not readily discernable. Although recent opioid treatment guidelines posit that there is insufficient evidence to recommend long-acting opioids versus short-acting opioids, [13] other investigators have stipulated that short-acting Schedule II opioids appear to increase the risk of misuse. [9] The absence of a higher prescribing of short-acting opioid to the patients using two to five providers argues against an increased misuse in this group.

In addition, the differences in demographic characteristics of patients with two to five providers compared to those with a single provider were not suggestive of individuals more prone to abusive behaviors. In point of fact, those with two to five providers were not associated with youth, male gender, or larger geographic areas. These first two demographic covariates are associated with substance abuse [8] and the third with doctor shopping. [7] These characteristics of the 2–5 provider patient group also do not support an increased likelihood of abuse.

To put these findings into context, it is important to consider other data published on this subject. The use of medical claims data (i.e., ICD-9-CM codes denoting 304.0 [opioid-type dependence], 304.7 [combinations of opioid type with any other], 305.5 [opioid abuse], or 965.0 [poisoning by opiates or related narcotics]) combined with prescription drug information has been exploited to produce regression models that identify patients at risk for prescription opioid abuse or misuse. [14] In this modeling, opioid prescriptions from 2 or more physicians measured over a 3-month period were associated with increased risk for prescription opioid abuse. On an annualized basis, this would suggest that 8 prescribers should arouse suspicion of aberrant use, a number not too different from that suggested by Parente et al. [3]

Others have also reported merit in using the number of prescribers as a surrogate measurement for defining a cut-off point of potentially harmful doctor shopping. Hall et al., when analyzing decedents from prescription overdose fatalities, defined problematic doctor shopping as having received prescriptions for controlled substances from five or more clinicians during the year prior to death. [15] A minority of decedents, roughly 1 in 5, met this definition of doctor shopping. The doctor shoppers in this study tended to come from higher-income counties, to be less likely to have been drinking when they overdosed, and to have taken their drugs orally. In this context, doctor shoppers were thought to represent that part of the drug-abusing population that is less willing to engage in diversion. [15] That these investigators found a negative association between diversion and doctor shopping highlights the need to utilize cut-offs with high specificity (low false-positive rates) so that legitimate patients are not inappropriately labeled as doctor shoppers with negative connotation.

Another recent study provided additional substantiation of the potential viability of a cut-off approximating 5–6 prescribers. [16] Medications evaluated with a potential for abuse (e.g., diazepam, carisoprodol and codeine combinations) were compared with non-addictive drugs (e.g., esomeprazole, metformin and salbutamol). More than 96% of the patients used one or two physicians for prescriptions of the same drug, and less than 0.5 % used five or more physicians. However, the proportion of patients who used five or more physicians for the addictive drugs was 9.5 times higher than that for a comparable proportion of patients using the non-addictive drugs.

Law enforcement authorities acknowledge that individuals and criminal groups divert controlled prescription medications, espousing the belief that prescription fraud is driven by

the increasing abuse and addiction to prescription drugs. [17] Insurance companies are responding and developing computer programs to detect fraud and corruption by patients who are doctor shoppers (i.e., those who visit several physicians simultaneously for prescriptions). [18] One large insurer reported that nearly half of its 1,065 member fraud cases in 2006 (the latest year for which data are available) involved prescription benefits, and most were related to doctor shopping. [19] Given that the new health care reform law enacted advocates deterrence of fraud, [20] it would be appropriate to monitor cases of potentially deceitful activity using PMPs. As such, anomaly detection and pattern recognition may become a quid pro quo if we are to be allowed to continue to help patients in pain in a consequential manner.

In 2007, administrators of operational PMPs generated more than 56,000 reports providing prescribers or dispensers with information on patients who may have been abusing prescription drugs and/or doctor shopping during that year. [2] Policy-makers and practitioners might benefit from understanding that some finite degree of using multiple prescribers might be justified and acceptable. Although we have not presented evidence suggesting a level at which suspicion of aberrant behavior might occur, epidemiological exploration via interviews with patients engaged in this activity should be the next step. As this is not feasible using a secondary data analysis containing de-identified PMP data, other types of methodologies will have to be devised. Similar studies have been performed involving the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace by interviewing club drug users, street-based illicit drug users, methadone maintenance patients, and HIV-positive individuals who abuse and/or divert drugs. [21] The same can be done with individuals involved in obtaining prescriptions from multiple practitioners. Presently, our data does not support targeting patients with 2–5 prescribers in a one-year period. Further studies that include interview data will be necessary to determine an appropriate cut-off point.

Although we validated the consensus of the expert panel specifying that 5 or less prescribers in a one-year period is not a risk factor of potential controlled substance misuse or mismanagement, [3] we did not have the requisite data to define a threshold to trigger PMP notification of providers and dispensers concerning potential misconduct. Another limitation of the present study is the fact that this was a secondary data analysis; we were not able to supplement the CURES database with additional potential covariates that could help to further distinguish users of multiple prescribers from patients with only one prescriber, such as a diagnosis of substance abuse or other psychiatric comorbidities. As these latter variables are commonly associated with prescription opioid abuse, [22–26] determining their correlation with the use of multiple prescribers would be of value.

Doctor shopping (i.e., the concurrent use of several physicians by a patient) is one of the most frequent ways of securing medications in order to divert prescription drugs. [27] Clearly, the use of multiple providers for this purpose is abusive. The partitioning of the pejorative term, doctor shopping, from the expression utilized to describe the use of a permissible number of providers is a worthy goal. Our study attempted to corroborate that patients who used 2–5 providers to obtain opioids did not differ consequentially in terms of their demographics and prescription utilization from patients who used only one provider during a one-year period. This is consistent with the proposition that many patients who use up to five prescribers in a one-year period might have justifiable reasons for doing so. Accordingly, PMP officials might consider adopting a threshold level above five providers in a one-year period when reporting potentially abusive patient activities to physicians. Likewise, providers should interpret reports from state PMPs with caution to constrain the number of false accusations levied against patients with justifiable reasons for utilizing 2–5 providers to obtain opioids in a one-year period. Hopefully, the guidance provided herein for

regulatory agencies and practitioners will improve the care of chronic pain patients while not adding to the burden of the nonmedical use of opioids through diversion.

Acknowledgments

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Table 1

Prescriber Categories and Independent Variables

		Putative Acceptable Use of Multiple Prescribers	No Use of Multiple Prescribers
Opioids[*]			
Schedule III	Hydrocodone	68.3%	57.4%
	Codeine	9.8%	21.2%
Schedule II	Immediate-Release Oxycodone	7.8%	10.1%
	Extended-Release Oxycodone	3.0%	2.2%
	Transcutaneous Fentanyl	4.0%	3.1%
	Extended-Release Morphine	3.2%	2.4%
	Methadone	1.5%	0.9%
	Hydromorphone	1.5%	1.4%
	Immediate-Release Morphine	0.6%	0.8%
	Oral Transbuccal Fentanyl	0.1%	0.1%
	Meperidine	0.1%	0.3%
	Levorphanol	0.02%	0.02%
Demographics			
	Age - years (SD)	50.7 (18.1)	46.4 (19.8)
	Gender - % female	57.8 (42.2)	56.9 (43.1)
	Population		
	< 20,000	0.29%	0.28%
	20,000–50,000	1.19%	0.95%
	50,000–100,00	2.74%	2.04%
	100,000–500,000	17.84%	16.02%
	500,000–1,000,000	15.67%	15.15%
	>1,000,000	62.26%	65.55%

[*] Note: Codeine schedule II, long-acting hydromorphone were excluded from consideration because their numbers were insignificant. Buprenorphine was not included as it was not utilized for the treatment of chronic pain during the period of study (1999–2007).

Table 2

Association of Independent Variables with Categories of Numbers of Prescribers[♦]

Effect	OR = exp (Estimate of coefficient)	95% CI for OR
Opioid type (reference category is Hydrocodone)		
Fentanyl Patch	1.078	(1.053, 1.104)
Levorphanol	0.736	(0.537,1.011)
Methadone	1.388	(1.333, 1.445)
Extended-Release Morphine	1.138	(1.108, 1.168)
Extended-Release Oxycodone	1.123	(1.092, 1.154)
Codeine	0.387	(0.382, 0.392)
Buccal Fentanyl	1.064	(0.938, 1.206)
Hydromorphone	0.904	(0.872, 0.938)
Meperidine	0.309	(0.279, 0.342)
Immediate-Release Morphine	0.709	(0.673, 0.747)
Immediate-Release Oxycodone	0.649	(0.639, 0.66)
Age		
	1.012	(1.012, 1.012)
Gender (reference category is Female)		
	0.964	(0.956, 0.973)
Population (reference category is > 1,000,000 population)		
<20,000	1.101	(1.016, 1.193)
20,000–50,000	1.317	(1.263, 1.374)
50,000–100,00	1.416	(1.376, 1.457)
100,000–500,000	1.173	(1.159, 1.187)
500,000–1,000,000	1.088	(1.075, 1.102)

[♦]Reference category: No Use of Multiple Prescribers