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Assessing Opioid Shopping Behaviour

A Large Cohort Study from a Medication Dispensing Database in the US

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Abstract

Background: Risks of abuse, misuse and diversion of opioids are of concern. Obtaining opioid prescriptions from multiple prescribers, known as opioid shopping, is a way in which opioids may be abused and diverted. Previous studies relied on counting the number of prescribers or number of pharmacies a subject goes to in a year to define shopping behaviour, but did not distinguish successive prescribers from concomitant prescribers.

Objective: The aim of the study was to assess the frequency of opioid overlapping prescriptions from different prescribers, compare it with diuretics and benzodiazepines, and provide a definition of shopping behaviour that differentiates opioids from diuretics, avoiding the inappropriate flagging of individuals with legitimate use of opioids.

Study Design: Population-based cohort study using the IMS LRx database. This database covers 65% of all retail prescriptions in the US and includes mail service and specialty pharmacy provider prescriptions independent of the method of payment.

Setting: Ambulatory.

Patients: Subjects with at least one dispensing for any type of opioid in 2008. Similar cohorts were created for subjects exposed to benzodiazepines or diuretics. Analyses were performed separately for naïve subjects and those with prior use.

Outcome: Frequency of overlapping prescriptions defined as at least 1 day of overlapping dispensing of prescriptions written by two or more different prescribers at any time during an 18-month period.

Results: A total of 25 161 024 subjects exposed to opioids were included, of whom 13.1% exhibited at least one episode of overlapping prescriptions during 18 months of follow-up. Almost 10% of subjects exposed to benzodiazepines and 13.8% of subjects exposed to diuretics exhibited a similar behaviour. Having overlapping prescriptions dispensed by three or more pharmacies differentiates opioids from the other medication classes. Using that criterion, the overall risk of shopping behaviour was 0.18% in subjects

exposed to opioids, 0.10% in subjects exposed to benzodiazepines and 0.03% in subjects exposed to diuretics. For opioids, subjects aged between 25 and 64 years exhibited shopping behaviour more commonly (0.25%) than subjects 65 years or older (0.07%), and subjects with a history of prior opioid use exhibited such behaviour more commonly (0.7%) than opioid-naïve subjects (0.07%).

Conclusion: Overlapping of prescriptions is not unique to opioids and therefore a criterion that incorporates number of pharmacies is needed to define shopping behaviour. Having two or more overlapping prescriptions written by different prescribers and filled at three or more pharmacies differentiates opioids from diuretics and likely constitutes shopping behaviour.

Background

Opioids are potent analgesics and are increasingly being prescribed for a variety of acute and chronic pain syndromes.[1] With their increasing use, there is growing concern about the risk of opioid abuse, misuse and diversion.[1,2] Obtaining opioid prescriptions from multiple prescribers, also known as doctor shopping, is a way in which opioids may be abused and their use diverted.[3] Diversion through family and friends is now the greatest source of illicit opioids.[4]

Studies that have assessed doctor-shopping behaviour traditionally rely on counting the number of prescribers or number of pharmacies a subject goes to in a year.[5-8] However, such analyses do not distinguish successive prescribers from concomitant prescribers, and thus may overestimate the risk of shopping behaviour and inappropriately flag individuals with legitimate use of opioids. It is concomitant prescriptions, the possession of overlapping prescriptions from different prescribers, that constitutes doctor shopping[9,10] and allows the subject to receive more than the therapeutic dose;[9,10] the current study focuses on these.

A large, retrospective, population-based cohort study was conducted to assess the frequency of overlapping opioid prescriptions from different prescribers, compare it with diuretics and benzodiazepines, and provide a definition of shopping behaviour that differentiates opioids from diuretics, avoiding the inappropriate flagging of individuals with legitimate use of opioids.

Methods

Data for this study were sourced from the IMS LRx database, which covers 65% of all retail prescriptions in the US, and includes mail service and specialty pharmacy provider prescriptions. For this study, only outpatient prescriptions were used. In the database, the de-identified subject, the pharmacy and the prescriber can be tracked, as well as all dispensed prescriptions regardless of the method of payment. Prescription records are collected directly from pharmacies, which provide encrypted patient identifiers compliant with HIPAA (Health Insurance Portability and Accountability Act) privacy regulations. To uniquely identify a subject who filled prescriptions at multiple pharmacies, a probabilistic match is performed using a proprietary algorithm based on encrypted, non-identifiable elements, such as sex, date of birth, last name, first name, address, city, state, zip code and payer ID.

The advantages of this longitudinal pharmacy database over other databases, such as the prescription monitoring programmes (Statewide electronic databases that collect data on controlled substances dispensed in the State) or the electronic healthcare databases, include the following: not being constrained by State lines as are the Statewide prescription monitoring programmes, and capturing the filling of prescriptions outside the health insurance system (e.g. by payment in cash), whereas such transactions are not captured in insurance payment databases. The disadvantage

is that, unlike those databases, this database does not include diagnoses.

This study compares the rate of overlapping opioid prescriptions and their filling at multiple pharmacies with rates observed in two other therapeutic classes, benzodiazepines, which are also believed to have abuse potential, and diuretics, which are believed to have minimal or no abuse potential, and suggests a definition for shopping behaviour that differentiates opioids from diuretics in an effort to avoid classifying a legitimate opioid user as an opioid shopper.

Inclusion Criteria

Subjects with at least one dispensing of any type of opioid (strong, weak, immediate release, extended release or in combination formulation) in 2008, with 3 months of data prior to the index date (date of first opioid dispensing in the database), and whose pharmacies consistently supplied data to the LRx database during the entire study period were included. A similar cohort was created for subjects exposed to benzodiazepines or any diuretic. The cohorts for each of these therapeutic classes were independent; a subject in the LRx database could be in all three of the cohorts. Subjects were followed for 18 months after the index date.

Outcome

The outcome of interest was shopping behaviour, which was defined as at least 1 day of overlapping dispensings of opioids written by two or more different prescribers at any time during the 18 months of follow-up. For each subject, the shopping episode with the maximum number of overlapping prescriptions during the 18 months of follow-up was tabulated and the number of distinct prescribers and pharmacies that filled prescriptions during the episode was captured. For subjects with multiple episodes with the same number of prescriptions, the first episode was selected for the analysis.

An overlap occurred when two or more dispensings by different prescribers were active on the same day (i.e. a prescription was dispensed during the days' supply of another dispensed prescription). The overlapping prescriptions could include the same or different opioids. Similar definitions of overlap were used for the other medication classes.

As a sensitivity analysis, the minimum time necessary to consider that prescriptions overlapped was extended from 1 day to 4 days to account for the possibility that a subject may not pick up a prescription on the same day the pharmacist entered the prescription into the system.

Additional analyses were performed for subjects who were opioid-naïve and for subjects who had prior opioid use. An opioid-naïve subject was defined as a subject who did not have any opioid dispensing (weak or strong opioid) in the 3 months before the index date. Similar stratifications on naïve versus non-naïve were used for the other medication classes. Analyses were also performed for subjects stratified by age (≤24 years, 25–40 years, 41–64 years and ≥65 years), and sex.

To assess whether the absence of 100% coverage of pharmacies in the LRx database could lead to distortions of the risk of doctor-shopping behaviour, the results were stratified by regional coverage of the LRx database (<80% coverage vs ≥80% coverage). If there were two or more States involved in overlapping prescriptions, all States involved had to have at least 80% coverage to be considered high coverage.

Among the quality checks performed were a search for missing values in the days' supply field (no missing values were found) and out of range values such as 0 days or 365 days' supply (found in 0.01% of the prescriptions). For these prescriptions, we imputed the median days supply from other prescriptions within the same medication class.

Results

A total of 25 161 024 subjects exposed to opioids met the inclusion criteria. The median days' supply for opioids was 10; for benzodiazepines and diuretics, the median was 30. Thirteen percent (13.1%; n = 3 297 891) of subjects exposed to opioids exhibited at least one episode of overlapping prescriptions by at least two different prescribers during the 18 months of follow-up.

9.8% of subjects exposed to benzodiazepines and 13.8% of subjects exposed to diuretics exhibited a similar behaviour (table I).

Overlapping prescriptions were more common in subjects who were non-naïve in all three medication classes, but were especially evident in non-naïve subjects exposed to opioids. Among those with a history of exposure to opioids, 38.3% exhibited overlapping prescriptions compared with 8.5% of those who were opioid-naïve (table I). The corresponding figures for benzodiazepines were 19.5% and 6.0%, respectively, and for diuretics were 17.5% and 10.8%, respectively. Having overlapping prescriptions was less common in the youngest subjects (≤24 years of age) compared with older subjects for all three medication classes. Sex did not affect the frequency of overlapping prescriptions.

Among those with overlapping prescriptions, the number of prescribers was slightly higher in subjects exposed to opioids than in the other groups (tables II, III and IV). For example, in the opioid group, 5.4% of subjects who had overlapping prescriptions had more than two prescribers versus 3.2% of subjects exposed to diuretics or 2.5% of subjects exposed to benzodiazepines (tables II, III and IV).

What differentiated the shopping behaviour with opioids from that of other medication classes more effectively than the number of prescribers was the number of pharmacies involved in the overlapping prescription episodes. Of the subjects who had overlapping prescriptions, dispensing occurred at two or more pharmacies for 21.3% of subjects exposed to opioids, 17.7% of those exposed to benzodiazepines and 8.3% of those exposed to diuretics. The differences in the respective percentages were even more pronounced if the criterion was set as three or more pharmacies (tables II, III and IV). Among subjects with overlapping prescriptions, this stricter criterion was met by 1.3% of those exposed to opioids, 1.0% of those exposed to benzodiazepines and 0.2% of those exposed to diuretics. In terms of all subjects exposed, rather than only those who filled overlapping prescriptions, the respective percentages for filling at three or more pharmacies were 0.18% of those exposed to opioids, 0.10% of

Table I. Characteristics of subjects with overlapping prescriptions in the three medication classes

Group	Opioid			Benzodiazepine			Diuretic		
	Number	Number with overlapping Rxs	Percent with overlapping Rxs	Number	Number with overlapping Rxs	Percent with overlapping Rxs	Number	Number with overlapping Rxs	Percent with overlapping Rxs
Total	25 161 024	3 297 891	13.1	8 595 179	843 654	9.8	8 433 456	1 168 462	13.8
Age, years									
≤24	3 683 278	196 136	5.3	498 217	30 318	6.1	110 563	10 421	9.4
25–40	6 080 704	714 687	11.8	1 764 162	160 241	9.1	642 534	60 468	9.4
41–64	10 535 348	1 661 329	15.8	4 164 038	436 262	10.5	3 719 238	472 545	12.7
≥65	4 750 887	711 623	15.0	2 125 913	213 382	10.0	3 918 944	619 890	15.8
Sex									
Female	15 202 977	2 022 036	13.3	5 810 417	576 818	9.9	5 482 819	733 680	13.4
Male	9 834 192	1 259 096	12.8	2 736 957	262 642	9.6	2 901 003	428 477	14.8
Prior use									
Naïve	21 242 668	1 796 684	8.5	6 188 700	374 242	6.0	4 601 928	499 340	10.8
Non-naïve	3 918 356	1 501 207	38.3	2 406 479	469 412	19.5	3 831 528	669 122	17.5

Rxs = prescriptions.

those exposed to benzodiazepines and 0.03% of those exposed to diuretics (table V).

Using this criterion, subjects between 25 and 64 years exposed to opioids or benzodiazepines more often exhibited shopping behaviour (0.25% and 0.16%, respectively) than subjects exposed to diuretics (0.03%) [table V]. In all three medication classes, subjects with prior use exhibited more shopping behaviour than naïve subjects, but this difference was most striking for opioids, Shopping behaviour was seen for only 0.07% of opioid-naïve subjects but 0.75% of opioid non-naïve subjects (table V).

Five States had 80% or more coverage involving 157 670 individuals with overlapping prescriptions. The degree of participation of pharmacies entering data into the LRx database (<80% coverage or ≥80% coverage) did not substantially affect the observed pattern of overlapping prescriptions for opioids (table VI).

Almost 74% of the subjects had ≤4 days of prescription overlap (table VII). As expected, changing the minimum number of required overlapping days (from at least 1 day to 4 days) to determine whether or not the prescriptions overlapped decreased the number of subjects with opioid overlapping prescription episodes, from 13.1% to 7.7%, but did not substantially change the pattern of overlapping (tables I and VIII). Similarly to the results with at least one day of overlap, what differentiated shopping behaviour with opioids from that of other medication classes was dispensings at three or more pharmacies; 1.25% of the subjects with overlapping opioid prescriptions filled the prescriptions in three or more pharmacies compared with 1.01% of the subjects exposed to benzodiazepines and 0.22% of the subjects exposed to diuretics (table VIII). By way of context for the choice of a 4-day overlap, rather than a longer one, the median number of days' supply was 10 days for opioids.

Discussion

This large-scale, population-based study measured the frequency of overlapping opioid prescriptions written by different prescribers, compared it with other medication classes and suggested

Table II. Number (%) of subjects with overlapping opioid prescriptions by number of prescribers and number of pharmacies involved

Number of prescribers	Number of pharmacies 1	2	3	4	5	6	7	8	9	Total
2	2 490 742 (75.5)	604 510 (18.3)	24 435 (0.7)	1351 (0.0)	112 (0.0)	7 (0.0)	1 (0.0)	2 (0.0)	0	3 121 160 (94.6)
3	101 740 (3.1)	48 765 (1.5)	14 096 (0.4)	1140 (0.0)	100 (0.0)	9 (0.0)	2 (0.0)	0	1 (0.0)	165 853 (5.0)
4	4 324 (0.1)	3 281 (0.1)	1 741 (0.1)	661 (0.0)	82 (0.0)	5 (0.0)	1 (0.0)	0	0	10 095 (0.3)
5	237 (0.0)	197 (0.0)	121 (0.0)	105 (0.0)	42 (0.0)	9 (0.0)	3 (0.0)	1 (0.0)	0	715 (0.0)
6	6 (0.0)	13 (0.0)	12 (0.0)	10 (0.0)	10 (0.0)	5 (0.0)	1 (0.0)	0	0	57 (0.0)
7	1 (0.0)	2 (0.0)	0	0	0	3 (0.0)	1 (0.0)	0	0	7 (0.0)
8	0	1 (0.0)	0	0	0	0	1 (0.0)	0	0	2 (0.0)
9	0	0	0	1 (0.0)	0	0	0	0	0	1 (0.0)
12	1 (0.0)	0	0	0	0	0	0	0	0	1 (0.0)
Total	**2 597 051 (78.7)**	**656 769 (19.9)**	**40 405 (1.2)**	**3 268 (0.1)**	**346 (0.0)**	**38 (0.0)**	**10 (0.0)**	**3 (0.0)**	**1 (0.0)**	**3 297 891 (100)**

Table III. Number (%) of subjects with overlapping benzodiazepine prescriptions by number of prescribers and number of pharmacies involved

Number of prescribers	Number of pharmacies						Total
	1	2	3	4	5	6	
2	682 592 (80.9)	134 713 (16.0)	5154 (0.6)	246 (0.0)	20 (0.0)	1 (0.0)	822 726 (97.5)
3	11 724 (1.4)	5 887 (0.7)	2195 (0.3)	189 (0.0)	14 (0.0)	0	20 009 (2.4)
4	293 (0.0)	262 (0.0)	194 (0.0)	85 (0.0)	18 (0.0)	1 (0.0)	853 (0.1)
5	9 (0.0)	7 (0.0)	15 (0.0)	17 (0.0)	7 (0.0)	3 (0.0)	58 (0.0)
6	0	0	2 (0.0)	1 (0.0)	1 (0.0)	3 (0.0)	7 (0.0)
8	0	0	1 (0.0)	0	0	0	1 (0.0)
Total	**694 618 (82.3)**	**140 869 (16.7)**	**7 561 (0.9)**	**538 (0.1)**	**60 (0.0)**	**8 (0.0)**	**843 654 (100)**

a definition for shopping behaviour that differentiated opioids from diuretics to avoid classifying a legitimate opioid user as an opioid shopper.

It found that overlapping of prescriptions is not unique to opioids. Not only is it present with benzodiazepines, but also with diuretics. This finding indicated that the use of simultaneous prescriptions written by different prescribers to define shopping behaviour, although better than counting successive prescriptions, prescribers or pharmacies, needed to be further refined by also including information on the number of different pharmacies where such overlapping prescriptions were filled to avoid classifying a legitimate opioid user as an opioid shopper.

There are many legitimate reasons for an individual to have many opioid prescribers in the course of a year or even overlapping opioid prescriptions written by different prescribers, including appropriate service by multiple specialized physicians, physician coverage arrangements for vacation or group practice, relocation of the subject to a different neighbourhood, or inadequate pain control. Therefore, any effort to classify a subject as an opioid shopper needs to have a high predictive positive value, both to ensure the classification is useful as a research tool and to limit the frequency with which erroneously flagged individuals might suffer inconvenience or undertreatment of pain. A study that assessed the impact of being aware of the information in the prescription monitoring programmes on prescribing behaviour showed that such knowledge resulted in fewer or no opioid medications prescribed to patients in the majority of the cases.[11]

Having overlapping prescription by different prescribers, filled at three or more pharmacies, clearly distinguishes opioids from diuretics and is highly predictive of shopping behaviour. Using this definition, 0.18% of subjects exposed to opioids and 0.03% of those exposed to diuretics had shopping behaviour, suggesting that using this definition only a small proportion of the subjects identified as shoppers are false positives. On the

Table IV. Number (%) of subjects with overlapping diuretics prescriptions by number of prescribers and number of pharmacies involved

Number of prescribers	Number of pharmacies							Total
	1	2	3	4	5	6	7	
2	1 040 802 (89.1)	89 090 (7.6)	1372 (0.1)	30 (0.0)	3 (0.0)	1 (0.0)	0	1 131 298 (96.8)
3	29 371 (2.5)	5 156 (0.4)	839 (0.1)	30 (0.0)	0	0	1 (0.0)	35 397 (3.0)
4	1 235 (0.1)	308 (0.0)	110 (0.0)	26 (0.0)	0	0	0	1 679 (0.1)
5	47 (0.0)	16 (0.0)	8 (0.0)	4 (0.0)	3 (0.0)	0	0	78 (0.0)
6	2 (0.0)	3 (0.0)	0	2 (0.0)	0	1 (0.0)	0	8 (0.0)
7	0	0	0	0	0	0	1 (0.0)	1 (0.0)
12	1 (0.0)	0	0	0	0	0	0	1 (0.0)
Total	**1 071 458 (91.7)**	**94 573 (8.1)**	**2 329 (0.2)**	**92 (0.0)**	**6 (0.0)**	**2 (0.0)**	**2 (0.0)**	**1 168 462 (100)**

Table V. Frequency of shopping behaviour defined as ≥2 overlapping prescriptions written by different prescribers and dispensed in ≥3 pharmacies

Group	Opioid			Benzodiazepine			Diuretic		
	Number	Number with overlapping Rxs and ≥3 pharmacies	Percent with overlapping Rxs and ≥3 pharmacies	Number	Number with overlapping Rxs and ≥3 pharmacies	Percent with overlapping Rxs and ≥3 pharmacies	Number	Number with overlapping Rxs and ≥3 pharmacies	Percent with overlapping Rxs and ≥3 pharmacies
Total	25 161 024	44 071	0.18	8 595 179	8167	0.10	8 433 456	2431	0.03
Age, years									
≤24	3 683 278	2 245	0.06	498 217	459	0.09	110 563	30	0.03
25–40	6 080 704	14 911	0.25	1 764 162	2751	0.16	642 534	210	0.03
41–64	10 535 348	23 459	0.22	4 164 038	4236	0.10	3 719 238	1142	0.03
≥65	4 750 887	3 450	0.07	2 125 913	718	0.03	3 918 944	1048	0.03
Sex									
Female	15 202 977	25 188	0.17	5 810 417	5113	0.09	5 482 819	1577	0.03
Male	9 834 192	18 836	0.19	2 736 957	3046	0.11	2 901 003	853	0.03
Prior use									
Naïve	21 242 668	14 643	0.07	6 188 700	3192	0.05	4 601 928	990	0.02
Non-naïve	3 918 356	29 428	0.75	2 406 479	4975	0.21	3 831 528	1441	0.04

Rxs = prescriptions.

other hand, a very specific definition might miss many individuals demonstrating genuine shopping behaviour, but for many study designs it is more important to have a low frequency of false positives than to identify all true cases.

Incorporating the number of pharmacies where medications were obtained to monitor the use of opioid prescription has been suggested before.[5] A study that assessed opioid prescribing in subjects receiving schedule II opioids using the prescription monitoring programme in Massachusetts from 1996 to 2006 defined 'questionable activity' as individuals receiving opioids through three or more prescribers and three or more pharmacies in a year. That study, however, counted successive prescribers and was restricted to schedule II opioids, and therefore, not surprisingly, reported a higher percentage of subjects with 'questionable activity'. It found that 1.6% of subjects receiving schedule II opioids had such activity.[5] Another study that grouped subjects with different degrees of 'deviant behaviour' exposed to buprenorphine in France using cluster techniques found that the number of pharmacies helped form the clusters and that the higher the number of pharmacies, the higher the proportion of subjects with doctor-shopping behaviour.[12]

Table VI. Number (%) of overlapping prescriptions in subjects exposed to opioids by coverage of pharmacies in the LRx database

	<80% of coverage [n (%)]	≥80% of coverage [n (%)]
Number of prescribers		
2	2 970 766 (94.6)	150 394 (95.4)
3	158 963 (5.1)	6 890 (4.4)
4	9 730 (0.3)	365 (0.2)
5	696 (0.0)	19 (0.0)
6	55 (0.0)	2 (0.0)
7	7 (0.0)	0
8	2 (0.0)	0
9	1 (0.0)	0
12	1 (0.0)	0
Number of pharmacies		
1	2 467 224 (78.57)	129 827 (82.34)
2	630 336 (20.07)	26 433 (16.76)
3	39 099 (1.25)	1 306 (0.83)
≥4	3 562 (0.11)	104 (0.89)
Total	**3 140 221 (100)**	**157 670 (100)**

Additional findings of the present study are that, for shopping behaviour as defined by overlapping prescriptions filled at three or more pharmacies, prior opioid use increases the risk of such behaviour 10-fold and that subjects aged 25–64 years of age more often exhibited shopping behaviour than older subjects. These results are consistent with the literature on opioid abuse. Age is a strong

Table VII. Number of days of overlap for opioid prescriptions

Overlap days	Percentage of subjects	Number of subjects
1	25.39	837 232
2	23.06	760 390
3	16.38	540 271
4	8.96	295 596
5	8.66	285 731
6	3.46	113 996
7	3.53	116 408
8	2.05	67 474
9	1.13	37 388
10	2.00	65 908
11–30	5.36	176 804
Missing	0.02	693
Total	**100**	**3 297 891**

predictor for opioid abuse – the risk decreases with increasing age – as is the longer the duration of exposure to opioids.[13,14] The lower frequency of shopping behaviour among those aged <25 years likely reflects the fact that many of the subjects in this age group were children.

In the present study, a 1-day overlap of prescriptions was part of the definition of shopping behaviour. It is important to emphasize that the overlapping had to be for prescriptions written by different providers, so prescriptions for short- and long-acting opioids written by the same physician will not meet the criterion. The 1-day rule could be considered very strict, so we conducted a sensitivity analysis using 4 days of overlap. The change of definition of overlap did not change the pattern of shopping behaviour in any of the groups and confirmed that the use of three or more pharmacies is what differentiated the drug classes.

To uniquely identify subjects who filled prescriptions at multiple pharmacies, a probabilistic match was performed. The algorithm could lead to false negatives or false positives. False negatives could arise when the algorithm fails to identify two subjects as the same individual because the minimum number of required encrypted attributes do not match. False positives could arise when two subjects have similar names, dates of birth and addresses. False positives could also arise when, for example, a subject changes doctors, gets a new prescription and fills the new prescription during

Table VIII. Characteristics of subjects with overlapping prescriptions using a definition of at least a 4-day overlap in the prescriptions

Group	Opioid			Benzodiazepine			Diuretic		
	Number	Number with overlapping Rxs	Percent with overlapping Rxs	Number	Number with overlapping Rxs	Percent with overlapping Rxs	Number	Number with overlapping Rxs	Percent with overlapping Rxs
Total	25 161 024	1 937 130	7.7	8 595 179	587 241	6.8	8 433 456	936 922	11.1
Number of subjects filling in ≥3 pharmacies	25 161 024	24 177	1.25	8 595 179	5 974	1.01	8 433 456	2 066	0.22
Age, years									
≤40	9 763 982	412 161	4.2	2 262 379	129 335	5.7	753 097	56 078	7.4
41–64	10 535 348	1 036 689	9.8	4 164 038	302 325	7.3	3 719 238	371 319	10.0
≥65	4 750 887	478 997	10.1	2 125 913	153 248	7.2	3 918 944	505 420	12.9
Sex									
Female	15 202 977	1 194 724	7.9	5 810 417	402 815	6.9	5 482 819	581 826	10.6
Male	9 834 192	731 472	7.4	2 736 957	181 559	6.6	2 901 003	350 079	12.1
Prior use									
Naïve	21 242 668	865 444	4.1	6 188 700	255 318	4.1	4 601 928	409 831	8.9
Non-naïve	3 918 356	1 071 686	27.3	2 406 479	331 923	13.8	3 831 528	527 091	13.7

Rxs = prescriptions.

the period covered by the old one for legitimate reasons. The relatively small frequency of shopping behaviour among diuretic users with our definition of shopping behaviour represents an estimate of the maximum false positive rate for opioid shopping behaviour.

The suggested definition of shopping behaviour – having two or more overlapping prescriptions written by different prescribers and dispensed in three or more pharmacies clearly differentiates opioids from diuretics and thus provides validation that what is being measured is indeed shopping behaviour. The fact that shopping behaviour is substantially more common among opioid non-naïve subjects than among opioid-naïve subjects also supports this view. Another way to validate it would be to assess whether or not subjects with shopping behaviour have a higher risk of opioid abuse. It was not possible to link our definition to a diagnosis of opioid abuse or addiction because the database lacks such information. Yet, the use of three of more pharmacies and more than 12 prescriptions in a year, as well as early refills, have already been associated with an increased risk of opioid abuse.[6]

The LRx database does not have 100% coverage of all pharmacy transactions in the US and underrepresents independent pharmacies, which could lead to an underestimation of the shopping behaviour. This could especially impact analyses involving opioids because opioid shoppers go to more pharmacies than subjects exposed to other medication classes, and some of those pharmacies may not provide data to the LRx database. To assess this potential limitation, States with at least 80% coverage were compared with those with <80% coverage. The similarity of the two groups of States in regard to the frequency distribution for the number of prescribers involved in overlapping opioid prescriptions provides further confidence in the results of this study.

Conclusions

This is the largest population-based study that quantifies the frequency of overlapping prescriptions and compares it with three medication classes. Its findings suggest that having two or more overlapping prescriptions written by different prescribers and filled at three or more pharmacies is uncommon, is substantially more common with two drug classes that are liable to abuse than with drugs in a class that is not, and is substantially more common among repeat users than among new users. It is likely that most, but not all, such episodes represent shopping behaviour. Results of this study suggest that until all states have prescription monitoring programmes that are integrated across States, commercial longitudinal pharmacy databases are a useful tool for monitoring opioid shopping behaviour and drug utilization.

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