

Stimulant Treatment Patterns and Compliance in Children and Adults With Newly Treated Attention-Deficit/Hyperactivity Disorder

AMY R. PERWIEN, PhD; JENNIFER HALL, MPH; ANDRINE SWENSEN, PhD; and RALPH SWINDLE, PhD

ABSTRACT

OBJECTIVE: To identify newly treated cases of attention-deficit/hyperactivity disorder (ADHD), assess the presence of comorbid psychiatric conditions, identify pharmacological treatment patterns, and examine treatment compliance rates among children and adults with newly diagnosed and pharmacologically treated ADHD in a managed care population.

METHODS: Children (aged 18 years or younger) and adults having newly treated ADHD were identified from medical and pharmacy claims in an administrative claims database from 6 health plans. Claims data for services or products provided between April 1, 1997, and September 30, 1999, was analyzed for the managed care population (604,538 children and 1,542,304 adults). Data on compliance, persistence, and pharmacological treatment patterns were collected for the 6 months prior to and the 18 months following each patient's initial ADHD pharmacological treatment. A medication possession ratio (MPR) was calculated by dividing the number of days supplied in a prescription by the number of days until the next prescription was filled. Compliance was defined as an MPR >0.8 and persistence as an MPR >0.3.

RESULTS: The prevalence of diagnosed ADHD in this population was 0.7% (11,962 [2%] of children and 2,636 [0.2%] of adults) and incidence of ADHD was 0.04% (735 [0.1%] of children and 162 [0.01%] of adults). The most common comorbid psychiatric condition for incident cases was depression (31.6% of children and 63% of adults). Few children and adults switched their initial ADHD treatment agent, 11% and 12%, respectively. Dose titration occurred in 67% of children and 54% of adults. On average, changes in treatment (switching, titrating) took place after 2 to 3 months of treatment. Although patients, on average, obtained more than 6 refills for a total 200 days supply, the majority of patients (84% of children and 88% of adults) were compliant for less than 2 months over the period they were refilling prescriptions.

CONCLUSION: Although the majority of patients had dosage changes, these changes typically occurred after several months of treatment. Results suggest that, even though patients continued their ADHD medication for several months, they did not consistently take medication for more than 2 months. Given these treatment patterns, pharmacologic treatment in newly treated ADHD patients may be suboptimal and may impact outcomes, including the effectiveness and cost of treatment.

KEYWORDS: Attention-deficit/hyperactivity disorder (ADHD), Compliance, Stimulant medication

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Attention-deficit/hyperactivity disorder (ADHD) is one of the most common childhood mental health conditions, with 3% to 7% of children affected by this disorder.¹⁻⁵ Core symptoms of ADHD include inattention and hyperactivity/impulsivity. ADHD has long been recognized as a mental health disorder in children, and research has shown that children with this disorder experience significant impairments in psychosocial functioning. Compared with children without the disorder, those with ADHD have higher rates of academic difficulties, such as learning disabilities and early school departure⁶⁻⁸; experience social difficulties⁹⁻¹¹; and are likely to have coexisting psychiatric conditions.¹²

Although ADHD has traditionally been thought of exclusively as a childhood disorder, research has indicated that symptoms often continue into adulthood.¹³ Despite the fact that epidemiological studies of adult ADHD have not been conducted, this disorder has been estimated as occurring in approximately 4% of adults.¹⁴ Given the prevalence of the disorder, associated negative outcomes, and presence over the life course, identification and treatment are of primary concern.

Research has consistently shown that ADHD is amenable to treatment. The most common and effective treatment methods include pharmacotherapy with stimulant medication, behavior therapy, and/or parent training or in combination.¹⁵⁻¹⁷ The 2001 American Academy of Pediatrics ADHD Treatment guideline¹⁵ strongly recommends the use of either stimulant medication (strength of evidence: good) and/or behavior therapy (strength of evidence: fair) as appropriate (Guideline #3).

The National Institute of Mental Health-funded Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (MTA) was a large-scale multisite randomized clinical trial that examined the effectiveness of different ADHD treatments.¹⁸ It was conducted to answer in a more

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definitive way the effectiveness of the various treatment modalities and their combinations in a large sample study (N = 579 children). The MTA study compared strict medication treatment alone (i.e., having a specified process of 3-times-daily dosing and closely monitored daily doses), medication treatment in combination with behavior therapy, behavior therapy alone, and community treatment. The study did not find significant differences in core ADHD symptoms between medication treatment, which was primarily composed of stimulants such as methylphenidate, and medication treatment in combination with behavior therapy. Behavior therapy alone was either equal to or less effective than medication alone or in combination depending on which outcome measure was examined. The community care treatment group, in which the majority of patients received ADHD medication but were not in the strict medication management treatment arm of the study, did not show as much improvement in core ADHD symptoms compared with the other groups that had medication treatment. These findings suggest that highly regimented treatment and compliance may play a role in achieving favorable treatment outcomes when pharmacological treatment is utilized.

The MTA study highlights the fact that despite the potential benefits of stimulant therapy for ADHD, poor compliance may lead to suboptimal symptom management and less-than-favorable outcomes related to psychosocial and academic functioning. Arguably the most cited definition of compliance was offered by Haynes,¹⁹ who refers to it as “the extent to which a person’s behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical advice.” Although it is noted that use of the term “adherence” may be preferable to “compliance” because it suggests a more active patient role,²⁰ the terms “compliance” and “persistence” are used throughout this article because each of these terms have different meanings within claims database research, and the term compliance is still widely used by health care providers.

Early studies have estimated stimulant compliance rates between 35% and 100%,²¹ with the variability in rates most likely due to differences in how compliance was measured and over what time interval. For example, Johnson and Fine (1992) found higher rates of compliance using urine tests compared with pill counts.²² Regarding long-term compliance with stimulant medication, a more recent study found that 81% of children complied with stimulant medications for the first year of treatment and 52% complied for 3 years.²³ Given the chronic nature of ADHD, these differences in compliance rates may have negative implications for long-term management of ADHD symptoms as well as psychosocial and academic outcomes.

Since ADHD is a mental health disorder that can result in significant psychosocial impairments and treatments are available for this disorder, it is of interest to understand patterns of treatment and compliance in both children and adults. Although studies have shed light on problems associated with

compliance to stimulant treatment, they have generally used small sample sizes, included only children, and focused on pill counts or verbal reports of compliance. Examination of medical and pharmaceutical claims data is another method that can be used to look at treatment patterns as well as prescription compliance. This type of data can be viewed as complementary to other study methodologies. Further, claims data allow for examination of treatment patterns and compliance within a managed care population to help avoid or overcome potential bias associated with self-reports.

Although there are some data regarding treatment patterns and compliance in children with ADHD, this type of data does not exist for adults with ADHD. Utilizing a large medical and pharmacy claims database, the present study seeks to (1) identify the prevalence of ADHD in a population of commercially insured children and adults; (2) examine related characteristics, including comorbid psychiatric conditions; and (3) describe pharmacological treatment patterns and compliance.

Methods

This study was a retrospective, longitudinal claims data analysis using enrollment, medical claims, facility claims, and pharmacy claims data. The data were derived from 6 United Healthcare-affiliated health maintenance organization plans located in 6 states throughout the United States. Two were located in the Southeast, 2 in the Midwest, 1 in the Northeast, and 1 in the West. The plans were selected for their large enrollee population, representative geographic spread, and similarity to one another. The 6 plans were composed of 2,199,203 commercial members enrolled in Ingenix Pharmaceutical Services provider networks in which the physicians were compensated on the basis of discounted, fee-for-service charges not capitation or financial risk. Patients were identified from medical claims for the 6-month service period from October 1, 1997, through March 31, 1998.

The *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR*, 4th ed., American Psychiatric Association, 2000) describes 3 subtypes of ADHD: primarily inattentive, primarily hyperactive, and combined. The terminology used in the diagnostic codes in the International Classification of Diseases, Version 9 (ICD-9) is slightly different, with 1 code (314.01) to distinguish between attention-deficit disorder with hyperactivity (ADHD) and attention-deficit disorder without hyperactivity (ADD; ICD-9 code 314.00). The term ADHD will be used throughout this paper to cover both ICD-9 subtypes of attention-deficit disorder.

Patients

Utilizing medical and pharmacy claims data, patients were defined as those members receiving both a diagnosis for ADHD and related pharmacological treatment within the 6-month patient identification period. Newly treated, or incident

patients, were defined as children and adults who had their earliest ADHD prescription (i.e., methylphenidate, pemoline, dextroamphetamine, amphetamine mixed salts, or methamphetamine) preceded by at least 6 months with no ADHD prescriptions. This "ADHD medication-free period" was determined by looking back at all claims records for each patient for the 6-month period preceding their initial ADHD prescription, even if this 6-month interval preceded the October 1, 1997, start frame for this study. Using this definition of newly treated, it is possible that patients could have received pharmaceutical treatment for ADHD prior to the 6-month washout period. Medical and prescription claims data were collected for 18 months following each patient's initial ADHD treatment date.

Pediatric patients were included in the analyses if they met the following conservative criteria: (1) had a total of at least 2 physician or facility claims with a primary or secondary diagnosis of ADHD (ICD-9 diagnostic codes 314.00 or 314.01), (2) had at least 1 pharmacy claim for an ADHD pharmacological treatment (methylphenidate, dextroamphetamine, methamphetamine, or amphetamine/dextroamphetamine), and (3) were aged 18 years or younger as of their first ADHD diagnosis or pharmacy claim during the study period. Adults were required to meet the following inclusion criteria: (1) had at least 1 physician or facility claim with a primary or secondary ICD-9 diagnosis code for ADHD, (2) had at least 1 pharmacy claim for ADHD pharmacological treatment, and (3) were aged between 19 and 64 years. Initially, the inclusion criteria were identical for adults and children, but analysis of the medical claims data showed that ADHD was less common as a diagnosis code in adults compared with children. Therefore, the inclusion criteria for adults was changed to 1 medical (physician or facility) claim with a primary or secondary diagnosis code for ADHD.

Because stimulants can be used to treat narcolepsy, children and adults were excluded if they had been diagnosed with narcolepsy (ICD-9 diagnostic code 347.) in the 6 months prior to the study period as well as during the study period. Out of 22,225 potential subjects with at least 1 psychostimulant prescription between October 1, 1997, and March 31, 1998, 4,349 were adults and 17,876 were children. Of the 4,349 adults, only 1,136 (26.1%) had an ADHD primary or secondary diagnosis on any of their medical claims and were retained for the study. Of the 17,876 children with a psychostimulant prescription, only 4,506 (25.2%) had an ADHD primary or secondary diagnosis on at least 2 of their medical claims and were retained for the study. Of the remaining children, 4,329 (24.2%) had only 1 ADHD primary or secondary diagnosis in looking through all of their claims, and 9,041 (50.6%) had no ADHD diagnosis on any claim during the study interval.

Comorbid psychiatric conditions in these ADHD patients were identified by 2 methods: either from ICD-9 diagnosis codes on medical claims or by prescription claims for drugs commonly used to treat these psychiatric conditions. Because

depression, anxiety, and conduct disorder are among the most commonly occurring comorbid mental health disorders in patients with ADHD,²⁴ these conditions were of particular interest. Depression was identified by the presence of a primary or secondary diagnosis of depression (ICD-9 diagnostic codes 296.2–296.9, 298.0, 300.4, 301.12, 308.0, 309.0–309.1, 309.4, 311.0, 313.1) or at least 1 prescription for an antidepressant drug (amitriptyline, amitriptyline HCL/perphenazine, nortriptyline/chlordiazepoxide, amoxapine, bupropion, citalopram, clomipramine, desipramine, doxepin, fluoxetine, fluvoxamine, imipramine HCL, imipramine pamoate, mirtazapine, nefazodone, nortriptyline, paroxetine, phenelzine, protriptyline, sertraline, tranylcypromine, trazodone, or venlafaxine) during the 6-month patient identification period (October 1, 1997, to March 31, 1998). The presence of concurrent anxiety was based on a primary or secondary diagnosis of anxiety (ICD-9 diagnostic codes 293.84, 300.0x, 300.20, 300.4x, 308.0x, 309.21, 309.24) or at least 1 prescription for an anxiolytic (alprazolam, buspirone butabarbital, chloral hydrate, chlordiazepoxide HCL, clorazepate, diazepam, estazolam, flurazepam, lorazepam, meprobamate, oxazepam, quazepam, secobarbital, temazepam, triazolam, or zolpidem). Prescriptions for antidepressants and anxiolytics were used as proxies for presence of depression and anxiety, respectively, because diagnoses may be underreported in claims databases.²⁵ Members were identified as having conduct disorder based solely on ICD-9 criteria (ICD-9 diagnostic codes 309.3x, 312.xx, 314.2x).

Measures

Several pharmacological treatment patterns were examined, including treatment augmentation, treatment switching, and dosage titration. *Treatment augmentation* was defined as a patient adding a second type of drug therapy to an existing course of drug therapy. *Treatment switching* occurred when a patient began a second type of ADHD drug therapy without continuing (i.e., refilling) their initial type of therapy. To analyze treatment augmentation and switching patterns, treatment periods were created for each prescription of an initial ADHD medication. Each treatment period began with the prescription fill date and continued for a period equal to 150% of the days supplied for that medication (e.g., if 30 days of medication were supplied, the treatment period was 45 days). For the purpose of this analysis, only the first therapy augmentation or switch was analyzed. *Dosage titration* was defined as an ADHD prescription dosage increase or decrease of at least 25% of the previous daily dosage for the same drug. The 25% increase or decrease was based on the administration and dosage guidelines for methylphenidate, which was the most commonly prescribed stimulant.

To examine prescription refill compliance (referred to as "compliance"), a medication possession ratio (MPR), as defined by Rizzo and Simons (1997),²⁶ was calculated. This ratio is a measure of the amount of drug a patient may have had access

to between prescriptions (fills and refills) and is calculated by dividing the number of days supplied in an ADHD prescription by the number of days until the next prescription is filled or the number of days until the end of the study period if it was the last prescription (days supply/days until next fill = MPR). For example, if 30 days are supplied in a prescription and the next prescription is filled after 35 days, the MPR would be 0.86. Compliance is the number of days the patient was compliant from initial fill date until the first lapse in refilling medication and was defined as an MPR >0.80. This is a stringent compliance estimate, as it allows for minimal lapses in medication coverage.

To balance this conservative estimate of compliance, a more liberal measure (“persistence”) was created to examine how long patients attempted to continue their medication regardless of the rate. Persistence is the length of time medications continued to be refilled, and was defined as an MPR <0.30. This compliance and persistence methodology is based on previous work conducted by Rizzo and Simons (1997).²⁶ Compliance and persistence rates were based on the date the first prescription was filled in the study period and subsequent refill dates. Therefore, it was possible that patients could have become more or less compliant at a later point within the 18-month follow-up period.

In this study, drug holidays (i.e., weekend and vacation periods of time when patients are off medication) were not included in the analysis for several reasons: (1) it was not possible to know which patients had been prescribed drug holidays, (2) there is not a consensus on the use of drug holidays,²⁷ and (3) the more liberal definition of persistence allows for longer time periods in which patients could be off medications. Although hospitalization could affect compliance and persistence rates, only 5% of patients were hospitalized during the 18-month follow-up period.

Results

Patient Characteristics

From the population of managed care enrollees in the claims database, 11,962 (2%) of children and 2,636 (0.2%) of adults were diagnosed with ADHD (i.e., had at least 1 physician or facility claim with an ADHD diagnosis). Children accounted for 82% of the ADHD patients, with a single diagnosis of ADHD identified in the population of managed care enrollees from the medical claims database. Based on study criteria, (i.e., age at time of ADHD diagnosis, documented diagnosis of ADHD, newly treated with pharmacotherapy, and absence of narcolepsy), 0.1% of child health plan members (N = 735, 6.1% of 11,962 children with a diagnosis of ADHD) and 0.01% of adult health plan members (N = 162, 6.1% of 2,636 adults with a diagnosis of ADHD) met the study criteria as being newly treated. The mean age for children was 9.9 years (SD = 3.5) and the mean age for adults was 35.2 years (SD = 10.6) (Table 1). Although the majority of patients were male (76.3% of children and 60.5% of adults), the overall percentage of females with ADHD increased with age (21.9% of 0 to 6-year-olds versus

TABLE 1 Patients by Age and Gender (N=897)

Age Range	N (% total)	% Male
Children (0-18 years)	735	76.3
0-6	137 (19)	78.1
7-12	396 (54)	76.3
13-18	202 (27)	75.3
Adults (19-64 years)	162	60.5
19-34	70 (43)	68.6
35-64	92 (57)	54.4

TABLE 2 ADHD Children and Adults With Depression, Anxiety, or Conduct Disorder

	Children (N=735)		Adults (N=162)	
	Males (n = 561)	Females (n = 174)	Males (n = 98)	Females (n = 64)
Depression	179 (31.9%)	53 (30.5%)	59 (60.2%)	43 (67.2%)
Anxiety	58 (10.3%)	18 (10.3%)	34 (34.7%)	25 (39.1%)
Conduct disorder	38 (6.8%)	12 (6.9%)	5 (5.1%)	1 (1.6%)

TABLE 3 Initial ADHD Treatment by Drug Type

Drug	Children (n = 735)	Adults (n = 162)	Total (n = 897)
Methylphenidate	488 (66.4%)	106 (65.4%)	594 (66.2%)
Amphetamine mixed salts	159 (21.6%)	19 (11.7%)	178 (19.8%)
Dextroamphetamine	62 (8.4%)	24 (14.8%)	86 (9.6%)
Pemoline	23 (3.1%)	12 (7.4%)	35 (3.9%)
Methamphetamine	3 (0.4%)	1 (0.6%)	4 (0.4%)

51% of 35 to 64-year-olds, $P < .001$).

Table 2 shows the number of patients with comorbid depression, anxiety, and conduct disorder. Depression was the most common of the 3 comorbid psychiatric conditions for both children (31.6%) and adults (63%). For adults, 70% were identified with depression based on an ICD-9 code and 30% were identified based on a prescription for an antidepressant. For children, 66% were identified based on an ICD-9 code for depression and 34% were identified based on a prescription. Anxiety was found in 36.4% of adults and 10.3% of children during the study period. The majority of adults and children were identified with anxiety based on an ICD-9 code for anxiety (66% and 86%, respectively) as opposed to a prescription for an anxiolytic. Conduct disorder was found in 6.8% of children and 3.7% of adults with newly treated ADHD, all identified by ICD-9 codes in medical claims.

TABLE 4 Mean Length of Compliance and Persistence by Initial Treatment Type

Initial ADHD Medication	Days Compliant		Days Persistent	
	Children Mean (SD*)	Adults Mean (SD)	Children Mean (SD)	Adults Mean (SD)
Methylphenidate	34.9 (75.0)	40.7 (90.1)	208.0 (202.7)	180.5 (210.8)
Amphetamine mixed salts	35.4 (79.2)	56.4 (127.4)	211.5 (218.1)	165.9 (201.6)
Dextroamphetamine	31.3 (81.6)	90.7 (171.5)	166.2 (196.8)	296.9 (245.4)
Pemoline	20.4 (46.3)	38.4 (59.6)	80.8 (124.2)	201.6 (232.8)
Methamphetamine	20.0 (34.6)	0.0†	135.0 (43.3)	547.0†
Total	34.2 (75.6)	49.5 (109.0)	200.9 (204.5)	199.9 (219.9)

* SD = standard deviation. † Only 1 case; no variance.

Treatment Patterns

Table 3 shows initial medication treatments for both children and adults. During the study period, the majority was initiated on methylphenidate (66.4% of children and 65.4% of adults). Children filled an average of 217.8 (SD = 152.2, range 7 to 684) days of their initial medication, compared with 213.0 (SD = 180.9, range 6 to 606) days for the adults. There was no significant difference between children and adults in the average days of drug therapy.

Changes in initial medication therapy were examined separately for children and adults. For a minority of patients, initial treatment was augmented with a second ADHD drug or initial therapy was discontinued and the patient was switched to a different ADHD drug. Augmentation was generally low, with only 1.9% of children and 1.2% of adults adding a second ADHD drug. Treatment switching occurred in 11.6% of children and occurred an average of 165.5 days (SD = 147.4) after initiating ADHD pharmacotherapy. In the adults, 11.1% switched from their initial ADHD therapy to a new stimulant after a mean of 125.3 days (SD = 110.9). There were no significant differences in treatment augmentation and switching rates between children and adults. In comparison with medication augmenting and switching, medication titration (upward or downward) occurred more frequently in both children and adults. All differences between switching and augmentation rates compared with titration were significant ($P < 0.001$) for both children and adults. Initial doses were slightly more likely to be titrated for children (67.1%) than for adults (53.7%). In the children, titration occurred an average of 116.5 days (SD = 127.2) after initiating ADHD therapy, approximately 30 days more than the average length of time to titration observed in the adults (mean = 85.3, SD = 111.2). This difference in the timing until dose titration between children and adults was significant ($P = 0.020$).

Compliance and Persistence

As described earlier, the MPR was used to define compliance and persistence. Children were compliant with their initial ADHD therapy an average of 34.2 days (SD = 75.6, range 0 to 547) while

FIGURE 1 Percentage of Children and Adults Who Were Compliant With Initial ADHD Medication Over Specified Time Periods

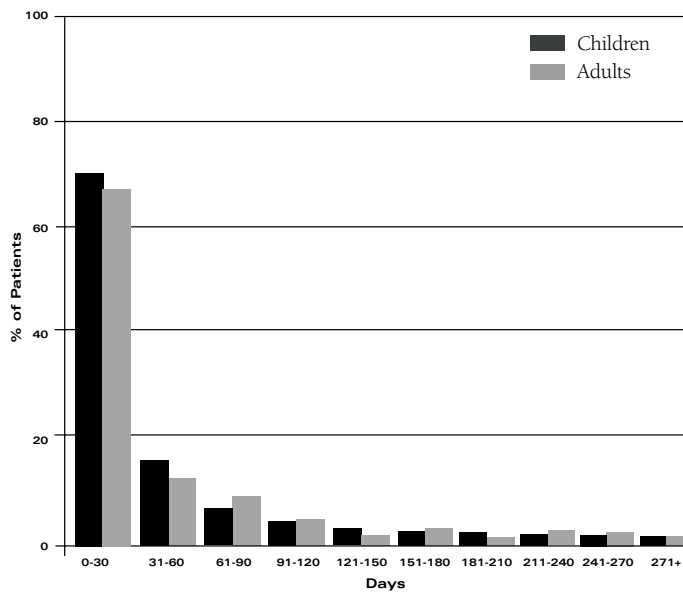
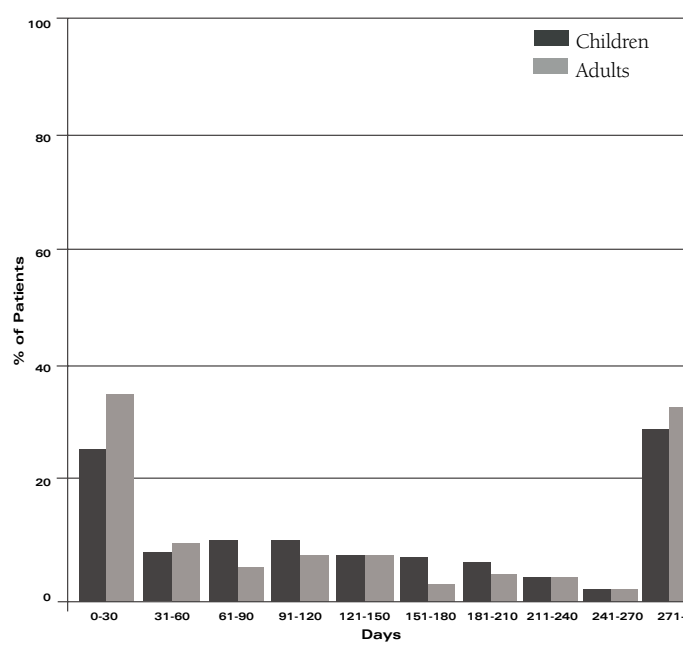


FIGURE 2 Percentage of Children and Adults Who Were Persistent With Initial ADHD Medication Over Specified Time Periods



adults were compliant for an average of 49.5 days (SD = 109.0, range 0 to 547) (Table 4). A value of 0 indicates that there were no refills to the index prescription (i.e., only the first prescription was filled). As depicted graphically in Figure 1, the majority of children and adults were only compliant for the first 30 days. The number of days persistent was similar for children (M = 200.9, SD = 204.5, range 0 to 547) and adults (M = 199.9, SD = 219.9, range 0 to 547). There were no significant differences between children and adults in terms of compliance ($P = 0.090$) and persistence rates ($P = 0.952$). Compared with compliance, children and adults were persistent with their initial ADHD medication for longer periods of time (Figure 2). However, the majority of patients were persistent for less than 6 months.

Discussion

This study examined treatment patterns within a population of managed care enrollees with newly treated ADHD. Although the occurrence of ADHD in the child population in this study (2%) was lower than previously published prevalence estimates (3% to 7%), gender differences (i.e., males outnumbering females) were consistent with the ADHD literature where there is a 4:1 male to female ratio. Based on diagnostic and pharmacological treatment information derived from claims data, 0.1% of children and 0.01% of adults met our definition of being newly treated for ADHD. Comorbid depression occurred frequently in these newly treated ADHD patients, in nearly one third of children (31.6%) and two thirds of adults (63%). Anxiety was found to be a comorbid condition in more than one third of adults (36.4%) and in 10.3% of children. These comorbidity rates are similar to the ranges reported in the literature.²⁴

One review found ranges of 10% to 75% for ADHD and mood disorders in children and youth.²⁸ A study of adults with ADHD found the majority with additional psychiatric comorbidities, including 53% with generalized anxiety disorder, 34% with alcohol abuse or dependence, 25% with dysthymia, and 25% with cyclothymia.²⁹ Finally, another adult study found 31% of adults with ADHD also had a comorbid affective disorder.³⁰

Relatively few children (11.6%) and adults (11.1%) changed medications during the study period; however, for children and adults to switch treatments, it took an average of more than 5 and 4 months, respectively. Dosage titration was more common, occurring in more than two thirds of the child cases and one half of the adult cases. Although the average number of days to titration for children (116.5 days) and adults (85.3 days) was shorter compared with medication changes, this is still a rather lengthy time period given the early onset of action of the stimulants. The tendency for treatment changes to occur earlier in the newly treated adults compared with the children may be related to adults being better able to advocate for changes in their own therapy. Because treatment patterns are inferred from the pharmacy claims data, it is not possible to know how treatment patterns are related to provider recommendations, patient compliance, and

clinical outcomes (e.g., lack of symptom alleviation and adverse events).

Consistent with previously published data related to medication compliance in children with ADHD,²¹ our data suggest relatively poor compliance given the chronic nature of the disorder. A conservative estimate of compliance, allowing for only minimal lapses in medication coverage, indicated that children and adults were compliant for rather brief time periods. A more liberal definition—persistence—suggested that patients continued to obtain ADHD prescription refills over a period of approximately 200 days. In addition, both children and adults had longer-than-expected periods of time between pharmacy refills, which could lead to inadequate amounts of available medication and possibly suboptimal pharmacological treatment. The more liberal definition of persistence may be a better estimate of compliance, as it indicates how long patients attempted to refill prescriptions and allows for drug holidays (i.e., weekends and summer time periods when medication is not prescribed) over the 18 months claims period that patients were followed from their initial prescription.

Limitations

Although this study highlights medication-use patterns and compliance problems in children and adults with newly diagnosed and pharmacologically treated ADHD from a large population of insured individuals (>2 million enrollees), several limitations are noted. Patients were excluded who did not have at least 1 ADHD diagnosis associated with a medical visit or pharmaceutical claim; children were excluded who did not have at least 2 ADHD diagnoses at some time during the 18 months of their claims. For children, this meant excluding 50.6% of all those with psychostimulant prescriptions and an additional 24.2% of children with only 1 ADHD diagnosis. In this way, the study insured more confidence that the results are specific to patients with ADHD. However, the findings cannot be generalized to children not diagnosed with ADHD for the reason of avoiding stigmatization, or where the stimulant is being used “diagnostically” to determine if it helps, or for inconclusive symptom configurations not meriting a repeated diagnosis in the physician’s opinion. This method also excludes early ADHD treatment “dropouts,” who receive a single diagnosis and 1 prescription, then fail to return.

Thus, the exclusionary criteria are very conservative, attempting to isolate patients who most probably have ADHD according to the claims record. More liberal inclusion criteria would have only made the compliance and persistence rates worse. The results do not address the “as needed PRN” or brief use of psychostimulants, except in documenting that there are sizable numbers of patients without probable ADHD diagnoses being prescribed psychostimulants. This is an important issue, but outside the scope of this study.

In addition to using medical claims to determine the pres-

ence of mental health conditions, this study used antidepressant and anxiolytic pharmaceutical claims as proxies for the presence of comorbid mental health conditions. Although it must be acknowledged that some of these medications are used to treat other conditions, there is evidence suggesting that medical claims underidentify patients with mental health conditions, such as depression.²⁵ Particularly in primary care, secondary and mental health comorbid diagnoses are often omitted. Thus, our method of identifying patients, although 2-fold (using either diagnostic and pharmacy data), is conservative and probably underestimates the true incidence of comorbid conditions.

Regarding compliance and persistence, pharmacy claims data may provide useful information, but the claims do not provide information about whether or not medication was taken as prescribed. The MPR is a proxy for examining compliance and persistence because it relies on pharmaceutical refill rates and assumes that medication that is dispensed is actually taken by patients. In addition, assumptions are made in terms of cut-offs for determining length of compliance and persistency. Further, some physicians and other health care providers recommend that children only take stimulant medications during the school week, thereby giving the children “drug holidays” on the weekends and during vacation time periods. The definitions used to determine compliance and persistence in our study allowed for some missed medication doses, but these definitions are not sensitive to extended drug holidays, perhaps making compliance and persistence rates appear worse in children.

Because medical and pharmacy claims data are collected for the purpose of payment and not research, variables not associated with reimbursement, such as severity of, and changes in, ADHD symptoms, are not available. In addition, patients could have received medications without the presence of a prescription claim by filling prescriptions outside of the health plan pharmacy system; drug samples are unlikely to be a factor in this study of ADHD drugs since all are controlled substances.

Future Directions

This study was undertaken prior to the use of longer-acting treatment agents and nonstimulant medications with ADHD indications (e.g., atomoxetine); therefore, future research should address compliance with these types of medications and compare rates between medications. Because other medications that are not indicated for the treatment of ADHD may be used in clinical practice, it may also be of interest to examine compliance with these medications used to treat ADHD.

The findings from this study should be replicated using other ways to measure compliance (e.g., microelectronic monitoring, pill counts, and direct questioning of physicians and patients). Each of these methods has advantages and disadvantages, and using them in combination may better estimate the scope of compliance problems. The compliance issues suggested in this study indicate that future research in this area could

examine factors that are potentially related to compliance to address barriers to compliance with ADHD medications. In fact, research suggests that, in children with ADHD, demographic characteristics (e.g., age) and disease variables (e.g., ADHD severity) may be predictive of compliance.²³ Other factors of interest may include medication costs; other comorbidities; and clinical outcomes, including side effects, symptom scores, and quality of life. It is possible that studies could identify different barriers for children and adults that would be amenable to intervention, which may lead to more effective, ongoing pharmacological treatment of ADHD.

Conclusion

This study highlights some patterns that may emerge during pharmaceutical treatment for ADHD. Specifically, dosage changes occurred with some frequency and after a 2- to 3-month course of treatment, on average. Although compliance estimates indicated that patients did not consistently take medications for extended periods of time, persistence estimates suggest that patients continued to refill prescriptions over longer periods of time. Given these treatment patterns, pharmacological treatment in newly treated ADHD patients may be suboptimal and may impact outcomes, including the effectiveness and cost of treatment. Therefore, there is an opportunity for health care providers to explore and address these issues with the goal of enhancing treatment outcomes.

DISCLOSURES

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