REPORT SUMMARY

This report contains the latest findings from research conducted by Express Scripts providing an in-depth analysis of the most current trends in the use of medications to treat Attention Deficit Hyperactivity Disorder (ADHD).

From an annual sample size of approximately 15 million privately insured individuals ages 0 to 64, the research examined the de-identified pharmacy claims of more than 400,000 individuals who filled at least one prescription for a medication indicated for the treatment of ADHD during the five-year study period. Prevalence, utilization and costs were evaluated from 2008 to 2012, including assessments of trends according to age, gender and geography. Because of the paucity of data on children under four years of age, only findings pertaining to those ages 4 to 64 are included in the report.
KEY FINDINGS OF THE RESEARCH INCLUDE:

• Use of ADHD medications among Americans rose 35.5% from 2008 to 2012, increasing the number of privately insured individuals on these drug therapies to more than 4.8 million in 2012.

• Boys ages 12 to 18 are the most prevalent users, with 9.3% of that population on an ADHD drug in 2012, up from 7.9% in 2008.

• While the number of girls on ADHD medications is less than half that of boys, women outnumber men in their use of these drug therapies.

• Unlike males, whose numbers significantly decrease after age 18, younger women ages 19 to 25 have higher rates of medication use than girls 4 to 18 years old.

• In 2012, the highest concentration of ADHD medication use was found in the South, with South Carolina experiencing the highest prevalence of ADHD medication use: 5.0% overall and 14.1% for 12 to 18 year old boys. The lowest rates were seen in the Western region of the U.S.

• Use of antipsychotic treatments among patients taking ADHD medication is substantially higher compared to non-ADHD medication users, especially in the age 4 to 11 category, where use of antipsychotics was 10 times higher than those not being treated for ADHD in 2012.

• Despite the high rate of antipsychotic use among those being treated for ADHD, Express Scripts data found that those numbers have actually declined among all age groups since 2009, reversing a significant upward trend that was identified in earlier research.

• Spending on ADHD medication rose 14.2% in 2012, the greatest increase seen among any traditional drug category; it is forecast to grow nearly 25% by 2015.¹
**BACKGROUND**

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most commonly diagnosed conditions of childhood in the U.S. According to the Centers for Disease Control (CDC), in 2012 11% of children ages 4 to 17 had been diagnosed with ADHD. In recent years, a recognition that ADHD can continue into adulthood has led to increased diagnosis and treatment in adults.

ADHD is characterized by exaggerated levels of inattention, impulsivity and hyperactivity that can result in social, academic and occupational impairment. While hyperactive behaviors are common in patients with ADHD, ADHD with inattentive presentation is more common among women who experience distracted and inattentive behaviors rather than hyperactivity and impulsive conduct.

Although severe inattentive behaviors were first described in 1902, ADHD was not recognized as a distinct mental condition until 1980, when the American Psychiatric Association (APA) published guidelines for diagnosis in children. Since then, the population treated for ADHD has exploded in the U.S., dwarfing its diagnosis and treatment seen in other countries.

Medication therapy is the most common treatment, although behavioral therapy is the recommended first-line approach in younger children. The psychostimulant Ritalin (methylphenidate) was the first widely used medication to treat ADHD. Stimulants continue to be the most popularly prescribed drug therapy for ADHD, while a smaller population of patients are treated with nonstimulant medications.

While stimulants are extremely effective in reducing ADHD symptoms, like many prescription medications, there are risks associated with their use, including addiction and adverse reactions in patients with cardiovascular disease or related conditions. ADHD medications may also increase risks of other psychiatric conditions and can cause seizures if taken in high doses. 2

There is also increased concern about abuse of prescription stimulant medications prescribed for ADHD and their wide availability on the black market in an academic setting. According to recent research, one in eight teenagers have misused or abused ADHD drugs. 3 In 2011 and 2012, the Drug Enforcement Administration (DEA) increased its efforts to combat illicit use of these drugs by implementing additional restrictions on their availability. These new restrictions required manufacturers to limit production of these medications to a forecasted amount, which combined with substantial increases in utilization, led to a significant shortage in supply.
THE NUMBERS DRIVING ADHD MEDICATION USE

Express Scripts research examined the latest data available to identify trends in the use of ADHD medications among Americans of different ages and genders.

The analysis shows that the number of adults and children using ADHD medications continues its meteoric rise, climbing 35.5% from 2008 to 2012. In 2012, almost 4.8 million privately insured Americans had taken a drug to treat ADHD.

PERCENT OF POPULATION ON ADHD MEDICATIONS

BY AGE 2008-2012

While children are still the primary users of ADHD medications, the number of adults on these drugs has been increasing at a much faster pace, up 53.4% vs. 18.9% from 2008 to 2012. The dramatic rise in both the diagnosis and treatment of ADHD in adults can largely be attributed to growing evidence that ADHD is not a condition exclusive to childhood. In fact, according to recent research approximately 30% of children with ADHD carry this disorder into adulthood.4

As has traditionally been the case, boys are the predominant users of these medications and far surpass the number of girls on ADHD drug treatments. However, the trend is the reverse among adults, with more women on ADHD medications than men.
DAVID J. MUZINA, M.D.
Vice President, Specialist Practice Clinical, Research and New Solutions at Express Scripts

THE NUMBERS DRIVING ADHD MEDICATION USE

There has been a dramatic shift in the way we think about ADHD in recent years. While still predominantly affecting children, we now know that ADHD is not just a childhood condition but can continue to impact behavior in adults. One unexpected development that has resulted from recognition of adult ADHD is that women have been receiving treatment to a greater extent than men.

Since females often present with the inattentive form of ADHD and do not display disruptive behaviors in school, their symptoms may be overlooked and frequently go undiagnosed and untreated. Later in life, when they become more aware of the condition, especially if their children are showing signs of ADHD, women may recognize their own symptoms related to the condition and consult with a physician about it. They also tend to be the parent who attends doctors’ visits when their child is being treated for ADHD.

Included in the growing numbers of women on ADHD medications may also be some who are being treated off-label for resistant depression since stimulants are sometimes used in these cases in conjunction with antidepressants.

For women with clinical diagnoses that warrant drug treatment, ADHD medications can be tremendously beneficial. Unfortunately there are less appropriate uses of the medication that may also be driving these increases but raise safety concerns given the potential side effects and addictive nature of stimulants. Since stimulants are known to decrease appetite, they are sometimes used improperly as a weight loss aid which can be an attractive alternative to willpower for dieting. These medications may also be utilized by women who may experience symptoms of attention disorders as a result of keeping up with the multiple demands on their time.
Gender differences are also seen when comparing prevalence among children and adults. Unlike males whose numbers fall precipitously as they enter adulthood, the prevalence of young women using these medications continues to rise past their childhood years, with 19 to 25 year old females actually eclipsing the number of girls taking ADHD medications by 27%.

**CHILDREN AND YOUNG ADULTS ON ADHD MEDICATIONS**

**BY GENDER 2012**

Unlike males, whose numbers plummet after age 18, younger women ages 19 to 25 have higher rates of medication use than girls 4 to 18 years old.
Utilization Trends in Children

Historically, the diagnosis and treatment of ADHD has been substantially higher in boys than girls, owing in part to more aggressive, disruptive and impulsive behaviors exhibited in young males, while girls are more apt to display the “distracted” symptoms of the condition which may be more easily overlooked.

Express Scripts data shows that this trend continues to hold true. In 2012, 7.8% of boys ages 4 to 18 were taking an ADHD medication, more than twice the number of girls the same age (3.5%).

Teenage boys, 12 to 18 years old, are by far the most prevalent users. In 2012, 9.3% of that population took an ADHD medication – up from 7.9% in 2008.

More than 80% of children taking ADHD medications use a stimulant form.
Increased awareness and acceptance of ADHD as a behavioral disorder over the past few decades has resulted in many children with this condition receiving treatment that they need to succeed in school and in their lives. However, there are also a variety of clinical and societal trends that have inflated ADHD diagnoses and drug treatments to questionable levels in the U.S.

One contributing factor is the heightened pressure on schools and students to boost academic performance in the current high-stakes testing environment where there is less tolerance for disruptive classroom behaviors. This is especially true among boys who often display the more impulsive and aggressive form of the condition.

While there are children who most certainly have ADHD and benefit greatly from drug treatments, ADHD has unfortunately become the go-to condition for children with behavioral issues, sometimes masking other problems such as mood, anxiety, oppositional defiant disorder or conduct disorder. Pediatricians and primary care physicians who often do not have the time or the training to conduct the thorough neuropsychological testing and clinical interviews needed to positively determine an ADHD diagnosis, are the ones primarily responsible for treating these children. Physicians can also find themselves pressured by parents who are not happy with their child’s grades or behaviors and are convinced that that it must be ADHD. Given the general lack of access to behavioral therapy and its expense, a drug prescription is usually the outcome once an ADHD diagnosis is made.

Another factor that may be adding to the prevalence of ADHD diagnosis and treatment is children’s exposure to “screen time” which has been shown to increase disruptive or distracted behaviors and lead to lower school grades. While there is no conclusive evidence that screen activities actually cause ADHD, video-game playing – especially among young children whose brains are developing – trains them to respond to very quick stimulus change and, without the balance of other activities requiring prosocial protracted attention, can result in behaviors that mimic ADHD symptoms. The pervasive use of technology at younger and younger ages is going to increasingly be a factor in ADHD diagnosis. It’s a phenomenon that both parents and clinicians need to be concerned about.
While the vast majority of children are treated with stimulants, there is a higher proportion of younger children on nonstimulant medications than is seen in teenagers. In 2012, 19.5% of 4 to 11 year olds taking an ADHD medication used a nonstimulant as compared with 14.2% of 12 to 18 year olds. Nonstimulants are considered easier to tolerate since they do not cause a number of the side effects associated with stimulants, including loss of appetite and difficulty sleeping. However, they may not be as effective as stimulants in treating ADHD in some patient populations.

The research also assessed the month-to-month utilization of ADHD medications and found that children’s use of these drugs dropped precipitously during the summer months. Among the reasons children may take these “drug holidays” is to reverse stunted growth which is another potential side effect of stimulant medications.

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SIDENOTE: In addition to using drug holidays to counteract impaired growth, some children are given medication breaks to lessen their exposure to a number of unpleasant side effects caused by stimulants. There is, however, some evidence that children with ADHD who remain on medications throughout the year have fewer problems than those whose treatment is interrupted.⁵
If ADHD medication side effects or growth issues are significant, then drug holidays are an important option for alleviating these problems. However, an individualized risk/benefit analysis and conversation with the patient and parents should be part of any determination about the need for a medication break. Ceasing treatment for a period of time may, in some cases, make it harder for a child to get back to taking ADHD medications on a regular basis, resulting in nonadherence or suboptimal use of the drug that can be problematic.

According to the analysis, more than three in four children using ADHD medications were prescribed the drug by a primary care physician rather than a specialist.
Utilization Trends in Adults

The Express Scripts analysis revealed a substantial spike in the adult population on ADHD drug treatments in recent years, with the largest gains seen among 26 to 34 year olds – up 84.4% from 2008 to 2012. Increases in prevalence among women in this age group were slightly higher, rising 85.1% over the five-year period.

While the increases are greatest among 26 to 34 year old women, younger females ages 19 to 25 showed the highest use of ADHD drug treatments compared to women in other age groups. Interestingly, they also surpassed girls in the use of these drugs, with 4.4% of them on an ADHD medication in 2012 compared to only 3.5% of 4 to 18 year olds.

Females and Males on ADHD Medication

As mentioned earlier in the report, the gender differences in adult use of ADHD medication are the opposite of those seen in children. There is only a slight difference between the number of men and women ages 19 to 25 using these drugs. After that, more women than men are on ADHD treatments and the relative gap between them widens as they get older.

The research showed that approximately two-thirds of adults were prescribed ADHD medications by a primary care physician rather than a specialist.

Sidetnote: In its updated edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) issued in May 2013, the American Psychiatric Association has for the first time provided specific guidelines to mental health practitioners on characterizing and diagnosing ADHD in adults. The DSM-5 reflects more than 20 years of published research demonstrating that while ADHD presents first by age 12, it can continue into adulthood. Adults with ADHD have higher rates of divorce, drug abuse, job loss and criminal behavior.
Utilization Trends in Adults

Very little research has been done on ADHD medication utilization among adults so the Express Scripts data adds important new information to our understanding of these trends.

The fact that we’re seeing a significant uptick in the number of adults prescribed ADHD medication in recent years is clearly tied to recognition that there is a proportion of individuals who continue to need treatment for ADHD in adulthood. What I find particularly intriguing are the gender differences that emerge in utilization of these medications in adults. It’s not surprising to see that there’s a significant drop in use of ADHD drugs in boys after they hit age 18 since once kids leave home, they tend to become far less compliant with their medications. However, it is striking that we’re not seeing that effect in females. The disparities may be related to the fact that females are going to college at a higher rate than males and students who go on to higher education utilize stimulants more than students who do not. Also, females tend to be far better patients than men and comply more readily with recommended care. Additionally, young women are often in more regular contact with their parents which can help support medication adherence.

It is also interesting that once they enter the workplace, women actually outpace men in their utilization of ADHD treatments. As mentioned, there is a tendency for females to adhere better to medical care which is part of what we see in these numbers. But another factor that has an appreciable effect in driving ADHD drug use, especially in career women, is the “superwoman syndrome.” For some women, stimulants may provide the extra energy and focus they need to perform at a high level both at home and on the job.

There is no doubt that there are adults who require ADHD medication to succeed in both their professional and private lives. However, the fact that there’s been a substantial spike in medicating adults for ADHD does raise the same questions we’ve asked about appropriate use of these treatments in children: are we now over-diagnosing and overmedicating in the adult population?
There are significant geographic differences in ADHD drug utilization throughout the U.S. According to Express Scripts research, the concentration of ADHD medication users in Southern states is higher than in other regions of the country. In 2012, the proportion of Southerners of any age who were taking ADHD medications was 3.6%, compared with 2.9% for the country as a whole. Boys between the ages of 12 and 18 who live in the South had the highest prevalence nationwide, reaching 10.5% while nationally, 9.3% of boys that age are using ADHD medications.

PREVALENCE OF ADHD MEDICATION USAGE

BY STATE & REGION 2012

<table>
<thead>
<tr>
<th>REGION</th>
<th>2012 PREVALENCE</th>
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<tbody>
<tr>
<td>MIDWEST</td>
<td>2.9%</td>
</tr>
<tr>
<td>NORTHEAST</td>
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</tr>
<tr>
<td>SOUTH</td>
<td>3.6%</td>
</tr>
<tr>
<td>WEST</td>
<td>2.2%</td>
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</tbody>
</table>
Individual Southern states show even greater differences. South Carolina had the highest proportion of residents in the country on an ADHD medication at 5.0%, 72% higher than the national average. Older boys living in that state showed an alarmingly high rate of use, with 14.1% of 12 to 18 year olds using an ADHD medication in 2012 vs. 9.3% nationally. Louisiana had the second highest prevalence rate in the country at 4.7% for the population as a whole and 13.6% for boys ages 12 to 18. Louisiana also stood out for having the highest number of older girls and young women on ADHD treatments. In 2012, 7.8% of girls ages 12 to 18 were on ADHD drugs, while 8.0% of 19 to 25 year olds were taking these medications – nearly double the number of females their age undergoing medication treatment nationwide.

The rate of ADHD medication use in South Carolina was **72% higher** than the national average.

**The Geography of ADHD Drug Utilization**

There are a number of factors that may be driving regional variations in ADHD medication use. One potential contributor in states with high treatment rates is lack of access to behavioral specialists who have the experience and training to properly diagnose ADHD. There is also evidence that high medication use is correlated with states that put a great deal of emphasis on high stakes testing and where schools and teachers are penalized for students’ poor performance. Furthermore, many of these school systems lack the resources to properly address behavioral problems, making them more apt to label kids as having ADHD. We also know that socio-economics plays a role, with lower-income children more likely to be diagnosed with ADHD.
The smallest proportion of the population on ADHD medication was found in the West; Hawaii ranked lowest among all states in the country with only 0.4% of its residents on an ADHD treatment – far below any other state.

Of note, while the number of people using ADHD medications is highest in the South, it is also the region where individual patients fill the fewest ADHD medication prescriptions. In 2012, the average number of ADHD medications filled per patient in the South was 6.87 as compared to 7.47 in the Midwest, the region with the greatest per patient fill rate. The fact that out-of-pocket costs are highest in the South could be a factor impacting patients’ use of medications. (See the section Cost of ADHD Treatments on page 22 for more details.)
TRENDS IN URBAN, SUBURBAN AND RURAL AREAS

The research also examined differences in the use of ADHD medications in urban, suburban and rural areas of the U.S.

There were more people living in suburban areas who used ADHD medications than in rural or urban areas of America. The concentration of suburban residents on these treatments was 3.2% in 2012, while 3.0% of those living in rural areas were using ADHD drugs. The lowest numbers were seen in urban areas, where the prevalence rate was 2.5%. Additionally, only 8.5% of ADHD medication users in urban areas filled prescriptions for nonstimulant medications compared to 9.5% in rural areas and 10.5% in suburban parts of the country.

PREVALENCE OF ADHD MEDICATION USE

IN URBAN, SUBURBAN & RURAL AREAS 2008-2012

THE GEOGRAPHY OF ADHD DRUG UTILIZATION

In suburban and wealthier communities, there is growing interest in ADHD medications as academic performance enhancers. There’s intense competition among high school students for spots in prestigious schools and for scholarship money. It’s been my experience that many parents in this economic stratum are looking for any advantage for their child including a drug that can help boost performance, especially around standardized testing times.
CONCURRENT TREATMENTS

To understand more fully how other medications and nondrug therapies are being utilized by patients with ADHD, Express Scripts researchers examined the use of antipsychotics, antidepressants and psychotherapy in this population.

ANTIPSYCHOTIC MEDICATION USE IN ADHD PATIENTS

The use of antipsychotics for the treatment of ADHD patients has long been controversial. Antipsychotics are powerful medications with potentially severe side effects. They are approved for use in patients with mood disorders, schizophrenia and other serious mental health conditions. They are not approved to treat ADHD. However, they are at times prescribed off-label for some ADHD patients with extreme behavioral problems since they can be very effective at quickly improving behaviors. A small subset of children with ADHD may also have other mental health conditions that warrant the use of antipsychotics.

Express Scripts data shows that children using ADHD medications are far more likely to be taking an antipsychotic than children who are not being treated for ADHD. The concomitant use of antipsychotic and ADHD medications in children ages 4 to 11 stands at 7.4%, more than 10 times higher than children not using ADHD drugs. However, children ages 12 to 18 with ADHD had the highest concomitant use of antipsychotic medication at 9.6%, more than seven times the rate of use seen in their peers not being treated for the disorder.

COMPARISON OF ANTIPSYCHOTIC USAGE IN CHILDREN

BY AGE GROUP WITH & WITHOUT ADHD MEDICATION, 2012

Children on ADHD medications are 10 times more likely to be using an antipsychotic than children who are not using ADHD medications.
This new data is set against a backdrop showing that 9.9% of the ADHD population of all ages took an antipsychotic medication in 2012 compared against just 1.5% of non-ADHD privately insured individuals. However, the research also reveals a trend of progressively lower annual use of antipsychotics in children and adults taking ADHD medications since 2009. The decrease was especially notable in adults with ADHD ages 26 to 34 who reduced their use of antipsychotics from 10.6% in 2008 to 7.6% in 2012. The Express Scripts data also shows a reversal in trend in the past three years when compared to an earlier study that reported a sevenfold increase in the use of antipsychotics in children and a nearly fivefold increase in adolescents from 1993 to 2009, many of whom were diagnosed with ADHD.  

CONCURRENT TREATMENTS

The fact that so many children with ADHD are also being treated with antipsychotics is alarming. While there are some cases that may warrant the use of these drugs along with stimulants, they should be treated as last resort therapies that are used only when other medications have been tried and failed. Atypical antipsychotics are very powerful drugs with potentially severe side effects. They can cause permanent neurological damage. They also increase risks of obesity, although in the ADHD population that may not be as significant a problem since stimulants may counter that effect. However, antipsychotics can increase triglyceride and lipid levels and raise the risk of type 2 diabetes in children independent of weight gain.

While the numbers are still far greater than they should be, it does appear that FDA warnings about these drugs and awareness of their dangerous side effects has begun to make an impact as seen in our data showing a slight dip in use since 2009.
ANTIDEPRESSANT USE IN ADHD PATIENTS

Depression is a common comorbidity of patients with ADHD, especially among females,11 and in some cases, ADHD medications have been used to treat major depression which does not respond to other treatments.12 The symptoms of one disorder commonly mimic the symptoms of the other, and misdiagnosis is a potential problem.

Express Scripts data shows that ADHD users of both genders and all ages are far more likely to be taking an antidepressant than those who are not being treated for ADHD. According to the analysis, use of antidepressants for those on ADHD treatments increases with age among both females and males, but starting at age 12, females with ADHD are far more likely to also be using an antidepressant than males. The rate of antidepressant treatment is 15.0% in children with ADHD and 40.5% in adults with ADHD but runs as high as 64.4% in females ages 50 to 64 and 47.0% in males of the same age.

Among children, the greatest increase in concurrent use was seen in children ages 4 to 11 from 2008 to 2011, with prevalence up about 10.6%. Antidepressant use declined over this time frame among most adults with ADHD with the one exception being males in the 19 to 25 age group, who saw a slight rise in the number of those also taking an antidepressant.

PREVALENCE OF ANTIDEPRESSANT USE

BY AGE & GENDER WITH & WITHOUT ADHD MEDICATION, 2012
**PSYCHOTHERAPY FOR CHILDREN WITH ADHD**

The Diagnostic and Statistical Manual of Mental Disorders–5, published in 2013 by the American Psychiatric Association, recommends psychotherapy as a first-line intervention in children with ADHD, supplemented with medication as needed in older children. This guideline notwithstanding, only one out of four insured children taking ADHD medication received any form of psychotherapy in a 2010 study conducted by Express Scripts with RAND Health. The study also identified a wide disparity in the rates of psychotherapy received across the U.S.

One outcome of the study validated that children in counties with the least number of psychologists were half as likely to be receiving therapy as those in counties with the most psychologists. But among other communities with comparable mental health resources, there was no apparent clinical explanation for the variation in psychotherapy among ADHD patients.

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**SIDENOTE:** Research has shown that while drug treatment for ADHD is extremely effective, the combination of medication and behavioral therapy can result in better academic performance and family relations. The combined approach may also lead to the prescribing of lower doses of medication.
COST OF ADHD TREATMENTS

The costs of ADHD medications on a per-member-per-year (PMPY) basis experienced a 91% increase over the five-year study period, from $18.57 in 2008 to $35.52 in 2012, driven primarily by a spike in utilization, although there was also an increase in the cost of these drugs. The average that plans paid per prescription increased 35.4% to $146.41, while beneficiaries’ out-of-pocket costs during this same period rose only 4.2% to $27.52.

The greatest increase in the average plan cost per prescription was seen in older patients, ages 50 to 64, at $236.92; while those ages 4 to 11 produced the lowest increase at $117.75. Plan costs per prescription differed by gender as well, with females averaging $153.29, but considerably lower for males at $140.98.

Regional differences in the average cost per prescription were also noted, with the highest costs in 2012 seen in the Midwest at $154.37, while the lowest per prescription costs were observed in the South at $140.61. However, the highest patient out-of-pocket costs are shouldered by those living in the South, with an average per prescription price of $32.27, while the lowest cost at $23.23 was observed in the West.

AVG. PLAN COSTS VS. MEMBER OUT-OF-POCKET COSTS

BY REGION PER ADHD PRESCRIPTION, 2012

- Avg. Plan Cost per Rx
- Avg. Member Cost per Rx

National spend on ADHD medications increased 91% from 2008 to 2012.
The type of medication prescribed as well as the physician prescribing it also significantly affected costs. On average, stimulant medications cost plans and members $142.86 per prescription compared to $159.74 for nonstimulants. The total per prescription cost when medication was prescribed by a specialist was $167.28 and $133.65 when written by a primary care physician. However, per patient out-of-pocket costs were slightly lower for medications prescribed by specialists. This may be related to a greater proportion of older patients – those more likely to be using expensive, branded medications without generic alternatives – being prescribed ADHD medications by specialists when compared to those prescribed by primary care physicians.
REFERENCES


APPENDIX

ADHD MEDICATION SPEND

In a separate analysis, the Express Scripts 2012 Drug Trend Report found that spending on ADHD medication rose 14.2% in 2012, the greatest increase seen among any traditional drug category including spend on diabetes treatments which has been rising dramatically in recent years due to the obesity epidemic in the U.S. The growth in ADHD drug spending was driven primarily by increased utilization, particularly among adults, but also to increased costs which were in large part due to the shortage in 2012 of active ingredients contained in many of the medications in this class.

<table>
<thead>
<tr>
<th>DRUG CATEGORIES</th>
<th>INCREASE IN DRUG SPEND (2012)</th>
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<tr>
<td>ADHD</td>
<td>14.2%</td>
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<tr>
<td>DIABETES</td>
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<td>DEPRESSION</td>
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<td>INFECTIONS</td>
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2012-2015 FORECAST

The Express Scripts 2012 Drug Trend Report also predicted that spending on ADHD medications will rise 24.8% between 2012 and 2015, even surpassing the increases in spending expected for diabetes treatments.

<table>
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<tr>
<th>DRUG CATEGORIES</th>
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<tr>
<td>ULCER DISEASE</td>
<td>-23.3%</td>
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TOP DRUGS BY MARKET SHARE IN 2012

The top ADHD medication in the market was amphetamine/dextroamphetamine (Adderall), followed by methylphenidate (Ritalin).

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>MARKET SHARE</th>
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<tbody>
<tr>
<td>AMPHETAMINE/DEXTROAMPHETAMINE</td>
<td>34.4%</td>
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<tr>
<td>METHYLPHENIDATE</td>
<td>21.9%</td>
</tr>
<tr>
<td>VYVANSE (LISDEXAMFETAMINE)</td>
<td>15.8%</td>
</tr>
<tr>
<td>FOCALIN XR (DEXMETHYLPHENIDATE)</td>
<td>4.6%</td>
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<tr>
<td>STRATTERA (ATOMOXETINE)</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

ADHD DRUG DEVELOPMENT TIMELINE

2007: FDA approves Vyvanse (lisdexamfetamine)
2009: FDA approves Intuniv XR (guanfacine hydrochloride)
2009: Adderall XR available as generic
2010: Desoxyn (methamphetamine) available as generic
2010: FDA approves Kapvay (clonidine hydrochloride)
2011: Concerta (methylphenidate) available as generic
2011: American Academy of Pediatrics (AAP) revises guidelines to include drug treatment for 4-5 year olds
2012: Ritalin LA (methylphenidate ER) available as generic
2012: Metadate CD (methylphenidate controlled release) available as generic
2012: Provigil (modafinil) available as a generic
2013: Kapvay (clonidine) available as a generic
2013: American Psychiatric Association (APA) includes guidelines for diagnosing ADHD in adults
2014: Intuniv (guanfacine) expected to lose patent protection
2016: Focalin XR (dexamethyphenidate) expected to lose patent protection
2017: Strattera (atomoxetine) expected to lose patent protection
ABOUT THE COMMENTATORS

Dr. Joseph Austerman is the current section head for the division of child and adolescent psychiatry at the Cleveland Clinic. He is also the director of the child and adolescent psychiatric consult liaison service and a member of the ADHD Center for Evaluation and Treatment Center (ACET) at the Cleveland Clinic.

Dr. Austerman specializes in the management of attention deficit/hyperactivity disorder, anxiety disorders, and psychiatric management of chronic pediatric illnesses. He currently sits on the American Academy of Child and Adolescent Psychiatry Counsel for the Physically Ill Child and a Counsel for Child Adolescent Emergency Psychiatry. His research focuses on the psychiatric aspect of chronic medical illnesses.

He has won numerous teaching awards, including the Dr. William and Roxanna Michener Award for the Development of Leadership, and completed both the distinguished educator certificate program and the Leading in Health Care program through the Cleveland Clinic Academy.

Dr. Austerman has held associate faculty positions at Case Western Reserve University School of Medicine, Ohio University Heritage College of Medicine, and the Cleveland Clinic Lerner College of Medicine. He completed a Bachelors of Science majoring in microbiology and chemistry at a Ohio University and the Doctor of Osteopathy degree from the Ohio University Heritage College of Medicine.
ABOUT THE COMMENTATORs

Dr. David J. Muzina joined Express Scripts in 2009 as vice president and National Practice Leader for the Neuroscience. Leading the company’s 15 specialized pharmacy practices, or Therapeutic Resource Centers (TRCs), he is responsible for continuous improvement across all practices with an emphasis on clinical quality, affordability and service for Express Scripts members. In addition, he has oversight for training specialist pharmacists and clinicians, research activities, and enhancing the practice of the specialized pharmacy care provided to all patients.

Prior to Express Scripts, Dr. Muzina was director, Center for Mood Disorders Treatment & Research, and Associate Professor of Medicine at the Cleveland Clinic. During his tenure there, he led the Cleveland Clinic’s participation in the NIMH Center of Excellence for Care and Study of Children and Adults with Bipolar Disorder and Alcohol/Drug Abuse at Case Western Reserve University. Dr. Muzina also served on the medical staff for several professional sports teams in Cleveland, as well as the Cuyahoga County Mental Health Board of Governors.

Additionally, Dr. Muzina directed Cleveland Clinic’s Adult Inpatient Psychiatry Program and oversaw integration of behavioral health units throughout the clinic’s regional hospital system. He was Founding Director of the Center for Mood Disorders Treatment and Research and in partnership with the University of Toronto formed the International Mood Disorders Consortium.

Dr. Muzina graduated magna cum laude from the University of Dayton (Ohio) in 1989 before pursuing his medical degree at Case Western Reserve University School of Medicine in Cleveland, Ohio. He completed his internship and psychiatry residency training at The Cleveland Clinic Foundation, serving as Chief Resident from 1996 to 1997.

Dr. Muzina is the author of more than 60 journal articles and book chapters that focus on Neuroscience, with an emphasis on diagnostic issues, the challenges of mood disorder treatment, and the importance of the Primary Care–Behavioral Health interface. Recent peer-reviewed publications have addressed antidepressant adherence, patterns of migraine headache treatment, and predictive value of early assessment of depression treatment published in prominent journals, including the Journal of Affective Disorders, Neuropsychiatric Disease and Treatment, and the American Journal of Managed Care.

He resides in Cleveland, Ohio with his wife Dr. Kathyrn Muzina and their three children. Dr. Muzina maintains a limited private practice in Northeast Ohio for specialty consultation in Psychiatry and Addiction Medicine. His personal mission statement is “make every health care moment matter.”
ABOUT EXPRESS SCRIPTS

Express Scripts manages more than a billion prescriptions each year for tens of millions of patients. On behalf of our clients – employers, health plans, unions and government health programs – we make the use of prescription drugs safer and more affordable. Express Scripts uniquely combines three capabilities – behavioral sciences, clinical specialization and actionable data – to create Health Decision Sciencesm, our innovative approach to help individuals make the best drug choices, pharmacy choices and health choices. Better decisions mean healthier outcomes.

Headquartered in St. Louis, Express Scripts provides integrated pharmacy benefit management services, including network-pharmacy claims processing, home delivery, specialty benefit management, benefit-design consultation, drug-utilization review, formulary management, and medical and drug data analysis services. The company also distributes a full range of biopharmaceutical products and provides extensive cost-management and patient-care services.

Visit Lab.Express-Scripts.com or follow @ExpressScripts on Twitter for more information.

ABOUT THE EXPRESS SCRIPTS LAB

Founded in 2010, The Express Scripts Lab was built to foster collaboration, accelerate learning and enhance care. In 2014, we expanded the facility in size, scope and function, by bringing the experts behind Health Decision Science together under one roof. The expanded Lab is a reflection of our passion for patient care and our alignment with the needs of our clients.

Located on our St. Louis campus, the Lab is where our experts collaborate to solve pivotal healthcare challenges, drive out waste and improve outcomes. Here, the combined strengths of behavioral sciences, clinical specialization and actionable data generate meaningful innovation and develop the best new ways to improve health decision-making. These insights and innovations are then translated into new solutions and deployed throughout our company. The Express Scripts Lab is at the frontline of health care innovation focused on one goal: better decisions for healthier outcomes.