

Persistence, Augmentation, and Consumption of Long-Acting Medications in ADHD Patients

Paul Hodgkins, PhD, MSc; Rahul Sasané, PhD; Laura Christensen, MS; Haim Erder, PhD; and Carolyn Harley, PhD

Attention-deficit/hyperactivity disorder (ADHD), a neurobehavioral condition,¹ affects approximately 4% of adults in the United States.² Stimulants such as methylphenidate (MPH) and amphetamine form the mainstay of ADHD pharmacotherapy.^{3,4} Three nonstimulant drugs are currently approved for use in the United States (guanfacine extended-release [ER], clonidine ER, and atomoxetine [ATX]).

Persistence is a measure of the time a patient continues taking the initial medication; lack of efficacy, tolerability issues, or difficulties with dosing compliance could cause persistence periods to end. Persistence among patients with mental health disorders is frequently suboptimal.^{5,6} However, data relating to treatment patterns for adults with ADHD are limited. One study indicated that adults persisted on therapy for a mean of 200 days, with the majority of patients persisting for less than 6 months.⁷ The study also found that 1.2% of adults augmented their index therapy with another stimulant, 11.1% switched to a new stimulant, and 53.7% required dose titration. In another study of adults with ADHD, only 50.5% of patients receiving immediate-release (IR) formulations of MPH and 61.4% of patients receiving ER formulations had more than 1 pharmacy claim for their index medication.⁸

Persistence and medication consumption patterns are appropriate metrics for comparing the utilization of medications. Daily average consumption (DACON) calculations are particularly relevant to healthcare payers because higher DACON values can be associated with increased medication costs and increased pharmacy budget. Although multi-therapy approaches impact medication costs, the pattern of augmentation of an index medication can provide information on its real-world effectiveness.

The present study focused on the utilization of long-acting ADHD medications within a US-based managed care system. Specifically, the study compared persistence, DACON, and augmentation rates for different long-acting ADHD

ABSTRACT

Objectives: To examine the relationship between pharmacy costs related to attention-deficit/hyperactivity disorder (ADHD) and persistence, daily average consumption (DACON), and augmentation in adults with ADHD.

Study Design: Retrospective analysis of pharmacy claims data from a commercial health plan between January 2007 and April 2008.

Methods: Costs were calculated as the sum of health plan and patient copayments for all ADHD medications; persistence as the total days patients remained on index therapy; and DACON as the quantity of medication supplied during the follow-up period divided by the total days of supply.

Results: In total, 2819 patients received long-acting ADHD medications (mixed amphetamine salts extended release [MAS XR], n = 1514; osmotic-release oral system methylphenidate [OROS-MPH], n = 546; atomoxetine [ATX], n = 513; lisdexamfetamine dimesylate [LDX], n = 246). Mean persistence was highest in LDX (116 days) and MAS XR (115 days) patients versus ATX (75 days) and OROS-MPH (83 days) patients. Higher DACON was associated with higher median cost for all medications ($P < .0001$ for each). Average costs were lowest for LDX. Overall, 235 patients (8.3%) augmented their index medication at an incremental burden of \$60 (LDX), \$244 (MAS XR), \$232 (OROS-MPH), and \$516 (ATX) added to median costs, equivalent to a 23% (LDX) to 141% (ATX) increase in acquisition costs.

Conclusions: LDX users had lower DACON and longer persistence, and were less likely to augment the index treatment resulting in higher index and total drug costs. Incremental cost associated with augmentation of index medication was lowest for LDX.

(*Am J Pharm Benefits*. 2012;4(6):e149-e158)

PRACTICAL IMPLICATIONS

This study examined the relationship between pharmacy costs related to attention-deficit/hyperactivity disorder (ADHD) and utilization variables: daily average consumption (DACON), augmentation, and persistence.

- Adult ADHD-related pharmacy costs were lowest for long-acting treatments and either associated with lower DACON or unaugmented with other ADHD medications.
- Among the long-acting ADHD medications, lisdexamfetamine dimesylate had the highest persistence and lowest DACON, and the lowest incremental cost burden associated with treatment augmentation.
- Payers managing pharmacy budgets for ADHD treatment should consider persistence on therapy, costs associated with DACON, and treatment augmentation, as well as direct acquisition costs.

medications, and their relationships to total ADHD-related pharmacy costs.

METHODS

This was a retrospective study of pharmacy claims data collected between January 2007 and April 2008. Costs included the amount paid by the insurance plan and the amounts paid by the patient.

Data Source

The claims data included medical and pharmacy claims, and eligibility information from a large, geographically diverse, national US health plan (>12 million enrollees with medical and pharmacy coverage). Medical claims included *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)* diagnosis codes, *ICD-9-CM* procedure codes, Current Procedural Terminology, version 4 procedure codes, Healthcare Common Procedure Coding System procedure codes, site of service codes, and health plan and patient costs. Outpatient pharmacy claims provided National Drug Codes for dispensed medications, quantity dispensed, drug strength, days of supply, and health plan and patient costs.

Patient Population

Adult patients with a preindex medical claim diagnosis of ADHD (*ICD-9-CM* diagnosis codes 314.00-314.9) and with 1 or more filled prescriptions for a long-acting ADHD treatment (index medication, including lisdexamfetamine dimesylate [LDX], mixed amphetamine salts extended release [MAS XR], osmotic-release oral system MPH [OROS-MPH], dexamethylphenidate extended release [d-MPH XR],

transdermal MPH, or ATX) between July 2007 and October 2007 were identified. Patients were aged 18 to 55 years at index date (date of earliest filled prescription), with continuous plan enrollment in pharmacy and medical benefits for 6 months prior to the index date (preindex period) and with pharmacy benefits for 6 months after the index date (follow-up period). Patients with prescription(s) for ADHD medications during the 6-month preindex period were excluded.

Outcomes

Outcomes were measured from the index date to the end of the follow-up period.

The number of prescriptions filled and the number of days of index medication supplied for the index medication were recorded. If the patient filled more than 1 prescription for the index medication on a given day, only 1 was counted in the calculation of persistence. If more than 1 prescription was filled on the index date, the prescription fill with the higher number of days of supply was used in calculations of days of supply. Counts of days supplied that were more than 183 were set to 183 (the duration of the follow-up period).

Persistence. Persistence was the total number of days the patient remained on index therapy. Patients were considered to have terminated therapy on the date of the last fill if the days of supply of that fill ran out more than 30 days prior to the end of the follow-up period. If the days of supply of the last fill ran out within 30 days of the end (or after the end) of the follow-up, persistence was set at 183 days.

DACON of the Index Medication. The DACON of the index medication was the quantity of medication supplied during the follow-up period divided by total number of days of supply. A DACON value of 1 indicated that a patient was dispensed 1 pill per day of the index medication. DACON values of more than 1 were indicative of a patient taking more than 1 pill daily. Mean DACON values and the proportion of patients with a DACON of 1 pill were recorded.

Augmentation. Augmentation was the filling of 1 or more prescriptions for any ADHD medication other than the index medication 30 days or more before the last prescription for the index medication was refilled. Thus, patients with a prescription fill for another ADHD medication before the last fill of the index medication were considered to have augmented the index therapy; those who switched ADHD medications (those with no prescription fills for the index medication after a prescription fill for another ADHD medication) were not captured in this definition. Augmentation medications were not limited to long-acting

Table 1. Characteristics of ADHD Patients, by Index Medication^a

Characteristic	Total (N = 2982)	LDX (n = 246)	MAS XR (n = 1514)	OROS-MPH (n = 546)	ATX (n = 513)	P (Across Index Medications)
Age, y						
Mean	30.0	30.1	29.5	29.1	32.1	<.0001
SD	11.0	10.2	10.7	11.4	10.9	
Median	27.0	29.0	26.0	23.5	32.0	
Range	18-55	18-55	18-55	18-55	18-55	
Age group, n (%)						
18-23	1252 (42.0)	87 (35.4)	661 (43.7)	273 (50.0)	158 (30.8)	<.0001
24-29	417 (14.0)	40 (16.3)	229 (15.1)	55 (10.1)	79 (15.4)	.0106
30-55	1313 (44.0)	119 (48.4)	624 (41.2)	218 (39.9)	276 (53.8)	<.0001
Sex, n (%)						
Male	1527 (51.2)	123 (50.0)	723 (47.8)	302 (55.3)	292 (56.9)	.0027
Female	1455 (48.8)	123 (50.0)	791 (52.3)	244 (44.7)	221 (43.1)	.0027
Health plan region, n (%)						
Northeast	198 (6.6)	11 (4.5)	89 (5.9)	53 (9.7)	33 (6.4)	.0328
Midwest	797 (26.7)	47 (19.1)	408 (27.0)	160 (29.3)	141 (27.5)	.0655
South	1674 (56.1)	173 (70.3)	865 (57.1)	272 (49.8)	268 (52.2)	<.0001
West	313 (10.5)	15 (6.1)	152 (10.0)	61 (11.2)	71 (13.8)	.0200
ADHD indicates attention-deficit/hyperactivity disorder; ATX, atomoxetine; LDX, lisdexamfetamine dimesylate; MAS XR, mixed amphetamine salts extended release; OROS-MPH, osmotic-release oral system methylphenidate; SD, standard deviation.						
^a Patients on index transdermal methylphenidate and dexmethylphenidate extended release were excluded from analyses by index medication because of low patient numbers (n = 39 and n = 124, respectively).						

medications, and included MPH (IR or ER, or transdermal system), d-MPH (IR or XR), MAS (IR or XR), dextroamphetamine (IR or sustained release), LDX, and ATX. The proportion of patients augmenting their index medication, the number of augmentations dispensed, and the most frequently used augmentation medications were calculated.

Pharmacy costs during follow-up were calculated from the claims data as the sum of health plan costs and patient-paid amounts for all ADHD medications (index, augmentation, and total). ADHD-related pharmacy costs and incremental cost burdens were also calculated separately by DACON (additional costs by DACON level) and augmentation (additional costs associated with augmentation vs no augmentation).

Statistical Analysis

Study variables were analyzed descriptively. Numbers and percentages were recorded for dichotomous and polychotomous variables. Means, medians, and SDs were calculated for analyses of cost, days of supply, and count of prescription fills. Means and standard deviations (SDs) were calculated for analyses of continuous DACON values. Results were stratified by index medication. Proportions were compared using the χ^2 test, and means were compared using the *t* test. Distributions of costs were compared using the Mann-Whitney *U* test because of the skewed nature of these data. Additional statistics

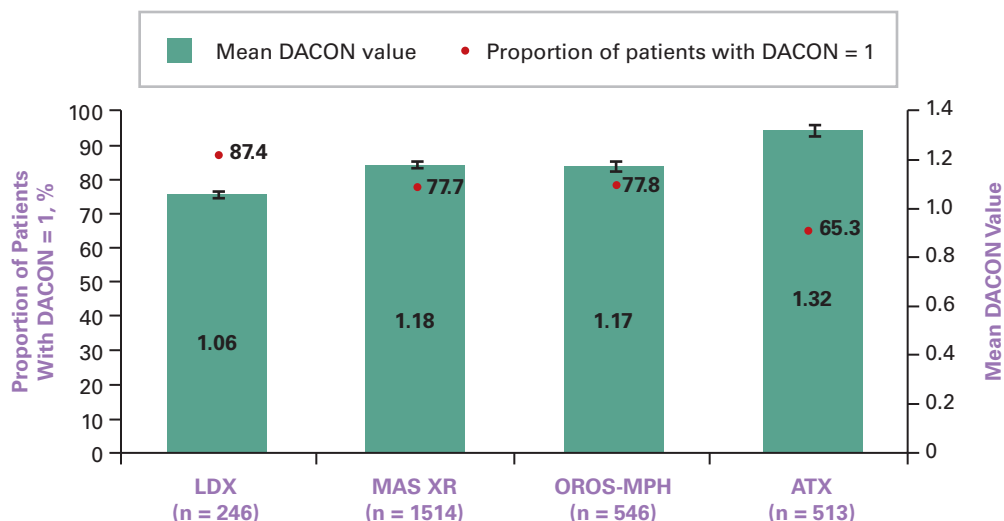
(minimum, maximum, 25th percentile, and 75th percentile) were calculated for persistence analyses, as the Mann-Whitney *U* test results were significant (indicating a difference in distributions) in some persistence analyses despite equal medians. To examine outcomes in those patients with longer persistence, additional analyses were undertaken for the subpopulation of patients with at least 90 days of supply of the index medication in the follow-up period. These included comparisons of the proportion of patients augmenting their index medication (using the χ^2 test) and of ADHD-related pharmaceutical costs during the follow-up period (using the Mann-Whitney *U* test). A *P* value of $\leq .05$ was considered statistically significant.

RESULTS Patients

A total of 126,022 patients were identified with a claim for a long-acting index medication between July and October 2007. Of these, 30,835 met the age requirements and continuous enrollment requirements for the 6 months prior to and 6 months after the index date, and 2982 patients were considered newly treated ADHD subjects and met all inclusion criteria for the study.

The mean age of patients was 30.0 years (Table 1). Approximately half of the eligible patients were male (males, n = 1527, 51.2%; females, n = 1455, 48.8%) and approximately half (1514/2982, 50.8%) received index

Figure 1. Mean DACON and Proportion of ADHD Patients With DACON of 1 Pill^a



ADHD indicates attention-deficit/hyperactivity disorder; ATX, atomoxetine; DACON, daily average consumption; LDX, lisdexamfetamine dimesylate; MAS XR, mixed amphetamine salts extended release; OROS-MPH, osmotic-release oral system methylphenidate.

^aError bars represent standard error. Patients on index transdermal methylphenidate and dexmethylphenidate extended release were excluded from analyses by index medication because of low patient numbers (n = 39 and n = 124, respectively).

treatment with MAS XR, followed by OROS-MPH (n = 546; 18.3%), ATX (n = 513; 17.2%), and LDX (n = 246; 8.2%). The sample sizes for the transdermal MPH (n = 39) and d-MPH XR (n = 124) cohorts were too small to allow for meaningful comparisons among groups; hence, they were excluded from subsequent analyses by index medication but were included in statistics reflecting the entire study population.

Persistence

The median length of time that patients continued their index therapy was 105 days (mean, 100.3 days). The median duration of persistence was longest for patients taking LDX (183 days; mean, 116.5 days) and MAS XR (183 days; mean, 115.4 days). The median duration of persistence was 36 days for ATX (mean, 74.9 days) and 58 for OROS-MPH (mean, 82.6 days). The Mann-Whitney *U* test revealed that longer persistence associated with DACON of more than 1 pill versus DACON of 1 pill was statistically significant for LDX (median 183 vs 183 days, respectively; mean 149.6 vs 111.7 days [*P* = .0213]) and MAS XR (median 183 vs 183 days, respectively; mean 129.6 vs 111.3 days [*P* = .0002]).

Of the 2819 patients, the number of prescriptions filled was highest for those receiving index therapy with LDX (4; mean, 3.66), followed by MAS XR (3; mean, 3.57), OROS-MPH (2; mean, 2.77), and ATX (2; mean, 2.58). The corresponding median numbers of days of supply of

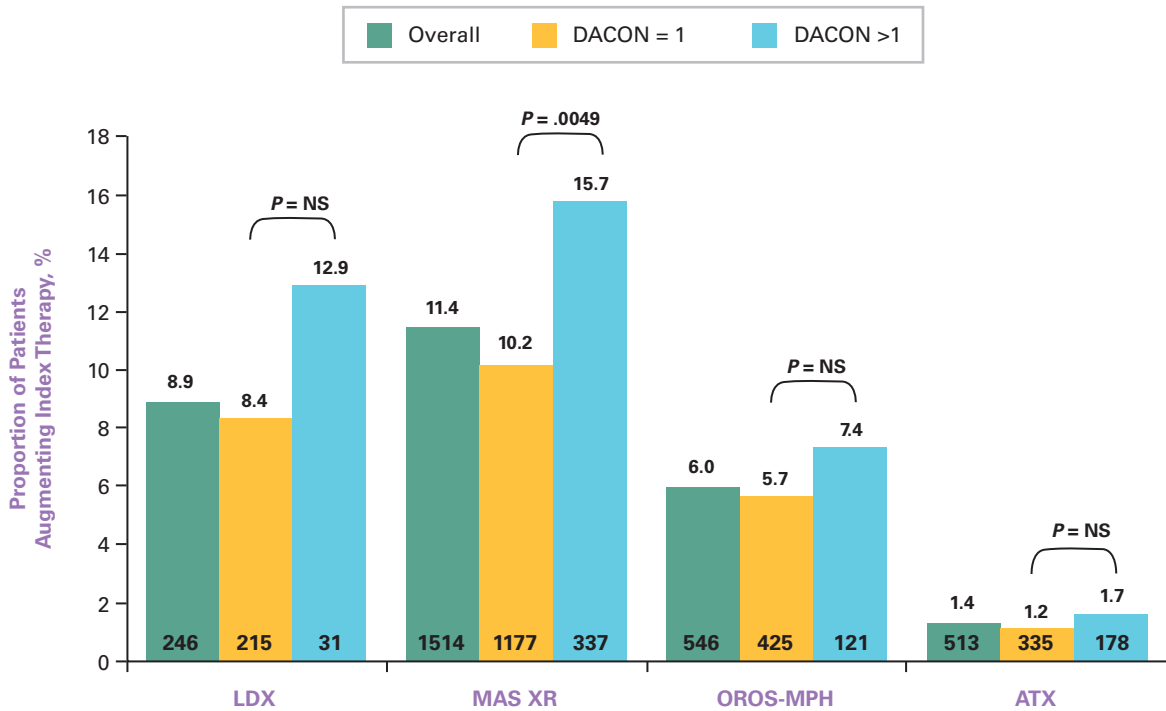
index medication were 113 for LDX (mean, 103.6), 91 for MAS XR (mean, 101.1), 60 for OROS-MPH (mean, 81.5), and 60 for ATX (mean, 79.8).

Daily Average Consumption. Of the 2819 patients, 2284 (81%) had a DACON of 1 pill; no patient had a DACON of less than 1 pill. Patients receiving index LDX had the lowest mean DACON (1.06 pills) and the largest proportion of patients with DACON of 1 pill (87.4%). Patients taking ATX had the highest mean DACON (1.32 pills) and the smallest proportion of patients with DACON of 1 pill (65.3%; **Figure 1**). Among the 698 patients with DACON of more than 1 pill, the mean (± SD) DACON was 1.45 (± 0.41) for LDX, 1.81 (± 0.57) for MAS-XR, 1.78 (± 0.51) for OROS-MPH, and 1.91 (± 0.44) for ATX.

Augmentation

Approximately 1 in 12 patients in the overall population augmented their index therapy (235/2819 patients, 8.3%). This proportion ranged from 1.4% for ATX to 11.4% for MAS XR; proportions for the other index medications were 6.0% (OROS-MPH) and 8.9% (LDX). A larger proportion of patients with DACON of more than 1 pill augmented their index therapy than those with DACON of 1 pill for all index medications, with this difference reaching statistical significance for MAS XR (15.7% of those with DACON >1 pill vs 10.2% of those with DACON = 1 pill; *P* = .0049; **Figure 2**).

Figure 2. Proportion of ADHD Patients Augmenting Their Index Therapy, by Index Medication and Mean DACON^a



ADHD indicates attention-deficit/hyperactivity disorder; ATX, atomoxetine; DACON, daily average consumption; LDX, lisdexamfetamine dimesylate; MAS XR, mixed amphetamine salts extended release; NS, not significant; OROS-MPH, osmotic-release oral system methylphenidate.

^aNumber inside base of each column indicates total number of patients in that group. Patients on index transdermal methylphenidate and dexamethylphenidate extended release were excluded from analyses by index medication because of low patient numbers (n = 39 and n = 124, respectively).

Patients with index amphetamines received augmentation mainly with other amphetamine formulations (141/173 patients augmented MAS XR with a generic AMPH salt combination). Similarly, most patients augmenting index OROS-MPH therapy did so with other MPH formulations (30/33 patients).

Cost Analyses

Medication Costs. Pharmacy costs per prescription fill at the drug level ranged from \$119 for index LDX to \$182 for index ATX. Pharmacy costs per prescription for the other medications were \$141 for MAS XR and \$139 for OROS-MPH (see [Appendix](#)).

Mean costs for nonindex ADHD medications (ie, those to which patients were switched or those that were used to augment index therapy) ranged from \$38 for patients taking index MAS XR to \$100 for those taking LDX. Median cost for nonindex ADHD medications was 0 for all index drug cohorts because fewer than half the patients in each group augmented therapy.

Overall, the mean ADHD-related pharmacy cost during the 6-month follow-up period was \$518 (median cost, \$460). Patients taking index ATX had the highest mean ADHD-related pharmacy costs (\$557), followed by

those taking MAS XR (\$542), LDX (\$536), and OROS-MPH (\$436) ([Table 2](#)).

DACON and Pharmacy Costs. Total mean pharmacy costs were lower for patients with DACON of 1 pill compared with those with DACON of more than 1 pill. The median ADHD-related total pharmacy costs for patients with DACON of 1 pill were significantly lower than the costs for those with DACON of more than 1 pill in the follow-up period ($P < .0001$ for all medications; [Figure 3](#)). Incremental costs for patients with DACON of more than 1 pill (calculated as the absolute difference in median costs or as a proportion of the mean costs of DACON of 1 pill) were lowest for LDX patients (\$234, 61%), followed by OROS-MPH (\$241, 80%), ATX (\$310, 88%), and MAS XR (\$342, 96%) patients.

Augmentation and Pharmacy Costs. Total mean ADHD-related pharmacy costs were higher for all index medications with augmentation than without augmentation ([Table 2](#)). Median costs were significantly higher for patients who augmented their index medication than for patients who did not ($P < .05$ for all medications). The difference in median costs between those who augmented and those who did not was smallest for LDX (\$603 vs \$543, difference \$60; $P = .0391$; increment 23%) and

Table 2. Total and Incremental ADHD-Related Pharmaceutical Costs During Follow-up, by Augmentation^{a,b}

Medication	Overall	Augmentation		Increment ^c	P
		No	Yes		
LDX					
Mean	\$536.25	\$525.33	\$647.40	23.2%	
SD	\$295.26	\$296.70	\$260.80		
Median	\$543.31	\$543.07	\$603.42	\$60.35	.0391
MAS XR					
Mean	\$542.19	\$511.92	\$776.82	51.8%	
SD	\$393.32	\$384.09	\$385.94		
Median	\$470.91	\$460.78	\$704.41	\$243.63	<.0001
OROS-MPH					
Mean	\$436.11	\$419.37	\$696.40	66.1%	
SD	\$325.08	\$310.06	\$432.78		
Median	\$341.05	\$334.22	\$566.54	\$232.32	<.0001
ATX					
Mean	\$556.89	\$546.39	\$1315.61	140.8%	
SD	\$421.32	\$402.33	\$918.11		
Median	\$468.84	\$467.40	\$983.26	\$515.86	.0046

ADHD indicates attention-deficit/hyperactivity disorder; ATX, atomoxetine; LDX, lisdexamfetamine dimesylate; MAS XR, mixed amphetamine salts extended release; OROS-MPH, osmotic-release oral system methylphenidate; SD, standard deviation.

^aTotal costs for index and nonindex ADHD medications.

^bPatients on index transdermal methylphenidate and dexamethylphenidate extended release were excluded from analyses by index medication because of low patient numbers (n = 39 and n = 124, respectively).

^cFor mean values, this is the difference in costs between the augmentation and no-augmentation groups, expressed as a percentage of the no-augmentation costs. For median values, this is the difference in costs between the augmentation and no-augmentation groups.

largest for ATX (\$983 vs \$467, difference \$516; P = .0046; increment 141%) (Table 2).

DISCUSSION

As pharmacotherapy is currently the mainstay treatment for ADHD,⁴ increased diagnosis rates will likely result in an increase in total spending on drug and nondrug therapies. The impact on pharmacy budgets in the United States from the increased unit costs of newer ER agents likely will be partly offset by the provision of these agents at higher copay levels than IR formulations. However, payers may be under increased pressure to approve the least costly treatments available that offer the best quality of care for patients. It is important to consider outcome measures in addition to the variety of cost measures. For example, augmentation of the index medication may cause an incremental increase to a pharmacy budget, but overall treatment outcomes may be improved, with lower overall healthcare costs.⁹⁻¹¹

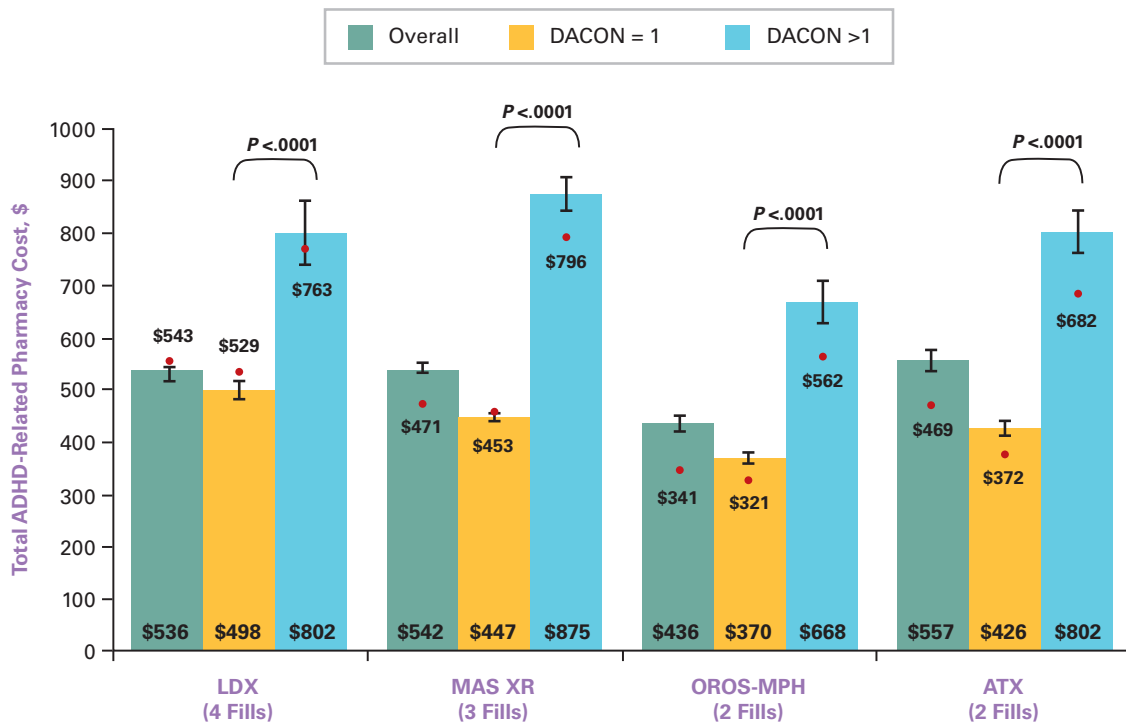
Our study population, with a mean patient age of 30.0 years, had a virtually equal male-female distribution (1:1), whereas in a recent community-based study higher male prevalence was noted.¹² However, the prevalence of diagnosed ADHD among adult females may

be on the increase, as a shift in the ratio of females to males, increasing from 0.55 to 0.76 over a period of 5 years, was noted.¹³ It is possible that this shift reflects the increasing recognition that ADHD is equally likely to affect females and males, although historically it has been more commonly recognized in males, particularly children.

In our study, LDX was associated with relatively high pharmacy costs during the follow-up, partly due to the long(er) persistence (mean persistence, 116.5 days) compared with the other long-acting drug classes evaluated (mean persistence, 74.9-115.4 days). Further, LDX users also had the highest number of prescription fills, resulting in the lowest mean per prescription costs of the long-acting medications evaluated.

Our results indicate that once-daily dosing was not always achieved. Most patients achieved DACON of 1 pill and did not require augmentation, but a sizable minority had DACON of more than 1 pill (~1 in 4) or required augmentation (~1 in 12). Patients taking index ATX had the highest mean DACON (1.32 pills), which is not surprising given that ATX can be prescribed for either once- or twice-daily dosing. For all 4 long-acting medications,

Figure 3. Total ADHD-Related Pharmacy Costs, by DACON Category^{a,b}



ADHD indicates attention-deficit/hyperactivity disorder; ATX, atomoxetine; DACON, daily average consumption; LDX, lisdexamfetamine dimesylate; MAS XR, mixed amphetamine salts extended release; OROS-MPH, osmotic-release oral system methylphenidate.

^aTotal costs for index and nonindex ADHD medications.

^bColumns represent mean costs; circles represent medians; error bars represent standard error. Number of fills in parentheses represents median number of prescription fills for the index medication. *P* values relate to comparisons of median costs. Patients on index transdermal methylphenidate and dexmethylphenidate extended release were excluded from analyses by index medication because of low patient numbers (*n* = 39 and *n* = 124, respectively).

higher DACON values were associated with higher pharmacy costs, likely due to the increased pill burden. The increase in ADHD-related pharmacy costs from DACON of 1 pill to DACON of more than 1 pill was lowest among index LDX users and highest among those taking MAS XR. The mean per prescription cost of LDX (\$119) was lower than that for the other medications, which may explain why LDX had the lowest cost increase associated with DACON of more than 1 pill. However, even for LDX, the cost increment associated with DACON values above 1 was large when expressed in absolute terms or as a proportion of the mean cost associated with DACON of 1 pill, confirming the importance of DACON calculations in determining the total impact of long-acting ADHD medications on pharmacy budgets.

Augmentation was higher among stimulant users than among ATX users. As previously reported,¹⁴⁻¹⁶ augmentation with 1 or more ADHD medications during follow-up was associated with higher median ADHD pharmacy costs for the entire follow-up period, regardless of index medication. The incremental cost of augmentation was highest

for ATX and lowest for LDX. For LDX, augmentation only added \$60 (23%) to median treatment costs, despite LDX having the lowest pharmacy cost per prescription brand, which meant that the augmenting medications may have been more expensive than LDX. In contrast, augmentation added more than 50% to the pharmacy costs for subjects with index MAS XR and OROS-MPH, and more than doubled the costs for subjects with index ATX. For LDX, MAS XR, and OROS-MPH, the cost increments were lower for augmentation than for increased DACON, although the increments associated with augmentation were still considerable.

The mean cost of nonindex ADHD medications was higher for LDX patients (\$100) than for other long-acting ADHD medications (the drugs commercially available for augmentation/switching may have been more expensive than LDX). However, fewer than half of patients in each group augmented therapy, so median costs for nonindex ADHD medications were 0 for all drugs. Notably, the mean costs of ADHD medications were higher in our study compared with the costs reported,

with differences attributed to methodology and patient population (6-month mean ADHD drug cost was \$282 for OROS-MPH, \$322 for MAS XR, and \$392 for ATX).¹⁷

Limitations

The data were derived from pharmacy claims data collected for payment and not for research. A filled prescription neither guaranteed that medication was consumed nor that it was taken as prescribed. No correction was made for length of prescription, and it is possible that prescription duration may have differed by drug; however, since the stimulants are controlled drugs and typically dispensed with a 30-day prescription, the impact of this possibility was considered limited. Although the number of prescriptions filled and the days of index medication supplied were recorded, the numbers of patients who filled multiple prescriptions for the index medication on a given day and who had multiple fills on the index date were not measured.

This study aimed to evaluate medication utilization among newly treated patients. On this basis, 19.7% of patients were excluded because of prior/ongoing treatment in the 6-month preindex period.

The numbers of patients receiving transdermal MPH or d-MPH XR was small (<5% of total population); hence, they were excluded from drug-specific analyses (but did contribute to overall analysis population). There were higher proportions of males in the OROS-MPH and ATX groups, which may have confounded comparisons with other groups; this is particularly relevant for patients receiving OROS-MPH, as responses to this medication have been reported to differ between male and female children.¹⁸

Diagnostic code requirements for ADHD as well as a prescription for an ADHD medication reduced the likelihood that a patient without ADHD would be incorrectly included. While a 6-month period with no prior ADHD medications was required for study entry, this did not guarantee that all patients were newly treated, as those on an extended “drug holiday” could have also fulfilled the inclusion criteria.

Finally, this study did not consider generic drugs. At present, the only long-acting drug formulation for the treatment of ADHD that has a generic equivalent is MAS XR. This generic form was introduced in the market in April 2009, after our data set was obtained and analyzed; therefore, no information on generic drugs could be obtained from our data.

CONCLUSIONS

Managing a pharmacy budget requires comprehensive evaluation of treatment outcomes and various costs.

Several factors affect the total pharmacy costs: the cost of all index medication prescriptions filled (a product of the per prescription cost and the number of prescriptions filled) and the cost of all nonindex medications filled for augmentation. In our study population, LDX users had lower DACON and longer persistence on the index drug, and were less likely to augment the index treatment, resulting in higher index and total drug costs. Thus, it is recommended that pharmacy managers consider the benefits of persistence on therapy as well as the costs associated with higher DACON and augmentation when choosing ADHD drug treatment.

Acknowledgments

The authors acknowledge the writing assistance of Andy Brown, PhD, of PAREXEL. Financial support for this assistance was provided by Shire Development LLC.

Author Affiliations: From Global Health Economics and Outcomes Research (PH, RS, HE), Shire Development LLC, Wayne, PA; Health Economics and Outcomes (LC), OptumInsight, Ann Arbor, MI; Health Economics and Outcomes (CH), OptumInsight, Palo Alto, CA.

Funding Source: This study was funded by Shire Development LLC.

Author Disclosures: Drs Hodgkins and Erder report that they are employees of Shire Development LLC and own stock/stock options in the company. The other authors (RS, LC, CH) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (PH, RS, LC, CH); acquisition of data (RS); analysis and interpretation of data (PH, RS, HE, LC, CH); drafting of the manuscript (PH, HE, RS); critical revision of the manuscript for important intellectual content (PH, RS, LC, HE, CH); statistical analysis (RS); obtaining funding (PH); administrative, technical, or logistic support (RS); and supervision (PH, RS, HE, CH).

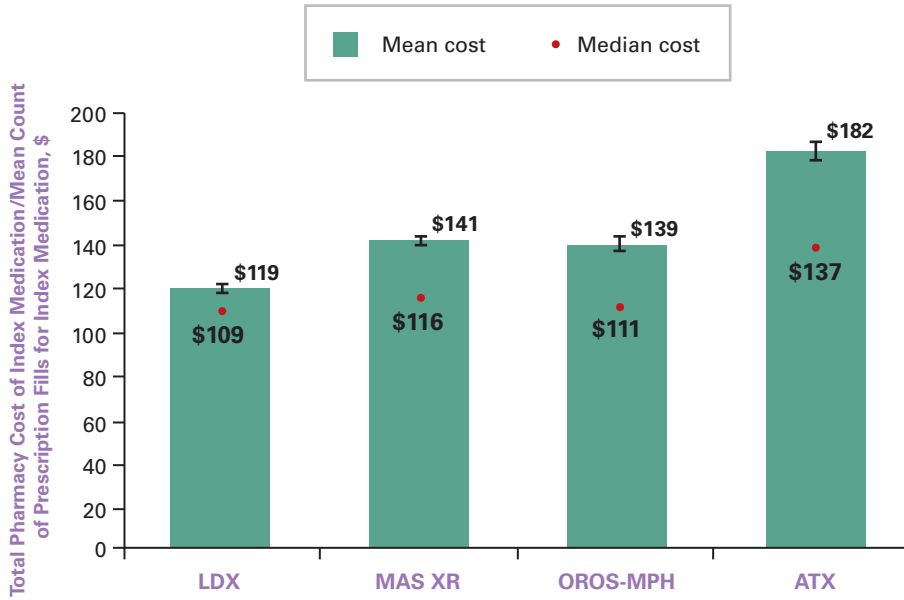
Address correspondence to: Paul Hodgkins, PhD, MSc, Senior Director Global Health Economics and Outcomes Research, Shire Development LLC, 725 Chesterbrook Blvd, Wayne, PA 19087. E-mail: phodgkins@shire.com.

REFERENCES

1. Harpin VA. The effect of ADHD on the life of an individual, their family, and community from preschool to adult life. *Arch Dis Child.* 2005;90(suppl 1):i2-i7.
2. Kessler R, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry.* 2006;163(4):716-723.
3. Biederman J, Faraone SV. Attention-deficit hyperactivity disorder [published correction appears in *Lancet.* 2006;367(9506):210]. *Lancet.* 2005;366(9481):237-248.
4. Brown RT, Amler RW, Freeman WS, et al; American Academy of Pediatrics Committee on Quality Improvement; American Academy of Pediatrics Subcommittee on Attention-Deficit/Hyperactivity Disorder. Treatment of attention-deficit/hyperactivity disorder: overview of the evidence. *Pediatrics.* 2005;115(6):e749-e757.
5. Cooper C, Bebbington P, King M, et al. Why people do not take their psychotropic drugs as prescribed: results of the 2000 National Psychiatric Morbidity Survey. *Acta Psychiatr Scand.* 2007;116(1):47-53.
6. Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. *Value Health.* 2008;11(1):44-47.
7. Perwien A, Hall J, Swensen A, Swindle R. Stimulant treatment patterns and compliance in children and adults with newly treatment attention-deficit/hyperactivity disorder. *J Manag Care Pharm.* 2004;10(2):122-129.
8. Olsson M, Marcus SC, Zhang HF, Wan GJ. Continuity in methylphenidate treatment of adults with attention-deficit/hyperactivity disorder. *J Manag Care Pharm.* 2007;13(7):570-577.

9. Faber A, van Agthoven M, Kalverdijk LJ, et al. Long-acting methylphenidate-OROS in youths with attention-deficit hyperactivity disorder suboptimally controlled with immediate-release methylphenidate: a study of cost-effectiveness in The Netherlands. *CNS Drugs*. 2008;22(2):157-170.
10. Zhu B, Ascher-Svanum H, Faries DE, Correll CU, Kane JM. Cost of anti-psychotic polypharmacy in the treatment of schizophrenia. *BMC Psychiatry*. 2008;8:19.
11. Gibson PJ, Damler R, Jackson EA, Wilder T, Ramsey JL. The impact of olanzapine, risperidone, or haloperidol on the cost of schizophrenia care in a Medicaid population. *Value Health*. 2004;7(1):22-35.
12. Ramtekkar UP, Reiersen AM, Todorov AA, Todd RD. Sex and age differences in attention-deficit/hyperactivity disorder symptoms and diagnoses: implications for DSM-V and ICD-11. *J Am Acad Child Adolesc Psychiatry*. 2010;49(3):217-228. e1-3.
13. Montejano L, Sasané R, Hodgkins P, Russo L, Huse D. Adult ADHD: prevalence of diagnosis in a US population with employer health insurance. *Curr Med Res Opin*. 2011;27(suppl 2):5-11.
14. Chen L, McCombs JS, Park J. The impact of atypical antipsychotic medications on the use of health care by patients with schizophrenia. *Value Health*. 2008; 11(1):34-43.
15. Stahl SM. Antipsychotic polypharmacy: evidence based or eminence based? *Acta Psychiatr Scand*. 2002;106(5):321-322.
16. Valuck RJ, Morrato EH, Dodd S, Oderda G, Haxby DG, Allen R; Medicaid Pharmacotherapy Research Consortium. How expensive is antipsychotic polypharmacy? experience from five US Medicaid programs. *Curr Med Res Opin*. 2007;23(10): 2567-2576.
17. Wu EQ, Birnbaum HQ, Zhang HF, Ivanova, JI, Yang E, Mallet D. Health care costs of adults treated for attention-deficit/hyperactivity disorder who received alternative drug therapies. *J Manag Care Pharm*. 2007;13(7):561-569.
18. Sonuga-Barke EJ, Coghill D, Markowitz JS, Swanson JM, Vandenberghe M, Hatch SJ. Sex differences in the response of children with ADHD to once-daily formulations of methylphenidate. *J Am Acad Child Adolesc Psychiatry*. 2007;46(6):701-710. [ajpb](#)

Appendix. ADHD-Related Pharmacy Costs for Index Medications Only per Prescription Fill^a



ADHD indicates attention-deficit/hyperactivity disorder; ATX, atomoxetine; LDX, lisdexamfetamine dimesylate; MAS XR, mixed amphetamine salts extended release; OROS-MPH, osmotic-release oral system methylphenidate.

^aMean number of prescription fills. Error bars represent standard error. Patients on index transdermal methylphenidate and dexamethylphenidate extended release were excluded from analyses by index medication because of low patient numbers (n = 39 and n = 124, respectively).