

Shopping Behavior for ADHD Drugs: Results of a Cohort Study in a Pharmacy Database

M. Soledad Cepeda · Daniel Fife · Joris Berwaerts · Yingli Yuan · Greg Mastrogiovanni

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Abstract

Objective Attention-deficit hyperactivity disorder (ADHD) medications are subject to abuse, misuse, and diversion. Obtaining ADHD prescriptions from multiple prescribers or filled across multiple pharmacies, known as ‘doctor shopping’, may reflect such unsanctioned use. We sought to create a definition of shopping behavior that differentiated ADHD medications from medications with low risk of diversion, i.e. asthma medications, and describe the incidence, frequency, and demography of shopping behavior.

Methods This was a retrospective cohort study in a pharmacy database—LRx—covering 65 % of US retail pharmacies. Subjects had ADHD or asthma medication dispensed between February 2011 and January 2012. We followed subjects for 18 months to assess the number with overlapping dispensings from different prescribers, and the number of prescribers and pharmacies involved in those dispensings.

Results We included 4,402,464 subjects who were dispensed ADHD medications, and 6,128,025 subjects who were dispensed asthma medications. Overlapping prescriptions from two or more prescribers dispensed by three or more pharmacies was four times more frequent in the ADHD cohort than in the asthma cohort. Using this definition, ADHD medication shopping behavior was more common among experienced users than naïve users, and

was most common in subjects aged 10–39 years. Among subjects who shopped, 57.4 % shopped only once (accounting for 22.4 % of episodes), and 9.2 % shopped six or more times (accounting for 42.0 % of episodes). Shoppers more often received stimulant ADHD drugs than non-stimulants.

Conclusions Overlapping prescriptions by different prescribers and filled at three or more pharmacies defines ADHD medication shopping. Shopping behavior is most common in adolescents and younger adults. A small proportion of shoppers is responsible for a large number of shopping episodes.

Key Points

Attention-deficit hyperactivity disorder (ADHD) medications may be subject to abuse, misuse, and diversion.

We found that overlapping prescriptions from two or more prescribers dispensed by three or more pharmacies defines ADHD medication shopping.

1 Introduction

Medications for the treatment of attention-deficit hyperactivity disorder (ADHD) are subject to misuse, abuse, and diversion [1–3]. The non-medical use of ADHD medications in high-school-age children in the US is estimated at around 9 %, and in college-age individuals goes from 5 to 35 % [1]. The increase in recent years in the number of emergency visits involving ADHD medications for non-

M. S. Cepeda (✉) · D. Fife · J. Berwaerts
Janssen Research & Development, LLC, 1125 Trenton
Harbourton Rd, Titusville, NJ 08560, USA
e-mail: scepeda@its.jnj.com

Y. Yuan · G. Mastrogiovanni
IMS Health, Collegeville, PA, USA

medical use (use not prescribed for the respondent by a physician or use only for the experience or feeling caused [4]) [5] reflects these problems. Obtaining ADHD prescriptions from multiple prescribers and/or filling prescriptions across multiple pharmacies, often called doctor or pharmacy shopping, may reflect such unsanctioned use [1, 6].

Doctor-shopping behavior is increasingly recognized for opioids [7–10], but less is known about doctor-shopping behavior for ADHD medications. On the basis of data from California's Prescription Monitoring Programs, 1.4 % of subjects dispensed ADHD medication had multiple providers in 2007 [11]. However, it is unclear how the behavior should be defined, how many individuals engage in the behavior (incidence), how often it occurs in a given subject or across subjects (frequency), the impact of age and sex on such behavior, or whether a small proportion of subjects are responsible for a large proportion of shopping episodes (concentration).

Developing a definition of shopping behavior for ADHD medications will help identify subjects who may be at higher risk of misusing/abusing or diverting. We sought to create an operational definition of shopping behavior that differentiated ADHD medications from medications with low risk of abuse or diversion, such as asthma medications. Such a definition will therefore decrease the risk of inappropriately identifying individuals with legitimate use of ADHD medications as being at increased risk of misusing/abusing or diverting those medicines. Such misclassification may adversely affect the individual who is misclassified (e.g. social stigma) and, secondly, it is potentially deleterious to research studies that assess shopping behavior and abuse because random misclassification would bias the studies toward the null and thus obscure the signals of interest. Once we defined shopping behavior, we also sought to describe its incidence and frequency, the impact of age and sex on shopping behavior, and the type of ADHD medication involved in the shopping episodes.

2 Method

2.1 Data Collection

We conducted a population-based retrospective cohort study using the LRx database, a longitudinal pharmacy database that covers 65 % of all retail dispensing in the US and includes all types of pharmacies—chains, food stores, mass merchandisers, and independent stores. From each of the pharmacies in the panel, the database captures *all* prescriptions that were dispensed, regardless of payment type. In particular, it includes prescriptions filled for

patients with any insurance type (commercial, Medicare, Medicaid) and prescriptions paid for entirely in cash. Dispensing records are collected directly from pharmacies, which provide encrypted patient identifiers compliant with Health Insurance Portability and Accountability Act (HIPAA) privacy regulations. The LRx database includes data on the subject (de-identified), the pharmacy, and the prescriber.

To uniquely identify a subject who filled prescriptions at multiple pharmacies, a probabilistic multi-level match was performed using a proprietary algorithm based on encrypted non-identifiable data elements including sex, date of birth, last name, first name, address, city, state, zip code, and payer identification.

2.2 Inclusion Criteria

We included all subjects dispensed an ADHD or asthma medication between 1 February 2011 and 31 January 2012 who had data available for at least 4 months prior to the first dispensing (index date), and whose pharmacies consistently supplied data to the LRx database during the entire study period. Each subject was followed for 18 months from his/her index date.

A subject who was dispensed ADHD and asthma medications could be a member of both cohorts.

2.3 Prescription/Dispensing Data

We included all ADHD medications whose ingredients were approved by the US FDA for the treatment of ADHD. These were the stimulants amphetamine, dexamethylphenidate, dextroamphetamine, lisdexamfetamine, methamphetamine, and methylphenidate, and the non-stimulants atomoxetine, clonidine, and guanfacine.

The asthma medications included were inhaled bronchodilators, inhaled steroids, inhaled steroid/long-acting β agonist combinations, and oral leukotriene inhibitors. Asthma medications were used as a comparator because they are frequently used by a population with roughly similar demographic characteristics as the population using ADHD medications [12], including a large representation of children and young adults, and are not believed to be widely abused or diverted [13].

Subjects who were not dispensed any ADHD medication during the 4 months before their index date were considered 'naive'. The 4-month period, rather than a shorter period, was adopted to decrease the risk of misclassifying as naive a subject who was receiving an ADHD medication during the school year but took a planned break in its use during 3 or 4 months of vacation (i.e. took a 'drug holiday').

2.4 Outcome

We assessed the number of subjects with overlapping dispensings of medications prescribed by different prescribers, and the number of prescribers and number of pharmacies involved in those dispensings, during the 18 months of follow-up. For subjects with more than one event of multiple overlapping filled prescriptions, we selected the one event with the maximum number of overlapping prescriptions. Note that a prescriber can write more than one prescription for a given individual, therefore the total number of pharmacies making dispensings for that individual may exceed the number of prescribers.

An overlap occurred when two or more dispensings of medications prescribed by different prescribers were active on the same day (i.e. a medication was dispensed during the days' supply of another dispensed medication). The overlapping dispensings could be for the same or different ADHD or asthma medications.

To set a definition of shopping behavior that differentiated ADHD medications from asthma medications, we qualitatively compared the frequency distribution of subjects across the number of prescribers and pharmacies between the two cohorts—the larger the ratio in the proportion of subjects, the larger the difference in behavior between the two cohorts. The best cut-off of number of pharmacies and number of prescribers also had to have a sufficient proportion of subjects to provide a useful marker of unsanctioned use.

Once the definition was selected, we identified subjects who met the definition, i.e. subjects with at least one event of overlapping prescriptions written by two or more prescribers and filled at three or more pharmacies. The index or qualifying event did not necessarily occur during the episode with the highest number of overlapping prescriptions. We then assessed how soon the shopping episode was observed during follow-up of a given subject (i.e. median time from index date to first shopping episode), the total number of events across all subjects according to age category, sex, and prior exposure (naïve or experienced), and the concentration of shopping (extent to which a relatively small proportion of shoppers accounted for a relatively large proportion of shopping episodes). Each time there was a new dispensing, the definition of shopping behavior was applied and, if the criteria were met, a new shopping episode was counted.

To make sure that the subjects dispensed prescribed asthma medication had a similar age distribution to the subjects dispensed ADHD medications, the asthma subjects were frequency-matched to the ADHD subjects by single year of birth.

This study used completely anonymized data and did not involve patient contact. The New England Institutional

Review Board determined that this was not human-subject research.

3 Results

A total of 4,402,464 subjects dispensed ADHD medications and 6,128,025 subjects dispensed asthma medications were included in the analysis. The age distribution (mean \pm SD) of the subjects was similar in the two cohorts—24.1 \pm 16.2 years of age in the ADHD medication cohort and 24.2 \pm 16.8 in the asthma medication cohort, as would be expected from the age matching. In the ADHD medication cohort, 43.9 % were female, and in the asthma medication cohort, 55.6 % were female.

The distribution of pharmacies and prescribers visited by subjects was markedly different in subjects who received ADHD drugs compared with those who received asthma drugs.

Overlapping prescriptions written by two or more prescribers and dispensed at two or more pharmacies were approximately twofold more frequent in the ADHD medication cohort than in the asthma medication cohort, and occurred in 198,923 subjects in the ADHD medication cohort (4.5 %) and in 120,163 subjects in the asthma medication cohort (2.0 %) [Tables 1 and 2].

Overlapping prescriptions written by two or more prescribers and dispensed at three or more pharmacies were approximately fourfold more frequent in the ADHD medication cohort than in the asthma medication cohort, and occurred in 11,861 subjects in the ADHD medication cohort (0.27 %) and in 4,226 subjects in the asthma medication cohort (0.07 %) [Tables 1 and 2].

Overlapping prescriptions written by two or more prescribers and dispensed at five or more pharmacies were approximately 28-fold more frequent in the ADHD medication cohort than in the asthma medication cohort; however, this occurred in only 143 subjects in the ADHD medication cohort (0.003 %), and in seven subjects in the asthma medication cohort (0.0001 %) [Tables 1 and 2].

We therefore adopted overlapping prescriptions written by two or more prescribers and filled at three or more pharmacies as the definition of ADHD medication shopping behavior. This definition of shopping behavior clearly discriminated between subjects dispensed ADHD medications and subjects dispensed asthma medications, and was sufficiently common to serve as a marker suggestive of unsanctioned use.

Using this definition, we found that ADHD medication shopping behavior was most commonly observed between 10 and 39 years of age. No large differences in frequency of shopping behavior were observed between men and women. Shopping behavior was observed in 13,707

Table 1 Number of subjects exposed to ADHD medications, with their number of prescribers and pharmacies visited^a

Number of pharmacies	1	2	3	4	5	6	7	Total
Number of prescribers								
1	3,555,122 (80.8)	(0)	(0)	(0)	(0)	(0)	(0)	3,555,122 (80.8)
2	640,049 (14.5)	182,818 (4.2)	9,056 (0.2)	611 (0)	44 (0)	8 (0)	2 (0)	832,588 (18.9)
3	8,183 (0.2)	4,141 (0.1)	1,616 (0)	278 (0)	48 (0)	4 (0)	1 (0)	14,271 (0.3)
4	184 (0)	100 (0)	88 (0)	57 (0)	20 (0)	3 (0)	(0)	452 (0)
5	3 (0)	2 (0)	4 (0)	7 (0)	6 (0)	5 (0)	1 (0)	28 (0)
6	(0)	1 (0)	1 (0)	(0)	1 (0)	(0)	(0)	3 (0)
Total	4,203,541 (95.5)	187,062 (4.2)	10,765 (0.24)	953 (0)	119 (0)	20 (0)	4 (0)	4,402,464 (100)

ADHD attention-deficit hyperactivity disorder

^a The figure in parentheses represents the percentage of the total number of subjects (4,402,464)

Table 2 Number of subjects exposed to asthma medications, with their number of prescribers and pharmacies visited^a

Number of pharmacies	1	2	3	4	5	9	Total
Number of prescribers							
1	5,320,404 (86.8)	(0)	(0)	(0)	(0)	(0)	5,320,404 (86.8)
2	650,913 (10.6)	106,486 (1.7)	2,748 (0)	68 (0)	2 (0)	1(0)	760,218 (12.4)
3	34,526 (0.6)	8,731 (0.1)	1,169 (0)	44 (0)	2 (0)	(0)	44,472 (0.7)
4	1,931 (0)	665 (0)	147 (0)	18 (0)	2 (0)	(0)	2,763 (0.1)
5	85 (0)	52 (0)	17 (0)	6 (0)	(0)	(0)	160 (0)
6	3 (0)	3 (0)	(0)	1 (0)	(0)	(0)	7 (0)
7	(0)	(0)	1 (0)	(0)	(0)	(0)	1 (0)
Total	6,007,862 (98)	115,937 (1.9)	4,082 (0.07)	137 (0)	6 (0)	1(0)	6,128,025 (100)

^a The figure in parentheses represents the percentage of the total number of subjects (6,128,025)

(0.6 %) of 2,360,546 non-naïve subjects, and in 4,423 (0.2 %) of 2,041,918 naïve subjects (Table 3). Note that this prevalence of shopping behavior is higher than that observed in Table 1 because of the different ways episodes were counted, as described in Sect. 2.4.

Among subjects who shopped, the median time from the first dispensing of ADHD medications to the first shopping episode was approximately 7 months, and was slightly shorter in non-naïve subjects than naïve subjects (Table 3).

Approximately 58 % of all subjects dispensed ADHD medications who exhibited shopping behavior had only one episode of shopping during the 18 months of follow-up, and these subjects accounted for 22.4 % of all shopping episodes. In contrast, the 9.2 % of shoppers who shopped six times or more accounted for 42.0 % of all the shopping episodes (Table 4). Relative to non-shoppers and the overall group of shoppers, these latter subjects were more likely to be between 30 and 39 years of age and not naïve to ADHD medications (Table 3).

Dispensing of stimulant ADHD medications was more common among subjects exhibiting shopping behavior than among subjects without such behavior; odds ratio 8.3, 95 % confidence interval 6.9–10.2 (Table 5).

4 Discussion

This large population-based cohort study suggests that the operational definition of ADHD medication shopping behavior has the greatest discriminative value when subjects have overlapping prescriptions for ADHD medications written by different prescribers and filled at three or more pharmacies. Similar behavior is very rare in subjects prescribed asthma medications.

A study conducted in a French claims database found, similar to our findings, that a small proportion of subjects (0.5–1 %) received their medication from a large number of distinct prescribers and pharmacies, which suggested abuse [14].

The definition of shopping behavior for ADHD medications is the same as for opioids [7, 8]. Similarly to opioid shopping behavior, shopping behavior is observed in less than 1 % of those dispensed ADHD medications and tended to occur in young adults; approximately half the subjects who exhibited shopping behavior did so only once, and a small proportion of subjects accounted for a disproportionately large percentage of shopping episodes. As for opioids, subjects with prior exposure were more likely

Table 3 Incidence of shopping behavior, time to first shopping episode, number of subjects with six or more shopping episodes, by age, sex, and prior use of ADHD medications

Group	Number of subjects exposed to ADHD medications (col. %)	Number (col. %) of subjects with shopping behavior	Number of days to first shopping episode (median)	Number (col. %) of subjects with six or more shopping episodes
Total	4,402,464	18,130 (0.4)	225	1,666 (9.2)
Age, years				
<10	640,430 (14.5)	2,322 (12.8)	287.5	70 (4.2)
10–19	1,714,153 (38.9)	3,794 (20.9)	246	193 (11.6)
20–29	743,932 (16.9)	4,517 (24.9)	227	418 (25.1)
30–39	457,853 (10.4)	3,789 (20.9)	190	506 (30.4)
40–49	392,840 (8.9)	2,084 (11.5)	202.5	253 (15.2)
50–59	296,421 (6.7)	1,275 (6)	195	175 (10.5)
60–69	116,655 (2.6)	302 (1.7)	163	45 (2.7)
≥70	40,180 (0.9)	47 (0.3)	207	6 (0.4)
Sex				
Female	1,934,829 (43.9)	8,807 (48.6)	214	910 (54.6)
Male	2,467,635 (56.0)	9,323 (51.4)	234	756 (45.4)
Prior use of ADHD medications				
Naïve	2,041,918 (46.4)	4,423 (24.4)	237	222 (13.3)
Non-naïve	2,360,546 (53.6)	13,707 (75.6)	221	1,444 (86.7)

Prior use of ADHD medications refers to the presence or absence of dispensing 4 months prior to the initial prescription in the study period
ADHD attention-deficit hyperactivity disorder, *Col.* Column

Table 4 Frequency of shopping episodes for subjects with shopping behavior

Number of shopping episodes during the follow-up period	Number (%) of subjects with shopping behavior	Number (%) of shopping episodes
1	10,413 (57.4)	10,413 (22.4)
2	3,345 (18.5)	6,690 (14.4)
3	1,443 (8.0)	4,329 (9.3)
4	795 (4.4)	3,180 (6.9)
5	468 (2.6)	2,340 (5.0)
6–9	915 (5.1)	6,637 (14.3)
10–20	585 (3.2)	7,834 (16.9)
21–83	166 (0.9)	4,992 (10.8)
Total	18,130	46,415

to become shoppers. Also in parallel with opioid shoppers, who tended to receive strong opioids, ADHD medication shoppers were more likely to receive ADHD medications that are stimulants.

The fact that the criteria that serve to identify subjects who engage in ADHD medication shopping behavior and opioid shopping behavior are similar seems to suggest that overlapping prescriptions written by different prescribers and filled at three or more pharmacies can be used as an operational definition to assess shopping behavior for medications that are prone to abuse and diversion in general. It is worth noting that subjects abusing a specific drug are likely to abuse other drugs or have a higher risk of

developing abuse when exposed to other medications with abuse potential [15–18].

In contrast to opioids for which 0.5 % of shoppers were aged 18 years or younger [8], we found that at least 13 % of shoppers were very young (less than 10 years of age); this finding likely represents diversion by their parents or caregivers [19]. We also found that a small number of subjects were responsible for a disproportionately large number of shopping episodes, which likely also represents diversion of ADHD medications. A survey of undergraduate students found that their leading source of ADHD medications for non-medical use was friends and peers [20].

Table 5 Type of ADHD dispensed to subjects with and without shopping behavior^a

	Number (%) of subjects without shopping behavior	Number (%) of subjects with shopping behavior	Odds ratio (95% CI) for shopping behavior vs. being dispensed any stimulant ADHD medication
Stimulants	4,179,353 (95.3)	18,024 (99.4)	8.3 (6.9–10.2)
No stimulants	204,981 (4.7)	106 (0.6)	
Total number (%) of subjects	4,384,334 (100)	18,130 (100)	

ADHD attention-deficit hyperactivity disorder, CI confidence interval

^a For subjects exhibiting shopping behavior, we looked for stimulants during any shopping episode; for non-shoppers we looked for stimulants during any dispensing

The low frequency of shopping behavior observed in this study is likely to be an underestimate of the true incidence. The LRx database does not have 100 % coverage of all pharmacy transactions in the US, and online transactions are not covered. Of note, the matching algorithm used to uniquely identify subjects could fail to identify two subjects as the same individual if a minimum number of required encrypted attributes did not match, and thus would fail to discern a subject who presented false identification. However, no other data source will permit an assessment across the whole of the US or will capture cash prescriptions, which are very relevant when evaluating the risk of diversion [8].

We aimed for a definition that would avoid false positives (subjects who, for many reasons, could have different prescribers and pharmacies but were not shopping). A definition that limits misclassification of subjects, especially by reducing the number of false positive subjects, is crucial for research and health policy. To obtain such definition, we compared subjects dispensed asthma medications, which are less likely to be abused, with subjects dispensed ADHD medications with a higher intrinsic risk of abuse. Asthma and ADHD medications differ with respect to scheduling, and may differ in patterns of prescription (e.g. number of prescribers involved in care). These distinctions may have differentially affected our estimates of the numbers of prescribers and pharmacies visited by subjects in the asthma medication cohort and thus confounded the observed differences in shopping behavior between the two groups. In addition, this study did not address possible differences in socioeconomic status between the asthma and ADHD medication cohorts. For example, if the prevalence of asthma and lack of continuity in care are associated with low socioeconomic status, then this could lead to a higher risk of a subject with asthma being classified as a shopper, with socioeconomic status being a mediating factor.

We found a small difference in the median time to first shopping episode between naïve and non-naïve

ADHD medication subjects. The small size of this difference may reflect misclassification error, with subjects who were non-naïve being classified as naïve because the look-back period that we implemented was limited to 4 months, while the recommended medication-free period ('drug holiday') for ADHD medications may have extended beyond 4 months. We also observed dispensings of ADHD medications to subjects aged 70 years or older. These dispensings could be for the treatment of conditions different from ADHD. However, we report the incidence of shopping behavior stratified by age category.

This study did not assess the intent of subjects who engaged in shopping behavior or the association with the comorbid diagnosis of substance abuse or dependence. It can be argued that counting the number of distinct pharmacies and prescribers is more objective and accurate than measuring a construct that is subjective and difficult to measure, such as abuse or dependence. Our intent was to find a combination of pharmacies and prescribers that differentiated between subjects prescribed ADHD medications who were more likely to engage in non-medical use, and subjects prescribed medications that are not prone to abuse or dependence, such as asthma medications. We found such a definition. Furthermore, the behavior was more commonly observed in young subjects, which strengthens the validity of the findings. In addition, the definition for ADHD medication shopping behavior was found to be the same as the one used to define opioid shopping behavior, and that definition has been explicitly linked to opioid abuse [21]. Nonetheless, understanding why subjects need to visit multiple pharmacies and prescribers, and determining whether or not they are misusing, abusing, or diverting the ADHD medications, will increase the acceptance of the definition of shopping behavior as it relates to ADHD medications, and will help health care providers or insurers implement monitoring to decrease the risk of abuse or diversion.

5 Conclusions

ADHD medication shopping behavior can be defined as subjects with overlapping prescriptions written by two or more prescribers and filled at three or more pharmacies. Shopping behavior is more commonly observed in younger ages, and a small number of subjects is responsible for a disproportionately large number of shopping episodes.

Declaration of interest M.S. Cepeda, D. Fife, and J. Berwaerts are employees of Janssen Research and Development, LLC, an affiliate of Janssen Pharmaceuticals, Inc. which markets CONCERTA® brand methylphenidate HCl, an ADHD medication. They hold stocks in Johnson & Johnson, the parent company of Janssen Research & Development, LLC.

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