Continuity in Methylphenidate Treatment of Adults With Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

BACKGROUND: Although stimulant therapy is commonly discontinued early in adults with attention-deficit/hyperactivity disorder (ADHD), the factors that contribute to continuity of stimulant therapy remain largely unknown.

OBJECTIVE: To (1) compare the continuity of methylphenidate (MPH) therapy among adults who use immediate-release methylphenidate (IR-MPH) for ADHD with adults who use extended-release methylphenidate (ER-MPH) formulations, and (2) examine some of the methodological issues involved in research with administrative claims for ADHD.

METHODS: An analysis of pharmacy and medical claims for 75 US managed care plans representing approximately 55 million beneficiaries for dates of service from January 1, 2000 through December 31, 2004. Patients had to be adults (aged 18 to 64 years) who had 1 or more outpatient medical claims for ADHD (*International Classification of Diseases, Ninth Revision, Clinical Modification* code 314.xx) during the study period and who had initiated ER-MPH or IR-MPH treatment for ADHD. The study cohorts did not have a pharmacy claim for MPHs, amphetamines, pemoline, or atomoxetine for 6 months preceding the first (index) MPH pharmacy claim. Stimulant treatment episodes were defined to start on the index date and terminate on the last date supplied of the index medication. Episodes of treatment were also defined as terminated if there was a gap of ≥ 30 days between the end of the days supplied on the pharmacy claim and the date of the next pharmacy claim for the index medication.

RESULTS: Less than one third (30.0%) of the adult patients who were prescribed MPH had 1 or more medical claims with a diagnosis code for ADHD. For the adult MPH patients with at least 1 medical claim with a diagnosis code for ADHD, the patients who initiated therapy with ER-MPH ($N = 2,833$) were significantly younger, were more likely to be male, and were less likely to be treated by a psychiatrist than were the patients who initiated therapy with IR-MPH ($N = 2,289$). Only 50.5% ($n = 1,156$) of IR-MPH patients and 61.4% ($n = 1,739$) of ER-MPH patients had more than 1 pharmacy claim for the index MPH medication. Adults treated with ER-MPH also had a significantly longer median duration of treatment with the index medication (ER-MPH: 68 days, 95% confidence interval [CI], 65–71 days vs. IR-MPH 39 days, 95% CI, 33–52 days). Controlling for group differences in age, gender, treatment by a psychiatrist, recently prescribed psychotropic medications, treated mental disorders, emergency mental health treatment, and inpatient mental health care, ER-MPH initiation was associated with an average 27% longer duration of treatment than with IR-MPH (survival time ratio: 1.27, 95% CI, 1.20–1.35).

CONCLUSION: In management of adult ADHD, use of ER-MPH formulations was associated with a longer median duration of the initially prescribed medication than was use of IR-MPH. It is unknown whether the observed absolute unadjusted difference of 29 days in median length of therapy is clinically important.

KEYWORDS: Attention-deficit/hyperactivity disorder, Methylphenidate, Treatment continuity

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Note: An editorial on the subject of this article appears on pages 617–19 of this issue.

What is already known about this subject

- Previous research indicates that episodes of treatment with stimulants such as methylphenidate (MPH) tend to be relatively brief in the community treatment of adult ADHD, with a mean of 50 days of therapy.

What this study adds

- Only 30% of adult patients who received either immediate-release MPH (IR-MPH) or extended-release MPH (ER-MPH) had a medical or facility claim with a diagnosis code for ADHD.
- For patients who received MPH and had at least 1 medical or facility claim with a diagnosis code for a diagnosis code for ADHD, ER-MPH had a longer median duration of therapy than did IR-MPH (68 days versus 39 days, respectively).
- The diagnosis codes for patients who received ER-MPH were distributed nearly equally between ADHD with hyperactivity (code 314.01, 46%) and ADHD without hyperactivity (code 314.00, 48%) compared with IR-MPH patients who had code 314.01 (ADHD with hyperactivity, 39%) and code 314.00 (ADHD without hyperactivity, 53%). The remainder, 5.5% for ER-MPH and 8.1% for IR-MPH, were ADHD other (code 314).

In the general adult population, the prevalence of attention-deficit/hyperactivity disorder (ADHD) is approximately 2% to 4%.^{1–4} Methylphenidate (MPH) effectively ameliorates many symptoms of adult ADHD.^{5–9} In 1 large 6-week randomized controlled trial of adults with ADHD,⁷ immediate-release methylphenidate (IR-MPH) was associated with a 76% response rate, compared with a 19% response rate for placebo. In a 6-week trial with the same response criteria, 66% of subjects treated with osmotic release oral system methylphenidate (OROS-MPH) responded, compared with 39% who received placebo.⁹ In both studies, response was defined as a 30% symptom reduction and, at least, much overall improvement.

Early discontinuation of treatment is common in the community care of patients initiating stimulant therapy.^{10–13} In 1 study,

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adults initiating pharmacological treatment for ADHD continued their medications for an average of only 50 days.¹³ Although early discontinuation of treatment commonly occurs in the care of adult ADHD, the factors that promote continuity of stimulant treatment remain largely unknown.

Among youth with ADHD, extended-release methylphenidate (ER-MPH) formulations are associated with significantly greater treatment continuity than immediate-release formulations.^{12,14} This higher rate of treatment continuity with ER-MPH may be related to the simpler dosing regimen in which a single dose provides clinical effects for about 8 hours compared with IR-MPH, which requires several daily doses to provide coverage throughout the day.¹⁵

In the present study, we evaluated whether ER-MPH formulations are associated with greater treatment continuity than are IR-MPH formulations in the community management of adults with ADHD under managed care. We compare the duration of MPH treatment episodes of adults from various US managed care health plans, following initiation with either ER-MPH or IR-MPH formulations.

Methods

Source of Data

Analyses of medical service and pharmacy claims from the PharMetrics (2000-2004) database are presented. This database contains standardized prescription, claims, and enrollment information from 75 managed care organizations that collectively cover more than 55 million lives,¹⁶ similar to the distribution of the US population by age and gender. Enrollment data include information on patient demographics and periods of eligibility for services. Claims data include diagnostic and provider information for all inpatient and outpatient services. Prescription claims include the name of the medication filled, the quantity of units dispensed, the days of supply, and the National Drug Code.

All study procedures were approved by the Institutional Review Board of the University of Pennsylvania.

Selection of Study Cohorts

Selected patients were between 18 and 64 years on the date of the first or index pharmacy claim for ER-MPH or IR-MPH. To assess patient characteristics before the index prescription and continuity of MPH after this prescription, the sample was limited to patients who were continuously enrolled in the health plan for 6 months before and 12 months after the index MPH prescription. Because we were interested in new stimulant treatment episodes, patients who received any stimulant prescription during the 6 months before the index MPH prescription were excluded from the analysis. The initial MPH claim was limited to a maximum of 90 days. To focus the analysis on patients receiving treatment for ADHD, we restricted the sample to adults who received 1 or more outpatient treatment claims for ADHD (*International Classifica-*

FIGURE 1 Patient Selection
(From Pharmacy Claims
for Approximately
55 Million Beneficiaries)

* A diagnosis of ADHD was based on 1 or more medical claims for ICD-9-CM 314 during the 6 months before or 12 months after the index prescription of methylphenidate.

ADHD=attention-deficit/hyperactivity disorder; ER=extended release; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; IR=immediate release; MPH=methylphenidate.

tion of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 314.xx) during the study period. Patients were excluded if they were prescribed pemoline or atomoxetine during the study period (Figure 1).

For the primary analyses, we partitioned the selected sample into 2 study cohorts: patients who received an index MPH prescription of an ER-MPH (N=2,833) or IR-MPH

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(N = 2,289) formulation. The ER-MPH group included patients whose index prescription was OROS-MPH (Concerta; n = 2,067), MPH-LA (Ritalin-LA, n = 84), MPH-CD (Metadate-CD, n = 109), a residual group of other long-acting MPH preparations (MPH-ER, MPH-SR, MPH-CR, MPH-SA, Metadate-ER, and Methylin-ER, n = 505). The group also included patients treated with more than 1 ER-MPH (n = 68). In some analyses, the 4 ER-MPH formulations were compared. All other selected patients were assigned to the IR-MPH group.

Duration of MPH Treatment Episodes

Stimulant treatment episodes were defined to start on the index date and terminate on the last date supplied of the index medication. Episodes of treatment were also defined as terminated if there was a gap of ≥ 30 days between the end of the days supplied on the pharmacy claim and the date of the next pharmacy claim for the index medication.¹² Each patient contributed only 1 stimulant treatment episode to the analysis. Once-per-day dosing was assumed to occur when the number of units in the pharmacy claim matched the number of days in the days supply field.

Background Characteristics

Study patients were first characterized with respect to patient age, gender, specialty of the prescribing physician (psychiatrist or other medical specialist treatment during the study period), and ADHD subtype. Three subtypes of ADHD were defined on the basis of the largest number of relevant claims for each patient during the study period: (1) ADHD without hyperactivity (ICD-9-CM code 314.00), (2) ADHD with hyperactivity (code 314.01), and (3) other ADHD subtypes (other code: 314). Mental health claims during the 6 months preceding the index MPH pharmacy claim were used to classify patients as having received treatment for mood disorders (codes 296, 300.4, 311), substance use disorders (codes 291, 292, 303-305), anxiety disorders (codes 300.0, 300.2, 300.3, 308.3, 309.81), and a residual diverse group of all other mental disorders, except mental retardation (codes 290-316, except above).

Analytic Strategy

Patients treated with ER-MPH or IR-MPH were first compared with respect to demographic and clinical background characteristics. Group comparisons are presented with 95% confidence intervals (CIs).

The mean and median duration of MPH treatment were calculated for both study groups with surrounding 95% CIs. Cox accelerated failure time regressions based on the Weibull distribution were performed, controlling for patient age, gender, treating specialist, other treated mental disorders, claims for other prescribed psychotropic medications, and claims for emergency and inpatient services in which the first listed diagnosis was a mental disorder (ICD-9-CM codes 290-316).

TABLE 1 Background Characteristics of Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Methylphenidate for ADHD

Characteristic	ER Methylphenidate (n = 2,833)	IR Methylphenidate (n = 2,289)	Statistics		
			t	df	P Value
Age in years - mean [SD]	31.2 [12.4]	33.3 [12.2]	6.1	5,120	<0.001
	%	%	χ^2	df	P Value
Age, years			22.2	2	<0.001
18-35	63.0	56.5			
36-50	28.3	33.1			
51-64	8.7	10.4			
Gender			10.5	1	0.001
Male	60.3	55.8			
Female	39.7	44.2			
Prescription by psychiatrist	31.9	35.6	7.4	1	0.006
ADHD subtype*			35.1	2	<0.001
Hyperactive	46.4	39.0			
Nonhyperactive	48.0	53.0			
Other	5.5	8.1			

PharMetrics database for claims from January 1, 2002, to December 31, 2004.

* ICD-9-CM code 314 is described as "hyperkinetic syndrome of childhood", and 314.0 is described as "attention deficit disorder". Modifiers to 314 include 314.00 for ADHD without mention of hyperactivity and 314.01 for ADHD with hyperactivity.

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Emergency department and inpatient service use were identified using Pharmetrics specified categories for place of service, procedure codes (Current Procedural Terminology [CPT-4], Healthcare Common Procedure Coding System [HCPS]), and revenue codes. In these analyses, the dependent variable was time to discontinuation of the index MPH medication. When the resulting parameter estimate for drug group was exponentiated, the regression provided a ratio of time to discontinuation between groups or the survival time ratio (STR). The time to discontinuation of the index MPH medication was also examined with a Kaplan-Meier survival curve, and the Wilcoxon test of equality over strata was used to compare the curves.

We also compared the mean and median duration of MPH treatment episodes among 4 subgroups of adult patients prescribed ER-MPH; those treated with OROS-MPH, MPH-LA, MPH-CD, or other extended-release MPH preparations. Separate

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TABLE 2 Characteristics of Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Methylphenidate for ADHD

Characteristic	ER Methyl- phenidate % (n=2,833)	IR Methyl- phenidate % (n=2,289)	Statistics		
			X ²	df	P Value
Treated comorbid disorders					
Substance use	5.0	5.4	.42	1	0.51
Mood disorders	28.2	27.6	.20	1	0.66
Anxiety disorders	11.9	12.0	.03	1	0.87
MH treatment					
Emergency	1.9	1.9	0	1	0.98
Inpatient	1.8	1.9	0.04	1	0.84
Medications					
Antidepressants	34.8	37.3	3.33	1	0.07
Antipsychotics	1.7	2.1	0.73	1	0.40
Mood stabilizers	4.7	4.4	0.18	1	0.67
Anxiolytics	12.6	14.6	4.30	1	0.04
Initial stimulant dosing			1,574.12	2	0.001
1 per day	62.3	7.6			
2 per day	24.2	32.2			
3 or more per day	13.5	60.2			
Proportion of patients with initial claim			11.42	2	0.003
≤30 days	77.7	81.6			
31-60 days	13.5	11.2			
61-90 days	8.8	7.3			

PharMetrics database for claims from January 1, 2000, to December 31, 2004. ADHD=attention-deficit/hyperactivity disorder; MH=mental health.

TABLE 3 Median Duration of Treatment Episodes for Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Methylphenidate for ADHD*

Stimulant Group	Overall Median in Days (95% CI)	Number (%) With 2 or More Stimulant Pharmacy Claims	Median in Days for Those With 2 or More Stimulant Pharmacy Claims (95% CI)
IR methylphenidate (n=2,289)	39.0 (33.0-52.0)	1156 (50.5)†	121.0 (113.0-130.0)
ER methylphenidate (n=2,833)	68.0 (65.0-71.0)	1739 (61.4)†	138.0 (130.0-149.0)
- Osmotic release oral system (OROS) methylphenidate (n=2,067)	73.5 (76.0-79.0)	1322 (64.0)‡	145.5 (132.0-156.0)
- Metadate CD (n=109)	58.0 (30.0-80.0)	65 (59.6)‡	98.0 (86.0-142.0)
- Ritalin LA (n=84)	57.5 (30.0-64.0)	46 (54.8)‡	92.5 (71.0-175.0)
- Other ER methylphenidate (n=505)	34.0 (30.0-58.0)	238 (47.1)‡	121.0 (102.0-139.0)

PharMetrics Data January 1, 2000 to December 31, 2004.

* The number of patients in the extended-release methylphenidate group (n=2,833) exceeds the sum of the OROS-MPH (n=2,067), MPH-CD (N=109), MPH-LA (n=84), and Other ER methylphenidate (n=505) groups because 68 patients who were treated with more than 1 ER-MPH formulation do not appear in the individual medication subanalysis.

† Significantly different values, chi square 61.0, P<0.001.

‡ Significantly different values, chi square is 49.3 (df=3) P<0.001.

CI=confidence interval; ADHD=attention-deficit/hyperactivity disorder; LA=long acting.

Kaplan-Meier survival curves were also calculated. All statistical analyses were conducted using SAS software version 9.1.3.¹⁷

Results

Background and Clinical Characteristics

In the selection of study patients, 30.0% (5,122 of 17,093) of those prescribed MPH had 1 or more medical claims for the treatment of ADHD during the study period (Figure 1). Among selected study patients, roughly one half (55.3%) were initially prescribed an ER-MPH. Compared with patients started on IR-MPH, patients started on ER-MPH were primarily young adults (aged 18-35 years), male, treated by a doctor who was not a psychiatrist, and treated for the hyperactive subtype of ADHD (see Table 1). A significantly larger percentage of the IR-MPH

patients received treatment with anxiolytic and antidepressant medications during the 6 months preceding the index MPH prescription (see Table 2). The two MPH groups did not differ significantly with respect to the proportion who received treatment for mood, anxiety, or substance use disorders or the proportion who received inpatient or emergency mental health treatment during the 6 months before the index prescription (Table 2). While 62% of ER-MPH patients had pharmacy claims with days supply that matched the units dispensed (i.e., once-daily use), only 8% of IR-MPH patients appeared to use only 1 unit per day (Table 2). Among the ER-MPH patients, those initiating OROS-MPH (68.1%) or MPH-LA (63.9%) were more likely than were those initiating MPH-CD (36.1%) or other ER-MPH preparations (45.8%) to start once-daily dosing regimens.

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FIGURE 2 Survival Distribution in Days of Methylphenidate Treatment for Adults With Attention-Deficit/Hyperactivity Disorder

Continuity of MPH Treatment

The overall median continuity of MPH treatment was significantly longer for patients treated with ER-MPH than with IR-MPH (Table 3). Only 50.5% ($n = 1,156$) of IR-MPH patients and 61.4% ($n = 1,739$) of ER-MPH patients had more than 1 pharmacy claim for the index MPH. Adults treated with ER-MPH also had a significantly longer median duration of stimulant treatment (ER-MPH: 68 days, 95% CI, 65-71 days vs. IR-MPH: 39 days, 95% CI, 33-52 days). A Kaplan-Meier curve revealed significantly greater time to index MPH discontinuation for patients treated with ER-MPH rather than IR-MPH (Wilcoxon² = 77.7, $df = 1$, $P < 0.001$; see Figure 2). In a multivariate analysis, which controlled for background demographic and clinical characteristics, ER-MPH patients had an estimated 27% (STR = 1.27) longer duration of index MPH treatment than did IR-MPH patients (Table 4). In this multivariate analysis, the duration of MPH treatment was also significantly related to treatment by a psychiatrist and treatment with an antidepressant medication or mood stabilizer prior to the index MPH prescription (Table 4). Mental health treatment in an emergency department during the 6 months before initiation of MPH therapy and younger age (18-35 years) were each significantly and independently related to a shorter duration of index MPH treatment (Table 4). The generalized R^2 for this model was 0.061.

Among patients treated with ER-MPH preparations, those treated with OROS-MPH had the longest median duration of

TABLE 4 Survival Time Ratios From an Accelerated Failure Time Model of Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Stimulants for ADHD

Characteristic (Versus Reference Category)	Survival Time Ratio	95% Confidence Interval	P Value
Stimulant			
ER-methylphenidate (IR-MPH)	1.27	1.20-1.35	<0.001
Patient age, years (51-64)			
18-35	0.62	0.55-0.69	<0.001
36-50	0.90	0.80-1.02	0.09
Patient gender			
Female (male)	1.01	0.95-1.08	0.72
ADHD subtype (other)			
With hyperactivity	0.99	0.87-1.13	0.90
Without hyperactivity	1.00	0.88-1.14	0.95
Treatment by psychiatrist (none)	1.18	1.10-1.27	<0.001
Comorbidities*			
Substance use (none)	0.92	0.79-1.07	0.27
Mood disorders (none)	0.98	0.90-1.07	0.63
Anxiety disorders (none)	1.01	0.91-1.12	0.85
MH treatment*			
Emergency (none)	0.76	0.59-0.98	0.03
Inpatient (none)	0.90	0.69-1.19	0.46
Medications			
Antidepressants (none)	1.19	1.10-1.29	<0.001
Antipsychotics (none)	0.84	0.66-1.06	0.14
Mood stabilizers (none)	1.15	0.98-1.35	0.08
Anxiolytics (none)	0.97	0.87-1.07	0.51

PharMetrics Data January 1, 2000 to December 31, 2004.

* Based on claims during the 6 months before the index MPH pharmacy claim.

ADHD = attention-deficit/hyperactivity disorder; LA = long acting;

MH = mental health.

index stimulant treatment, followed by MPH-CD, MPH-LA, and the other ER-MPH group. The times to index MPH discontinuation of the 4 extended-release groups are displayed in Figure 3. The survival times of the 4 curves significantly differ from each other (Wilcoxon² = 49.1, $df = 3$, $P < 0.001$). Controlling for group differences in age, gender, treatment by a psychiatrist, recently prescribed psychotropic medications, treated mental disorders, emergency mental health treatment, and inpatient mental health care, OROS-MPH initiation was associated with an average 46% longer duration of treatment than was the other ER-MPH group

FIGURE 3 Survival Distribution in Days of Various Extended-Release Methylphenidate Treatments for Adults With Attention-Deficit/Hyperactivity Disorder

ER-MPH=extended-release methylphenidate; MPH-CD=Metadate CD;
MPH-LA=methylphenidate long-acting;
OROS-MPH=osmotic release oral system methylphenidate.

(STR=1.46, 95% CI, 1.32-1.62). In this analysis, MPH-CD (STR = 1.15, 95% CI, 0.92-1.43) and MPH-LA (STR = 0.99, 95% CI, 0.77-1.26) did not significantly separate from the other ER-MPH group. The generalized R^2 for this model was 0.092 (data not shown).

Discussion

In this managed care population, adults starting ER-MPH formulations for the treatment of ADHD had greater continuity of treatment with the initially prescribed medication than adults starting IR-MPH formulations had. After controlling for several basic demographic, clinical, and treatment characteristics, ER-MPH was associated with a 27% longer duration of treatment than IR-MPH was, but the absolute difference was fewer than 30 days.

The reasons for the difference in treatment continuity are not known. It is possible that greater ease of administration associated with once-a-day dosing may help to account for the longer observed stimulant therapy episodes of patients treated with ER-MPH rather than with IR-MPH. Compared with once-a-day dosing, multiple daily doses may make patients more prone to missed doses and consequent decline in treatment response. In the management of several medical conditions, more complex

dosing regimens have been related to problems with treatment continuity and poorer clinical outcome.¹⁸⁻²¹ At the same time, some patients and physicians may prefer IR-MPH because it allows for greater ease in dose titration and permits more flexible dosing schedules that may minimize side effects.²²

Of the ER-MPH products, OROS-MPH had the longest treatment continuity. This finding extends similar results concerning the continuity of MPH treatment for children and adolescents.¹² Detailed clinical assessments, not available in administrative data, might help to reveal reasons for the differences in treatment duration among the ER-MPH formulations. It is possible that the greater treatment continuity of OROS-MPH compared with the other ER-MPH formulations is related to its longer half-life. Administration of OROS-MPH results in an immediate release of MPH, followed by a slower release of MPH over approximately 12 hours.

MPH-LA, MPH-CD, and the other extended-release preparations have somewhat faster release. After a single dose of MPH-LA, MPH is released over an 8-hour period. MPH-CD typically results in a peak MPH plasma concentration approximately 1.5 hours after dosing, followed by a second peak approximately 4.5 hours after dosing.²³ It is also possible that the differences in the continuity of the ER-MPH formulations are explained by differences in unmeasured patient or physician characteristics that have confounded associations between MPH formulation and treatment continuity. Although the model controlled for several covariates, the generalized R^2 of 6.1% indicates that 94% of the variance in treatment continuation is attributed to unmeasured confounding factors.

The observed differences in stimulant continuity among MPH preparations occurred against a background of widespread early discontinuation of treatment. For both groups, the median duration of MPH treatment episodes was less than 70 days. An important priority remains the identification of patient, treatment, and contextual factors that contribute to pervasive early MPH discontinuation. An understanding of the most common reasons for early discontinuation may provide a framework for developing effective interventions to reduce premature discontinuation of MPH treatment in adults with ADHD. It may be especially important to determine the extent to which early MPH treatment discontinuation reflects problems with medication tolerability or side effects, including sleep difficulties, reduced appetite, stomach ache, exacerbation of tic disorders, or cardiovascular concerns.

Limitations

First and foremost among the study limitations is the fact that the clinical significance of MPH discontinuation cannot be determined from the current analysis. More specifically, it is not possible to distinguish clinically appropriate treatment discontinuation from premature treatment termination for cause, such as perceived lack of efficacy or adverse effects. Second,

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patients initially prescribed IR-MPH may differ from those initially prescribed ER-MPH in important unmeasured clinical or treatment characteristics that may place the IR-MPH group at increased risk of early MPH discontinuation. In a variety of contexts, patient education, increased number of hours when the clinic is open, and improved communication between physicians and patients have been demonstrated to improve adherence to medication regimens.²⁵

Third, the present analysis was limited to patients treated with MPH rather than with mixed amphetamines, atomoxetine, or other medications commonly used to treat adult ADHD. Fourth, although pharmacy claims databases tend to be reliable and valid,²⁶⁻²⁷ a pharmacy claim does not guarantee actual medication consumption. In addition, some patients may take medications without generating a claim (e.g., out-of-pocket purchases), while other patients may take less than the amount prescribed. Fifth, because the study involved participants in private managed care plans, the results may not be generalizable to other patient populations, such as those insured by Medicaid or the Veterans Administration.

Conclusions

In this observational study of adults treated for ADHD, ER-MPH was associated with significantly longer treatment episodes than was IR-MPH. In 1 study of pediatric ADHD, patients who were adherent with stimulants exhibited significantly greater symptom improvement at long-term follow-up than did patients who were nonadherent with stimulants.²⁴ An important challenge for future research involves determining the effects of extending stimulant therapy continuity on key clinical and functional outcomes in the community treatment of adult ADHD.

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