

# Emerging Trends in Prescription Stimulants Indicated for Treatment of Attention-Deficit/Hyperactivity Disorder: Mississippi, 2011 and 2014



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**INTRODUCTION:** Prescribed for treatment of such conditions as attention-deficit/hyperactivity disorder (ADHD), narcolepsy, and obesity, central nervous system (CNS) stimulants are associated with serious risks including the potential for abuse and addiction. State Prescription Monitoring Programs (PMP) data can be applied to establish the population-level consumption of amphetamines and similar CNS stimulants. Utilizing the 2011-2014 statewide PMP data, the goal of this study was twofold: to assess prescription rates and trends and to evaluate the demographics implicated in the use of stimulant medications in Mississippi. We analyzed prescriptions for CNS stimulants indicated for ADHD treatment and we excluded wakefulness-promoting and weight-loss medications. This study included prescriptions issued to Mississippi residents only. The unit of analysis was prescriptions not individual patients.

**PREVALENCE AND TRENDS OF ADHD:** In 2011, Mississippi had the 13th highest prevalence of childhood ADHD in the nation according to the Centers for Disease Control and Prevention (CDC).<sup>1</sup> Based on a national survey using parental reports, an estimated 8.8% of American children and 10.9% of children in Mississippi between the ages of 4 and 17 years had a current ADHD diagnosis in 2011. The majority of these ADHD-positive children were treated with drugs in 2011 - 6.1% of American children and 7.5% of children in Mississippi were reported as receiving an ADHD medication. In addition to such high rates of diagnosed and medicated ADHD, the same study revealed a steep upward trend in the prevalence of this childhood condition. Between 2003 and 2011, the number of children diagnosed with ADHD increased by 11.0% nationally and by 14.0% in Mississippi. A chronic health issue, ADHD often continues into adulthood. As a result, the National Institute of Mental Health estimates that the current prevalence of ADHD among the adult American population is 4.4%.<sup>2</sup>

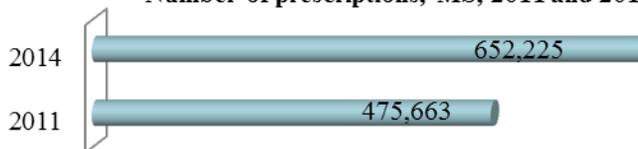
### CNS STIMULANTS, 2011 AND 2014:

Between 2011 and 2014, the number of prescriptions for the studied group of stimulants surged by 37.1% from 475,663 to 652,255 prescriptions (Figure 1). During the same period, the rate increased from 16 to 22 prescriptions for stimulants per 100 residents.

The number of dosage units (pills) increased even more rapidly by 41.0% from 20,016,148 in 2011 to 28,228,842 dosage units in 2014 (Figure 2). Between 2011 and 2014, the rate increased from 672 to 943 stimulant pills per 100 residents.

In parallel with these findings, the total days of supply rose from 14,379,522 in 2011 to 19,659,744 in 2014. This was an increase of 36.7% or (Figure 3).

**Figure 1. CNS Stimulants:  
Number of prescriptions, MS, 2011 and 2014**



**Figure 2. CNS Stimulants:  
Number of Dosage Units, MS, 2011 and 2014**



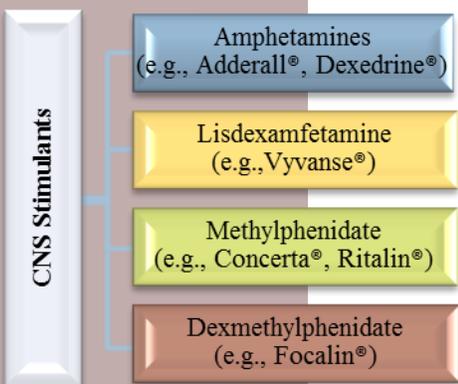
**Figure 3. CNS Stimulants:  
Total Days of Supply, MS, 2011 and 2014**



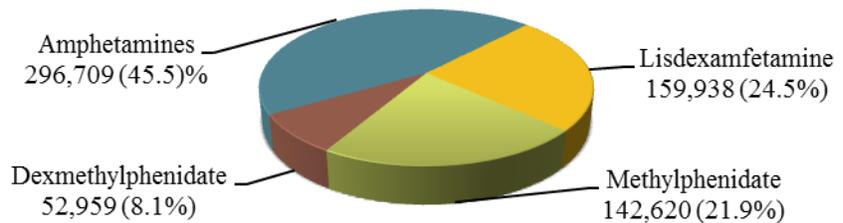
**MAJOR GROUPS:** Various stimulants have been used to treat ADHD for decades and remain the first line of therapy for the majority of newly diagnosed cases. Despite sharing clinical indications, different stimulant medications used for treatment of ADHD exhibit different pharmacological properties. Variation between stimulants in such pharmacological properties as mechanism of action, metabolism and elimination can have, however, a crucial effect on their dosing, benefits of use, and side effects. To evaluate the distribution and prescription trends of different prescription stimulants, we separated all studied medications into four groups: amphetamines, lisdexamfetamine, methylphenidate, and dexmethylphenidate.

Amphetamines were the most widely prescribed stimulant medications in 2014, accounting for almost half of all such prescriptions (45.5%). Lisdexamfetamine (e.g., Vyvanse®) was the second most prescribed stimulant group with 24.5% of all prescriptions (Figure 4). Methylphenidate, a group including Concerta®, Ritalin®, and Quillivant®, accounted for one fifth (21.9%) of all studied stimulants.

**Lisdexamfetamine:** Approved by the Food and Drug Administration (FDA) in 2006, Vyvanse® is the most recently released ADHD drug. The medicine has been marketed as having less abuse potential compared to other stimulants - a concept derived from the drug’s unique formulation and pharmacokinetic properties. Studies suggest, however, that the safety and tolerability of Vyvanse® are similar to those of other ADHD stimulant medications.<sup>3</sup> In addition, FDA requires a “black box warning” indicating a high potential for abuse and dependence for all stimulants, including Vyvanse®. Such labels are designed to call attention to serious or life-threatening risks.

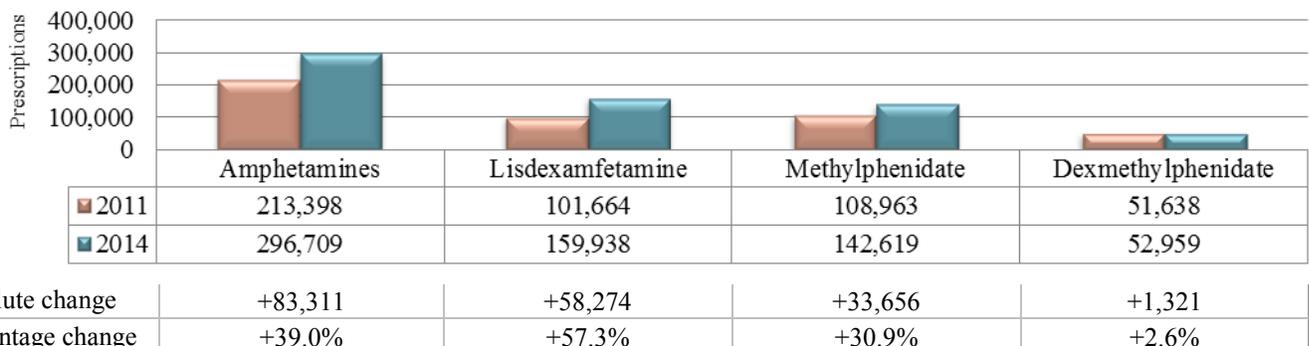


**Figure 4. Prescriptions for CNS Stimulants by Major Groups, MS, 2014**



**TRENDS BY MAJOR GROUPS, 2011 AND 2014:** While all classes of stimulants demonstrated an upward trend, there were significant variations in the scale of this increase. Between 2011 and 2014, the number of amphetamine and methylphenidate prescriptions increased, respectively by 39.0% and 30.9% (Figure 5). Vyvanse®, the only drug in the class of lisdexamfetamines, exhibited the highest rate of increase, growing 57.3% from 2011 through 2014 (Figure 5). Compared to 2011, there were 58,274 more Vyvanse® prescriptions dispensed in 2014. Reasons for this steep increase may include the marketing of Vyvanse® as a low-abuse potential stimulant drug.

**Figure 5. Prescriptions for CNS Stimulants, Change, MS, 2011 and 2014**

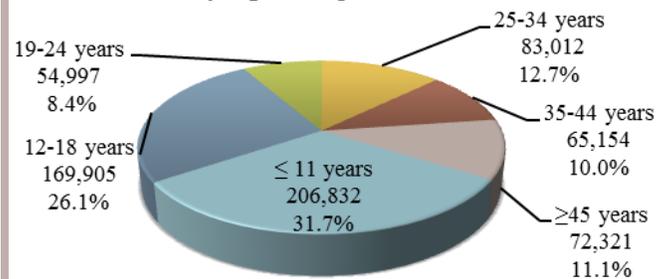


**SEX AND AGE DISTRIBUTION, 2014:** Almost one-third (31.7%) of all amphetamine prescriptions were disseminated among children 11 years of age or younger during 2014 in Mississippi. Over one quarter (169,905 or 26.1%) were dispensed among children between 12 and 18 years of age. A total of 275,484 (42.2%) stimulant prescriptions were disseminated to the adult population (≥ 18 years) during the same year (Figure 6).

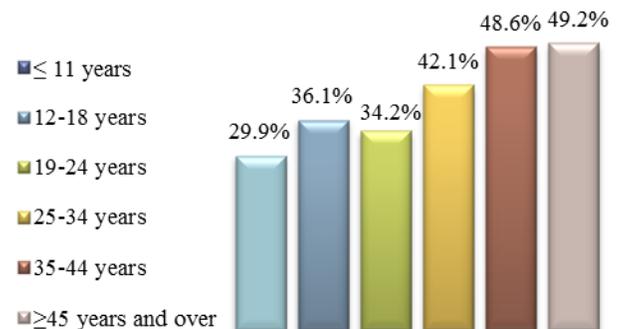
More than half of all stimulant prescriptions in Mississippi were dispensed to males (56.3%) versus females (43.7%) in 2018. Prevalence studies have shown that male children are two times more likely to be diagnosed with ADHD compared to female children nationwide.<sup>4</sup> Our study, however, revealed that the sex distribution of stimulant use was age dependent : After the age of 18 years, the proportion of prescriptions filled by females was greater than the proportion of prescriptions filled by males (Figure 8).

**TRENDS BY SEX AND AGE, 2011 AND 2014:** The prescribing trends for all of the studied age groups demonstrated an upward movement. From 2011 to 2014, the number of prescriptions increased by 29.9% for children ≤ 11 years and by 36.1% for children between the age of 12 and 18 years. The greatest increase in stimulant consumption, however, occurred among adults of 25 years of age and older (Figure 7). The increase in the amphetamine consumption was higher for females compared to males. Between 2011 and 2014, the number of stimulant prescriptions grew by 41.3% for females and by 33.9% for males.

**Figure 6. Prescriptions for CNS Stimulants by Age Group, MS, 2014**

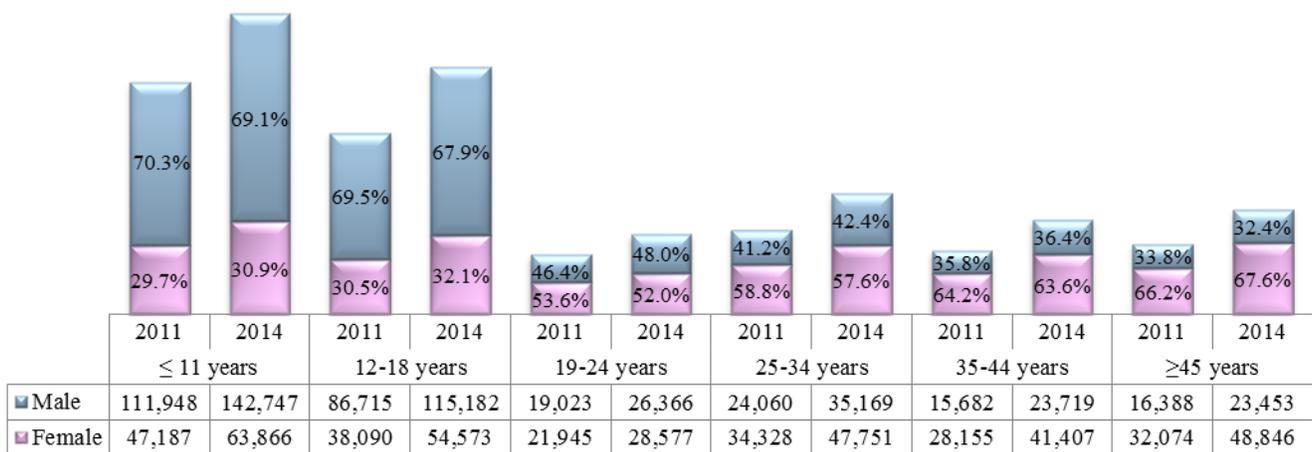


**Figure 7. Prescriptions for CNS Stimulants by Age Group, Percentage Change, 2011 and 2014**



Note: Records with missing values for age and records indicating unknown age were excluded from this analysis.

**Figure 8. Prescriptions for CNS Stimulants by Sex and Age Group, 2011 and 2014**



**NATIONAL TRENDS:** In support of our findings, recent research by CDC revealed some concerning trends in stimulant medication use: The percentage of privately insured reproductive-aged women who filled a prescription for an ADHD medication increased by 344% between 2003 and 2015 nationally.<sup>5</sup> The increase was confined to stimulant medications only and occurred across all geographic regions. The CDC report also warns about the paucity of scientific research on the safety of stimulant use during pregnancy.

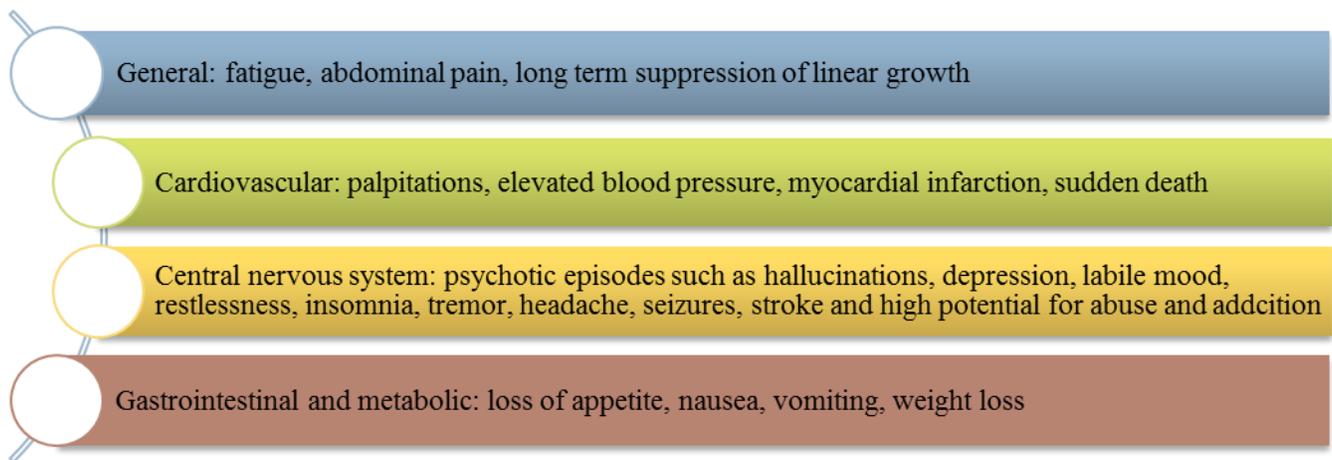
**CAUSES:** While further research is needed, the following factors may have led to such a sizable expansion in prescription stimulant usage in Mississippi.

**Widening of diagnostic criteria:** The upward movement in prescribing of stimulant medications may be due to a potential increase in late onset ADHD diagnoses. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), published in May of 2013 revised some of the ADHD diagnostic criteria.<sup>6</sup> Previously, the diagnosis of ADHD required presence of symptoms before the age of 7 years; the new guidelines increased this age to 12 years. In addition, DSM-5 removed the requirement for clinical impairment and reduced the number of symptoms required for diagnosis of adult ADHD from six to five. Research has estimated that this shift in diagnostic criteria increases the expected prevalence of ADHD among young adults by 27.0%.<sup>7</sup> An early adoption of these guidelines may have increased the diagnosed and medicated ADHD cases during the study period.

**Non-medical use and diversion:** Another contributing factor may be the widespread belief that stimulants enhance academic and athletic performance. Such misconceptions may coexist with inadequate patient and family literacy about the dangers of these drugs and their widespread misuse and diversion for non-medical purposes. For example, the estimated nationwide prevalence of nonmedical stimulant use in the past year ranges from 5% to 9% for school-age children and from 5.0% to 35.0% for college-age persons. The lifetime prevalence of drug diversion, defined as the unlawful transfer of prescription medications, ranges from 16.0% to 29.0% among school or college students.<sup>8</sup>

**Off-label use:** Nationwide, the consumption of stimulant medications has been expanding over the last two decades. Changing patterns of stimulant use also have been documented. Between 1996 and 2013, the number of prescriptions for methylphenidate increased by 8.2 fold and the number of prescriptions for amphetamines increased by 40 fold, according to recent research.<sup>9</sup> The same study reports that off-label use accounts for at least 40% of total stimulant consumption and states that adults are more likely to use stimulants for non-ADHD-related treatments. During 2006-2009, only 63.0% of adolescents and 34.0% of adults with stimulant prescriptions had a diagnosis of ADHD. Such off-label use may include weight loss, fatigue, depression, and cognitive enhancement.

**BENEFITS AND RISKS OF ADHD TREATMENT:** Symptomatically, attention-deficit/hyperactivity disorder is characterized by inattention and hyperactivity/impulsivity. This disorder can lead to poor academic performance, as well as behavioral and social problems. Pharmacological treatment has been shown to ameliorate the symptoms of ADHD. At the same time, the long list of serious, treatment-related side effects highlights the need to evaluate carefully all risks associated with ADHD medications.<sup>10</sup>



During 2014, the Mississippi State Department of Health reported one unintentional child overdose death caused by Concerta®, a prescription ADHD medicine.<sup>11</sup> Parents, teachers, and the medical community in Mississippi should be aware of the potential for fatal outcomes related to ADHD treatment.

**DRUG-RELATED HARM REDUCTION:** The following measures could improve ADHD-related outcomes.

**Pediatric population:** The American Academy of Pediatrics and the American Association of Child and Adolescent guidelines/parameters for clinical practice highlight the need for accurate criteria based diagnosis and management with monitoring of progress in at least two settings. Assessment for mental and physical co-morbidity is likewise recommended.<sup>12</sup> A less than optimal mental health provider ratio in the state significantly impacts children with ADHD because of the following two factors. First, a large majority of children with ADHD have a concurrent mental health diagnosis, which affects treatment and adherence to treatment. Second, the first line of therapy for many preschool children with ADHD is behavioral therapy. Therefore, the following prevention strategies may assure accurate diagnosis and mitigate treatment-related adverse effects.

- Engaging in a thorough and comprehensive diagnostic protocol, including assessing patients for other behavioral, development and physical conditions.
- Monitoring the outcomes of drug-related treatment with standardized tools. Such monitoring should include evaluating patients for psychotic symptoms and signs of chronic intoxication, abuse, and dependence.
- Informing adolescents and parents of preschool and school aged children of the serious potential side effects of drug-related ADHD treatment, including the potential for misuse and diversion.

**Adults:** Health care providers should also consider comprehensive diagnostic approaches of adult ADHD and review the Mississippi's Prescription Monitoring Data for potential non-medical use of amphetamines and other stimulants. Careful monitoring is necessary because it is unclear if the increase in stimulant prescriptions dispensed among adults in Mississippi was due to persistent symptoms of ADHD or off-label use of these stimulants.

**Public health initiatives:**

- Establishing a surveillance system monitoring rates and trends of stimulant use.
- Increasing awareness of risk factors associated with medical and non-medical use of stimulants.
- Implementing effective school-based interventions for children with ADHD and providing training opportunities for teachers to study appropriate teaching techniques for students affected by this condition.
- Educating patients and family about ADHD. The Centers for Disease Control and Prevention has built a comprehensive and resourceful website on ADHD, including symptoms, diagnosis, treatment, and research.

**Focus for the Future** is a CDC initiative that connects families with tools and resources to help kids with ADHD thrive. For more information, please visit: <https://www.cdc.gov/ncbddd/adhd/index.html>.

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