Continuity of Methylphenidate Treatment for Attention-Deficit/Hyperactivity Disorder

Steven C. Marcus, PhD; George J. Wan, PhD, MPH; Jason E. Kemner, MPH; Mark Olfson, MD, MPH

Objective: To compare the continuity of methylphenidate hydrochloride (MPH) therapy among youth Medicaid beneficiaries treated for attention-deficit/hyperactivity disorder with immediate-release (IR) or extended-release (ER) MPH formulations.

Method: An analysis was conducted of statewide California Medicaid claims (2000-2003) focusing on children and adolescents, ages 6 to 17 years, who started ER-MPH or IR-MPH treatment for attention-deficit/hyperactivity disorder. The study cohorts were limited to youth who had not filled a prescription for MPHs, amphetamines, pemoline, or atomoxetine for 6 months preceding the index prescription and remained eligible for Medicaid benefits for the following 12 months. The study groups were compared with respect to background demographic traits and clinical characteristics. Mean and median duration of MPH treatment episodes were defined to terminate if a gap of 30 or more days occurred from the end of the last prescription supply to the start of the next prescription. Survival time ratios were used to assess treatment duration controlling for group differences in background characteristics.

Results: As compared with patients initiating IR-MPH treatment, patients initiating ER-MPH treatment had a significantly longer mean estimated duration of treatment (ER-MPH, 140.3 days [95% confidence interval CI], 136.3-144.4 days] vs IR-MPH, 103.4 days [95% CI, 101.3-103.4 days]). Similar results were found in analyses stratified by patient age, race/ethnicity, and sex. Controlling for group differences in age, sex, race/ethnicity, coprescribed psychotropic medications, other treated mental disorders, case management, managed care participation, and seasonal effects, ER-MPH treatment initiation was associated with an average 37% longer duration of treatment than IR-MPH treatment (survival time ratio, 1.37 [95% CI, 1.32-1.42]). Among patients treated with ER-MPH, treatment initiation with an osmotic release oral system MPH (Concerta) was associated with significantly longer mean duration (147.2 days [95% CI, 142.6-151.7 days]) than treatment initiation with Metadate CD (controlled delivery) (113.0 days [95% CI, 100.9-125.1 days]) or Ritalin LA (long acting) (101.1 days [95% CI, 91.2-111.0 days]), respectively.

Conclusions: Extended-release MPH formulations were associated with greater continuity of MPH treatment than IR formulations in the study population. Initial selection of an ER formulation may help to prolong continuity of MPH therapy among youth Medicaid beneficiaries with attention-deficit/hyperactivity disorder.

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received only 1 prescription, 19.3% received 2 prescriptions, 15.8% received 3 or 4 prescriptions, and only 10.9% of the children received 5 or more prescriptions during a 1-year period.9

In several medical contexts, simplifying the dosing regimen tends to improve treatment adherence.11 Although little is known concerning the effects of regimen complexity on treatment continuity in ADHD, it is conceivable that formulations with less complex dosing requirements contribute to greater continuity than formulations that require more complex dosing.

Standard IR-MPH has a short half-life and therefore requires several daily doses to provide coverage throughout the day.12 The clinical effects of the IR-MPH formulations occur during the first 30 minutes following dosing, reach maximal effect across approximately 2 hours, and are no longer clinically apparent at 5 hours.13 For continuous daytime coverage with traditional IR-MPH formulations, a typical regimen for school-aged patients involves a dose following breakfast, 1 following lunch, and a third dose right after school to provide coverage for homework and other after-school activities. By contrast, newer extended-release (ER) MPH formulations provide continuous clinical effects throughout an 8-hour school day and beyond. This extended coverage eliminates in-school and midday dosing.14

Three ER-MPH formulations, Ritalin LA (long acting), Metadate CD (controlled delivery), and an osmotic release oral system MPH (Concerta), are currently available. Ritalin LA relies on a wax-matrix vehicle to release the medication slowly across an 8-hour period following ingestion. Metadate CD, which combines 30% of IR-MPH and 70% of extended-release MPH beads, typically results in a peak plasma concentration approximately 1.5 hours after dosing and a second peak approximately 4.5 hours after dosing. Administration of OROS MPH results in an immediate release of MPH from the outer covering of the capsule followed by a slower release of MPH across approximately 10 hours.15

In the current report, we evaluate whether ER-MPH formulations are associated with greater treatment continuity than IR-MPH formulations. We examine claims of child and adolescent Medicaid beneficiaries who are starting MPH treatment for ADHD to compare the duration of MPH treatment associated with ER and IR formulations.

**METHODS**

**SELECTION OF STUDY COHORTS**

Data were collected from statewide California Medicaid claims files for the period spanning January 1, 2000, through December 31, 2003. The study was approved by the institutional review board of the University of Pennsylvania, Philadelphia. To select study cohorts, we first limited the sample to youth aged 6 to 17 years who were prescribed MPH. We selected only those beneficiaries who were eligible for California Medicaid benefits for at least 6 months preceding and 12 months following an index MPH prescription. The 12 months following the index prescription are referred to as the follow-up period. We further limited the sample to youth who did not have a prescription claim for an ADHD medication during the 6 months preceding the index MPH prescription and did not have any inpatient claims during the follow-up period. Medications for ADHD were defined to include MPHs, amphetamines, pemoline, and atomoxetine. Finally, we restricted the sample to youth who received 1 or more outpatient treatment claims for ADHD (International Classification of Diseases, Ninth Revision [ICD-9] code 314) during the 6 months preceding the index MPH prescription to focus the analysis on ADHD rather than narcolepsy or off-label uses, such as traumatic brain injury or stroke, that may be associated with different patterns of MPH continuity.

For the primary analyses, we partitioned the selected sample into 2 study cohorts: patients who received an index MPH prescription of either an ER-MPH (n = 3444) or IR-MPH (n = 8093) formulation. Patients whose index prescription was Concerta (n = 2858), Ritalin LA (n = 287), or Metadate CD (n = 299) were defined as ER-MPH. All other selected patients were assigned to the IR-MPH group. Subsequent analyses compared the treatment duration of the 3 ER formulations.

**DEMOGRAPHIC AND CLINICAL CHARACTERISTICS**

On the basis of claims and eligibility files, variables were constructed to define patient ages (6-12 years and 13-17 years), sex (male and female), and race/ethnicity (white, black, Hispanic, and other). Study patients were also classified by prescription of other psychotropic medications during the 12-month follow-up period, including antidepressants, antipsychotics, anxiolytics, sedatives/hypnotics, and mood stabilizers. Mood stabilizers were defined as lithium and anticonvulsants prescribed without a diagnosis of epilepsy (ICD-9 code 345) during the follow-up period.

To control for other mental disorders treated prior to the index MPH prescription, mental disorder variables were defined from claims data during the 6 months preceding the index prescription. The other treated mental disorders included mood disorders (ICD-9/Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV] codes 296, 300.4, and 311), adjustment disorders (309), conduct disorder and related disorders (312), oppositional disorder (313.8), anxiety disorders (300 [except 300.4], 308.3, 309.81), schizophrenia and related disorders (295, 297-299), substance use disorders (291, 292, 303-305), tic disorders (307.2), and a residual group of other mental disorders (290-319).

Patients who received 1 or more billed services from a private managed care contractor during the follow-up period were classified as having received managed care. Similarly, patients who received 1 or more case management visits during the follow-up were considered to have received case management. A variable was also defined to denote patients who received inpatient treatment for a mental disorder (ICD-9/DSM-IV codes 290-319) during the 6 months preceding the index prescription.

**DURATION OF PHARMACOLOGICAL TREATMENT**

The duration of the MPH treatment episode for each patient was calculated by sequentially counting the unduplicated continuous prescriptions using the date of the prescription and the number of days of medications supplied. Episodes of treatment were considered to have terminated if a gap of 30 or more days occurred from the end of the last prescription supply and the start of the subsequent prescription.
Table 1. Demographic and Service Characteristics of Patients Initiating Treatment for ADHD With Extended-Release and Immediate-Release Methylphenidate Preparations*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients Taking Extended-Release Methylphenidate (n = 3444)</th>
<th>Patients Taking Immediate-Release Methylphenidate (n = 8093)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-12</td>
<td>62.4 (60.8-64.0)</td>
<td>74.3 (73.4-75.3)</td>
</tr>
<tr>
<td>13-17</td>
<td>37.6 (36.0-39.2)</td>
<td>25.7 (24.7-26.6)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>77.5 (76.1-78.9)</td>
<td>78.2 (77.3-79.1)</td>
</tr>
<tr>
<td>Female</td>
<td>22.5 (21.1-23.9)</td>
<td>21.8 (20.9-22.7)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>49.2 (47.5-50.9)</td>
<td>43.8 (42.7-44.9)</td>
</tr>
<tr>
<td>Black</td>
<td>20.8 (19.4-22.2)</td>
<td>23.8 (22.9-24.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>24.8 (23.4-26.2)</td>
<td>26.5 (25.5-27.4)</td>
</tr>
<tr>
<td>Other</td>
<td>5.2 (4.4-5.9)</td>
<td>5.9 (5.4-6.4)</td>
</tr>
<tr>
<td>Inpatient psychiatric care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Managed care</td>
<td>36.1 (34.5-37.7)</td>
<td>42.5 (41.4-43.6)</td>
</tr>
<tr>
<td>Case management</td>
<td>2.0 (1.5-2.4)</td>
<td>1.4 (1.1-1.7)</td>
</tr>
<tr>
<td>Summer start of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summed</td>
<td>27.2 (25.7-28.7)</td>
<td>18.3 (17.5-19.1)</td>
</tr>
<tr>
<td>Summer</td>
<td>20.3 (18.9-21.6)</td>
<td>25.0 (25.0-25.9)</td>
</tr>
</tbody>
</table>

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval.
*Data are from the California Medicaid program (2000-2003).
Methylphenidate was given as methylphenidate hydrochloride.

Some analyses concern the total duration of all consecutively prescribed ADHD pharmacological treatments. In these analyses, duration of ADHD treatment includes the total duration of days supplied from the index MPH prescription to the first gap of 30 or more days of any ADHD medication (MPHs, amphetamines, pemoline, or atomoxetine). These analyses examine duration of any continuous ADHD pharmacological treatment rather than duration of only the initial MPH treatment.

The duration of pharmacological treatment analyses were truncated at 1 year from the index prescription. Other analyses concern only the duration of treatment for the index medication.

**ANALYTIC STRATEGY**

Patients treated with ER-MPH and IR-MPH were compared with respect to demographic traits, prescription of other concurrent psychotropic medications, other treated mental disorders, managed care services, case management, and inpatient treatment prior to the index prescription. The proportions of patients in each study group who received their index MPH prescription during the school summer months (June-August) were also determined and compared. Comparisons between patient groups were presented with 95% confidence intervals (CIs).

The mean and median duration of MPH treatment were calculated for the study groups overall and stratified by age, sex, and racial/ethnic groups. Confidence intervals were calculated around the means. Accelerated failure time regressions based on the Weibull distribution were performed overall and separately by demographic traits controlling for these characteristics, prescription of other psychotropic medications, other treated mental disorders, managed care services, case management, season of index prescription, and inpatient psychiatric treatment prior to the index prescription. In these analyses, the dependent variable was time to treatment discontinuation by exponentiating the resulting parameter estimate for drug group, the regression provides a ratio of the adjusted median time to discontinuation between groups or survival time ratio (STR). Group comparisons are also presented of the total number of days supplied of MPH during the follow-up period.

We performed 4 additional analyses. First, to control for planned stimulant discontinuation during school summer vacation, a subgroup analysis was performed limited to patients with index MPH prescriptions in September or October and a 9-month follow-up period. Next, we compared the duration of MPH treatment of patients initially prescribed Concerta Ritalin LA, or Metadate CD. We also compared the IR and ER study groups with respect to duration of any ADHD treatment including prescriptions for MPHs, amphetamines, pemoline, and atomoxetine that occurred without a 30-day gap in the prescription supply. We then computed the mean total number of MPH medication days for each study group during the 12-month follow-up period. Finally, we examined group differences by the specialty of the prescribing physician in cases where this variable was available.

**RESULTS**

**BACKGROUND CHARACTERISTICS**

Approximately 7 (70.1%) in 10 study patients were initially prescribed ER-MPH formulations. As compared with patients who were initially prescribed IR-MPH formulations, patients initially prescribed ER-MPH were significantly more likely to be between 13 and 17 years of age, white in race/ethnicity, and to receive case management, but they were less likely to receive managed care or fill their first prescription during the summer months (Table 1). Inpatient psychiatric treatment during the 6 months prior to the index prescription was rare in both groups.

**CLINICAL CHARACTERISTICS**

A significantly greater proportion of patients taking ER-MPH than IR-MPH received treatment for a mental disorder other than ADHD during the 6 months preceding the index prescription. Specifically, patients taking ER-MPH were significantly more likely than patients taking IR-MPH to have also been previously treated for a mood disorder or oppositional defiant disorder (Table 2).

Patients in the ER-MPH group were significantly more likely than those in the IR-MPH group to have been prescribed antidepressants, antipsychotic medications, and mood stabilizers during the follow-up period (Table 2). Fewer than 5% of both groups of study patients were treated with amphetamines, pemoline, or atomoxetine during the follow-up period.

**CONTINUITY OF MPH TREATMENT**

The mean continuity of MPH treatment was significantly longer for patients taking ER-MPH than those taking IR-MPH (Table 3). In a multivariate analysis, several covariates were independently and significantly related to the duration of MPH treatment. Specifically, in relation to white patients, treatment duration was inversely related to black race (STR, 0.77 [95% CI, 0.73-0.80]), Hispanic ethnicity (STR, 0.81 [95% CI, 0.78-
A substantially greater proportion of patients taking ER-MPH (8.3% [n = 288]) than Ritalin LA (8.0% [n = 285]) and other ethnicities (STR, 0.81 [95% CI, 0.75-0.87]). As compared with patients aged 6 to 12 years, patient age between 13 and 17 years was inversely related to treatment duration (STR, 0.79 [95% CI, 0.76-0.82]). Treatment with other classes of psychotropic medications tended to increase the duration of the index MPH treatment episode (antidepressants, STR, 1.42 [95% CI, 1.34-1.51]; sedative hypnotics, STR, 1.41 [95% CI, 1.08-1.84]; antipsychotic medications, STR, 1.37 [95% CI, 1.20-1.38]; anxiolytic medications, STR, 1.26 [95% CI, 1.19-1.34]; multiple ADHD medications, STR, 1.20 [95% CI, 1.13-1.26]). Treatment duration was directly related to use of case management services (STR, 1.47 [95% CI, 1.40-1.53]) but inversely related to treatment of a comorbid mental disorder (STR, 0.95 [95% CI, 0.92-0.99]), inpatient psychiatric care during the 6 months preceding the index MPH treatment episode (STR, 0.81 [95% CI, 0.70-0.93]), and treatment under managed care (STR, 0.85 [95% CI, 0.82-0.88]). Duration of MPH treatment was not significantly related to patient sex, prescription of anxiolytic medications, or whether the episode started during the summer months. In this multivariate analysis, which controlled for background demographic, service, and clinical characteristics, patients taking ER-MPH had an estimated 37% (STR, 1.37) longer mean duration of MPH treatment than patients taking IR-MPH.

In stratified analyses, initial treatment with ER-MPH was associated with significantly longer mean continuity of treatment than IR-MPH among children aged 6 to 12 years and adolescents aged 13 to 17 years, boys and girls, and each of the 4 racial/ethnic groups (Table 3). Group differences in continuity became apparent approximately 30 days after the index prescription (Figure 1). However, a great majority of both groups discontinued MPH treatment during the 1-year follow-up period.

An analysis was also performed of the total number of MPH treatment days during the 12-month follow-up period. This analysis included MPH treatment days at any point during the 12-month period rather than only those days that were part of 1 continuous treatment episode as described earlier. This analysis revealed that during the follow-up period, patients taking ER-MPH were treated for a significantly greater number of total days (mean, 193.5 days [95% CI, 190.0-197.0 days]) than patients taking IR-MPH (mean, 171.2 days [95% CI, 169.1-173.4 days]).

A substantial and similar proportion of patients initiating ER-MPH and IR-MPH treatment restarted a pharmacological treatment for ADHD within 90 days of the end of their last MPH prescription for their index treatment episode (ER-MPH, 43.8% [95% CI, 41.9%-45.6%]; IR-MPH, 44.1% [95% CI, 43.0%-45.3%]). However, patients initiating ER-MPH treatment were slightly more likely than those initiating IR-MPH treatment to receive any treatment for ADHD during this period following their index treatment episode (ER-MPH, 58.8% [95% CI, 56.9%-60.6%]; IR-MPH, 55.6% [95% CI, 54.4%-56.7%]).

**ER-MPH FORMULATIONS**

A substantially greater proportion of patients taking ER-MPH were treated with Concerta (83.0% [n = 285]) than Ritalin LA (8.3% [n = 287]) or Metadate CD (8.7% [n = 299]). Patients starting Concerta treatment had significantly longer mean MPH treatment episodes (147.2 days [95% CI, 142.6-151.7 days]) than those who started taking either Ritalin LA (113.0 days [95% CI, 100.9-125.1 days]) or Metadate CD (101.1 days [95% CI, 91.2-111.0 days]) (Figure 2).

### TREATMENT CONTINUITY DURING THE SCHOOL YEAR

To control for possible confounding by planned MPH discontinuation during school summer vacation, we examined 9-month treatment continuity for patients who started taking ER-MPH (n = 774) or IR-MPH (n = 1681) formulations in September or October. In this subgroup, as in the overall analysis, patients taking ER-MPH had significantly longer mean MPH treatment durations (139.0 days [95% CI, 134.5-143.5 days]) than patients taking IR-MPH (103.1 days [95% CI, 100.7-105.5 days]).

In a separate analysis, initiation of ER-MPH formulations during the summer months was also associated with a significantly longer mean duration of treatment (143.3 days [95% CI, 136.1-154.9 days]) than initiation of IR-MPH formulations (104.2 days [95% CI, 100.0-108.4 days]).
A minority of patients who started taking ER-MPH (12.6%) or IR-MPH (16.0%) were treated with another ADHD medication, such as amphetamines, pemoline, or atomoxetine, during their MPH treatment episode. Among this subgroup, the mean duration of MPH treatment did not significantly differ between patients taking ER-MPH (101.2 days [95% CI, 92.8-109.6 days]) and patients taking IR-MPH (102.9 days [95% CI, 98.4-107.4 days]).

CONTINUITY OF ADHD TREATMENT

Patients taking ER-MPH had a significantly longer total mean duration of ADHD treatment (157.9 days [95% CI, 153.7-162.1 days]) than patients taking IR-MPH (128.1 days [95% CI, 125.6-130.6 days]) (Figure 3). In this analysis, total duration of ADHD medication treatment included prescriptions for MPHs, amphetamines, pemoline, and atomoxetine that occurred without a 30-day gap in the prescription supply.

CONCURRENT ADHD TREATMENTS

Table 3. Mean and Median Treatment Duration of Patients Initiating Extended-Release Methylphenidate (ER-MPH) and Immediate-Release Methylphenidate (IR-MPH) Preparations, Stratified by Demographic Groups*

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean, d (95% CI)</th>
<th>Median, d</th>
<th>STR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>140.3 (136.3-144.4)</td>
<td>103.4 (101.3-103.4)</td>
<td>90</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-12</td>
<td>149.5 (144.2-154.9)</td>
<td>107.5 (105.0-110.0)</td>
<td>97</td>
</tr>
<tr>
<td>13-17</td>
<td>125.1 (119.0-125.1)</td>
<td>91.3 (87.7-91.3)</td>
<td>80</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>140.9 (136.3-145.5)</td>
<td>101.8 (99.4-104.1)</td>
<td>90</td>
</tr>
<tr>
<td>Female</td>
<td>138.4 (130.0-146.9)</td>
<td>109.1 (104.5-113.6)</td>
<td>92</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>154.9 (148.8-160.9)</td>
<td>116.8 (113.4-120.2)</td>
<td>100</td>
</tr>
<tr>
<td>Black</td>
<td>125.7 (117.5-133.8)</td>
<td>90.8 (87.9-94.7)</td>
<td>85</td>
</tr>
<tr>
<td>Hispanic</td>
<td>126.2 (118.4-134.0)</td>
<td>94.9 (91.1-98.8)</td>
<td>75</td>
</tr>
<tr>
<td>Other</td>
<td>130.4 (112.9-147.9)</td>
<td>93.9 (85.9-101.9)</td>
<td>66</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; STR, survival time ratio.

*Data are from the California Medicaid program (2000-2003). Survival time ratios are adjusted for patient age, sex, race/ethnicity, concurrent other classes of psychotropic medication prescriptions, managed care, previous inpatient psychiatric care, case management, and season initiating methylphenidate hydrochloride treatment.
portion of patients taking ER-MPH (41.6% [95% CI, 39.0%-44.2%]) than patients taking IR-MPH (35.2% [95% CI, 32.7%-37.7%]; IR-MPH, 36.1% [95% CI, 34.4%-37.8%]), and physicians of other specialties prescribed to a significantly larger proportion of patients taking IR-MPH (33.4% [95% CI, 31.8%-35.1%]) than patients taking ER-MPH (23.2% [95% CI, 21.0%-25.5%]). Across all 3 physician groups, the mean duration of ER-MPH treatment was significantly longer than IR-MPH treatment (psychiatrists, ER-MPH, 162.0 days [95% CI, 151.6-172.4 days] vs IR-MPH, 132.0 days [95% CI, 124.9-139.1 days]; pediatricians, ER-MPH, 138.6 days [95% CI, 127.7-149.5 days] vs IR-MPH, 103.8 days [95% CI, 98.3-109.3 days]; other physicians, ER-MPH, 143.6 days [95% CI, 130.6-156.6 days] vs IR-MPH, 104.2 days [95% CI, 98.6-109.9 days]).}

**COMMENT**

In this Medicaid population, young people initiating ER-MPH formulations for the treatment of ADHD had greater treatment continuity than their counterparts initiating IR formulations. This difference was observed among children and adolescents, boys and girls, across the major racial/ethnic groups, and across specialties of the prescribing physician. After controlling for a range of relevant background characteristics, ER formulations were associated with an estimated 37% increase in duration of initial MPH treatment. Initiating treatment with an ER-MPH formulation was also associated with a significantly longer mean duration of receiving any pharmacological treatment for ADHD.

Greater patient acceptance and ease of administration may help to account for the increased treatment continuity associated with ER-MPH formulations. Multiple daily dosing may risk embarrassing young people in front of their peers and increase the chance of the loss of clinical effectiveness that follows from missing a dose. During the school year, a school nurse or other school staff is generally required to dispense a midday MPH dose. Some schools may not reliably administer midday doses, while other schools may prohibit administration of medications altogether. At the same time, some patients and physicians may prefer IR preparations because they allow for greater ease in titration of doses and permit more graduated dosing schedules that may minimize adverse effects during the early phase of treatment. Other patients, especially younger children, cannot swallow pills whole so stimulant preparations must be opened and sprinkled on their foods. This is not possible with some ER-MPH formulations.

Among the ER formulations, Concerta was associated with the longest treatment continuity. Detailed clinical assessments, not available in administrative data, may be required to determine the reasons for the differences in treatment duration among the ER formulations. It is possible that the continuity differences among the ER formulations are related to differences in their underlying pharmacokinetic profiles. Alternatively, the observed differences may be related to differences in unmeasured patient or physiologic characteristics that have confounded associations between MPH preparation and treatment continuity.

Modest formulation-related differences in MPH treatment duration exist in the context of widespread early treatment discontinuation. Overall, less than one half of the study patients continued MPH therapy beyond 90 days and fewer than 1 in 5 continued for 1 year. Further research is needed to determine whether such pervasive MPH discontinuation occurs in other patient populations and, if so, the most common reasons for early discontinuation. It is especially important to determine the extent to which early MPH treatment discontinuation reflects problems with medication tolerability and adverse effects, such as difficulty falling asleep, reduced appetite, stomach ache, exacerbation of tic disorders, or limitations in the clinical effectiveness of MPH in complex cases that populate routine practice.

Youth at especially high risk for early treatment discontinuation included adolescents, young people not receiving case management services, and youth of African American or Hispanic ancestry. The association between stimulant treatment continuity and younger patient age is consistent with previous research. Although race and ethnicity did not emerge as related to treatment nonattendance among subjects enrolled in a recent large controlled trial of ADHD treatments, the current findings suggest that within a Medicaid population, Hispanic and African American youth are at increased risk for early treatment discontinuation. Frequent early MPH discontinuation among low-income youth with ADHD underscores the need to develop intervention strategies to promote greater continuity of care.

This study has several limitations. First, though data from prescription claims tend to be reliable and valid, a prescription claim does not confirm that the patient actually took the prescribed medication. Moreover, some patients may take medications without generating a claim (e.g., out-of-pocket purchases) while other patients may take less than prescribed. For example, a patient may be prescribed enough IR medication for doses 3 times a day 7 days a week, but the family opts to defer the afternoon dose or skip weekend doses; over time this leads to gaps in the prescription record, though not treatment discontinuation. Second, patients initially prescribed IR-MPH may differ from those prescribed ER-MPH in important unmeasured clinical characteristics, such as level of attention, difficulty following instructions, or motivation for treatment, that may render the former group more likely to discontinue MPH therapy. In addition, physicians may select long-acting formulations for young people who they believe have a need for longer-term stimulant therapy. Third, the clinical significance of MPH discontinuation cannot be determined from the current analysis. We have no means of distinguishing clinically appropriate treatment discontinuation from premature treatment termination. In this regard, more than one half of the patients who discontinue their index MPH treatment receive some treatment for ADHD within the subsequent 90 days. Fourth, the study is limited to Medicaid beneficiaries, so the results may not be safely generalized to privately insured or uninsured patient populations.
Methylphenidate formulations offer a range of pharmacokinetic profiles and durations of action to help meet the diverse and changing needs of youth with ADHD. For some patients, long-acting formulations may enhance medication adherence, perhaps by eliminating the midday, in-school medication dose and reducing the need for an after-school dose. At the same time, though, it is unreasonable to assume that simply selecting a stimulant regimen with an appropriate pharmacological profile will ensure long-term medication adherence. In practice, promotion of long-term treatment continuity may be facilitated by actively engaging the child, his or her parents, teachers, and, when clinically indicated, a case manager in monitoring key problem behaviors and encouraging appropriate coping strategies.

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