Factors Associated With Musculoskeletal Injuries in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder

Jeffrey A. Guy, MD[a]; Lisa M. Knight, MD[b]; Yinding Wang, MSPH[c]; and Jeanette M. Jerrell, PhD[d,*]

ABSTRACT

Background: Musculoskeletal injuries may be associated with attention-deficit/hyperactivity disorder (ADHD) symptom severity, comorbid psychiatric or medical conditions, and the prescribed psychostimulant.

Methods: A population-based, retrospective cohort design was employed using South Carolina's Medicaid claims data set covering outpatient and inpatient medical services and medication prescriptions over an 11-year period (January 1, 1996, through December 31, 2006) for patients ≤ 17 years of age with ≥ 2 visits for *ICD-9-CM* diagnostic codes for ADHD. A cohort of 7,725 cases was identified and analyzed using logistic regression to compare risk factors for those who sustained focal musculoskeletal injuries and those who did not.

Results: The risk of sustaining sprains, arthropathy and connective tissue disorders, or muscle and joint disorders was significantly related to being diagnosed with comorbid hypertension (adjusted odds ratios [aORs] = 1.60, 2.09, and 1.46, respectively) and a substance use disorder (aORs = 1.58, 1.38, and 1.28). Having a substance use disorder was also related to incident fractures and dorso/spinal injuries (aORs = 1.42 and 1.21). Diagnosed hypertension was related to incident concussions (aOR = 2.00), a diagnosed thyroid disorder was related to an increased risk of sprain and concussion (aORs = 1.44 and 2.05), a diagnosed anxiety disorder was related to an increased risk of dorso/spinal disorders (aOR = 1.71), and diagnosed diabetes was related to incident bone and cartilage disorders (aOR = 1.61).

Conclusions: Comorbid hypertension, substance use disorders, and thyroid disorders deserve increased clinical surveillance in children and adolescents with ADHD because they may be associated with an increased risk of more than one musculoskeletal injury.

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[a]Departments of Orthopedics and [b]Pediatrics, University of South Carolina School of Medicine, Columbia

[c]Department of Epidemiology and Biostatistics, University of South Carolina Arnold School of Public Health, Columbia

[d]Department of Neuropsychiatry and Behavioral Science, University of South Carolina School of Medicine, Columbia

**Corresponding author:* Jeanette M. Jerrell, PhD, Department of Neuropsychiatry and Behavioral Science, University of South Carolina School of Medicine, 15 Medical Park, Ste 301, Columbia, SC 29203 (Jeanette.Jerrell@uscmed.sc.edu).

There has been a noteworthy decline in the daily amount of physical activity that children and adolescents engage in over the past few decades and a concomitant "explosion" in the number of children diagnosed at an early age with obesity, hypertension, and diabetes. These conditions lead not only to a lower baseline of fitness level in children engaging in recreational or competitive sports, but also to a higher prevalence of comorbid chronic medical conditions and the perfect venue for incident musculoskeletal traumatic or other microtraumatic/repetitive, overuse musculoskeletal injuries.[1–4] Overuse, microtraumatic injuries represent approximately 50% of all pediatric sports-related injuries.[2]

Simultaneously, attention-deficit/hyperactivity disorder (ADHD) has become one of the most commonly diagnosed cognitive-behavioral disorders in children and adolescents.[5,6] ADHD is characterized by impaired cognitive function, impulsivity, and lack of coordination. Children with comorbid conduct disorder/oppositional defiant disorder (CD/ODD) and anxiety disorders may be more aggressive, impulsive, defiant, or oppositional and likely to engage in risky behavior when compared to children with ADHD alone.[7–9] Furthermore, in postmarketing studies,[10–16] the adrenergic stimulants prescribed to treat ADHD have been associated with adverse medical reactions: endocrine and metabolic (weight loss, growth suppression), cardiovascular (hypertension and arrhythmias), and neuromuscular and skeletal (tremors, arthralgia, and dyskinesia) in ≤ 10% of exposed patients. ADHD has also been closely associated with an increased risk of sports-related concussion[17–20] and extremity fractures, proximal humerus fractures in particular, and accidents involving bone fracture.[21,22]

Therefore, the constellation of ADHD-related symptoms, comorbid medical disorders, and the adverse effects of psychostimulant medications deserves further investigation to determine if youth with ADHD are more susceptible to sustaining various types of musculoskeletal injuries.[23] Our study will focus on the increased risk for traumatic fractures, sprains, and concussions and nontraumatic overuse orthopedic injuries associated with an ADHD diagnosis complicated by comorbid CD/ODD, anxiety, or substance use compared to the risk imparted by being prescribed certain psychostimulants, controlling for other chronic conditions of childhood, which could be pathogenically related to ADHD, the psychostimulants, or musculoskeletal injuries, most notably obesity, diabetes or other endocrine disorders, hypertension, or cardiac arrhythmias.

METHODS

Data for this study were obtained retrospectively from the South Carolina Medicaid database during an 11-year period from January 1, 1996, through December 31, 2006. Medical claims were used

Clinical Points

- A high percentage of youth with attention-deficit/hyperactivity disorder (ADHD) sustained traumatic fractures and sprains, primarily in the upper extremities, and had multiple fractures, sprains, and concussions.
- The majority of nontraumatic, overuse musculoskeletal injuries represented muscle and joint pain, stiffness, or swelling, primarily in the lower leg, ankles, and feet.
- From a population-based perspective, children with hypertension, substance use disorders, and thyroid dysfunction were more likely to experience multiple types of incident musculoskeletal injuries, such as sprains, concussions, and muscle, joint, and connective tissue pain and stiffness.
- Practitioners should maintain vigilant surveillance of patients with ADHD with comorbid hypertension, substance use disorders, and endocrine disorders, which are associated with incident musculoskeletal injuries.

to identify a service encounter, date of service, and the *International Classification of Diseases*, Ninth Revision, Clinical Modification (*ICD-9-CM*) diagnosis codes related to that visit. Selection criteria were age ≤ 17 years, continuous enrollment in Medicaid for a minimum of 9 months in any calendar year, and at least 1 initial service encounter with an *ICD-9-CM* ADHD diagnosis of 314.00 or 314.01. *ICD-9-CM* codes of 314 or 314.1–314.9 indicating hyperkinesis not associated with ADHD were excluded from this study. The Medicaid database is routinely cleaned as billings are submitted to eliminate duplicates and correct obvious coding errors. The methods involved in this study were approved by the University of South Carolina Institutional Review Board as exempt from human subject research guidelines (45 Code of Federal Regulations part 46) because existing medical database records were used for secondary analysis.

Within this ADHD cohort, primary or secondary diagnosis codes for 9 categories of musculoskeletal injuries were coded as follows: fracture (800–829); dislocation (830–839); sprain (840–848); concussion (850–854); thorax, abdomen, and pelvis (860–869); arthropathies and connective tissue disorders (710–719); dorso/spinal disorders (720–724); muscle and joint disorders (725–729); and bone and cartilage disorders (730–739). Diagnosed CD/ODD (312.x, 313.81), anxiety (300.0x), or substance use disorder (304.x or 305.x) were coded in the analyses as indicators of ADHD disease severity, since their presence exacerbates the fundamental attention and behavioral control deficits. The following categories of diagnosed comorbid disorders were also evaluated as follows: obesity (278, 278.00, 278.01), diabetes (250.0–250.9), dyslipidemia (272.0–272.9), thyroid disorder (240.0–246.9), essential hypertension (401.x), or acquired cardiac arrhythmia (427.x). Cases with congenital heart defects (747.0–747.9), other congenital anomalies (740–742.53), cardiovascular disease (410.0–414.9, 415.0–417.9, 420.0–429.9, 440.0–448.9, 451.0–459.9), organic brain disorders or mental retardation (310, 310.0–310.9, 318, 318.1, 318.2, 317.xx, 319.xx), or genetic syndromes or diseases were excluded from these analyses.

Descriptive statistical analyses were performed to determine the prevalence of each injury and any bivariate associations between the predictor variables of interest, ie, individual risk factors (age at ADHD diagnosis, sex, race), comorbid conditions, and pharmacologic interventions received for ADHD (ie, coded separately as the medication prescribed or not prescribed and as the number of months each medication was filled or refilled from the Medicaid pharmacy file).

Because musculoskeletal injuries result from a complex interaction of multiple risk factors, a multivariate statistical analysis approach was used.[24] To address our primary research questions regarding the factors that significantly increase the odds of a child or adolescent with ADHD being diagnosed with a musculoskeletal injury, 7 separate multiple logistic regression equations were constructed to assess the relative odds associated with having each of 7 diagnosed musculoskeletal injury categories (only the fracture, sprain, concussion, arthropathies and connective tissue disorders, dorso/spinal disorders, muscle and joint disorders, and bone and cartilage disorders categories contained enough cases for multivariate analysis). Individual risk factors (dichotomously coded sex and ethnicity), comorbid psychiatric disorders (CD/ODD, anxiety disorder, and substance use disorder as disease severity indicators),[7–9] comorbid medical conditions (obesity, hypertension, cardiac arrhythmia), and the prescribed psychostimulant medication or atomoxetine (coded as yes/no in each regression equation) were used as predictor variables based on the likelihood ratios apparent in the bivariate analyses. Each full regression model was then reduced through a stepwise procedure to reflect only the statistically significant variables associated with being diagnosed with each musculoskeletal injury category, using a preset significance level of $P \leq .05$. The measure of association reported for these results is the adjusted odds ratio (aOR) with a corresponding 95% confidence interval. All statistical analyses were performed in SAS software, version 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

The ADHD cohort for this study consisted of 7,725 child and adolescent cases. Descriptive results regarding this cohort indicate that 68.5% of the cohort was male and 50.6% was black, with a mean age at diagnosis of ADHD of 7.7 years in the Medicaid system. Thirty-five percent of the ADHD cohort was diagnosed with CD/ODD, 11.2% with anxiety disorder, and 4.4% with a substance disorder. Comorbid medical conditions diagnosed in the ADHD cohort and their prevalence in this cohort were obesity (8.0%), diabetes (2.2%), thyroid disease (2.3%), dyslipidemia (1.9%), hypertension (2.8%), and cardiac arrhythmia (1.0%) (Table 1). The most frequently diagnosed thyroid disease was hypothyroidism (54.9%). Some children and adolescents diagnosed with hypertension were being treated with antihypertension medications (22.9%). However, only

Table 1. Descriptive Analysis of the Cohort of 7,725 Youth Diagnosed With Attention-Deficit/Hyperactivity Disorder (ADHD)

Indicator	Cohort
Gender, male, n (%)	5,290 (68.5)
Race, black, n (%)	3,905 (50.6)
Age at first ADHD diagnosis, mean (SD), y	7.7 (2.71)
Comorbid psychiatric diagnoses, n (%)	
Conduct disorder/oppositional defiant disorder	2,661 (34.5)
Anxiety	862 (11.2)
Substance use disorder	343 (4.4)
Comorbid medical conditions, n (%)	
Obesity	615 (8.0)
Diabetes	172 (2.2)
Thyroid disorder	174 (2.3)
Dyslipidemia	148 (1.9)
Hypertension	214 (2.8)
Cardiac arrhythmia	75 (1.0)
Musculoskeletal injuries, n (%)	
Fracture	1,640 (21.2)
Sprain	2,099 (27.2)
Concussion	346 (4.5)
Dislocation	214 (2.8)
Thoracic/pelvis injury	48 (0.6)
Arthropathies and connective tissue disorders	2,250 (29.1)
Dorso/spinal disorders	1,330 (17.2)
Muscle and joint disorders	2,277 (29.5)
Bone and cartilage disorders	940 (12.2)
ADHD medication exposure	
Methylphenidate, n (%)	4,707 (61.1)
No. of months exposed to methylphenidate, mean (SD)	15.5 (16.3)
Mixed amphetamine salts/dextroamphetamine, mean (SD)	4,272 (55.5)
No. of months exposed to amphetamines, mean (SD)	14.6 (15.7)
Atomoxetine, n (%)	1,738 (22.6)
No. of months exposed to atomoxetine, mean (SD)	7.0 (8.1)

Table 2. Adjusted Odds Ratios for Having 7 Types of Musculoskeletal Injuries Related to Comorbid Medical Conditions or Individual Risk Factors (regression models reduced to significant predictors)

Parameter	Adjusted Odds Ratio	95% CI
Fracture		
Female	1.15*	1.03–1.29
Substance use diagnosis	1.42*	1.11–1.82
Sprain		
Black	1.14*	1.03–1.26
Hypertension diagnosis	1.60*	1.21–2.12
Substance abuse diagnosis	1.58**	1.26–1.99
Thyroid diagnosis	1.44*	1.05–1.98
Concussion		
Hypertension diagnosis	2.00*	1.22–3.29
Thyroid diagnosis	2.05*	1.19–3.52
Arthropathies and connective tissue disorders		
Hypertension diagnosis	2.09**	1.59–2.74
Substance use diagnosis	1.38*	1.10–1.73
Dorso/spinal disorders		
Anxiety diagnosis	1.71**	1.33–2.20
Substance abuse diagnosis	1.21*	1.01–1.45
Muscle and joint disorders		
Hypertension diagnosis	1.46*	1.11–1.94
Substance abuse diagnosis	1.28*	1.02–1.60
Bone and cartilage disorders		
Diabetes diagnosis	1.61*	1.08–2.39

*$P \le .01$.
**$P < .0001$.

1 child (0.6%) was prescribed insulin for 3 months or more, and no thyroid medications were noted as being prescribed and billed through the Medicaid pharmacy database during the study period.

During the 11-year period of this study, these ADHD patients were diagnosed with traumatic musculoskeletal injury as follows: sprains (27.2%), fractures (21.2%), concussions (4.5%), dislocations (2.8%), and thoracic and pelvic injuries (0.6%). Due to their low prevalence rates, cases in the dislocation and thoracic and pelvic injury categories were not subjected to further multivariate analysis. Diagnosed sprains were most frequently ankle and foot injuries (36.0%), wrist and hand injuries (21.9%), and back and lumbar injuries (16.7%), followed by knee and leg or nose, neck, and chest injuries (8.2% each). Diagnosed fractures were most frequent in the upper extremities (60.5%), particularly the radius and ulna, hand, and humerus, and to the lower extremities (25.7%), particularly the ankle and foot. Patients in this ADHD cohort had multiple recorded visits for sprains (mean = 2.87, SD = 2.71), fractures (mean = 5.45, SD = 4.78), and concussions (mean = 2.38, SD = 4.89). If we assume that these visits represent 1 episode of each injury, 36.2% of the cohort sustained 2 or more episodes of fractures, 22.6% sustained multiple episodes of sprains, and 4.1% sustained multiple concussions, which were treated by a physician within the Medicaid system.

Among the overuse injury categories, specific arthropathies and connective tissue disorders were diagnosed in 29.1% of individuals with ADHD, and the vast majority represented unspecified joint pain, stiffness, or swelling, primarily in the lower leg and ankles and feet. Dorso/spinal disorders were diagnosed in 17.2% of individuals with ADHD, primarily in the back and spine region and in the cervical region. Muscle and joint disorders were diagnosed in 29.5% of individuals with ADHD, predominantly for soft tissue pain and stiffness. Bone and cartilage disorders were diagnosed in only 12.2% of individuals with ADHD, primarily representing juvenile osteochondrosis of the hip and pelvis or lower extremities and feet, osteochondrosis dissecans, and unspecified bone and cartilage conditions. All of the traumatic and overuse injuries developed, on average, several years after the child was diagnosed with ADHD during adolescence.

This cohort was being treated with a range of adrenergic stimulant medications: 61.1% were taking methylphenidate, on average, for 15.5 months; 55.5% were taking mixed amphetamine salts/dextroamphetamine for a mean of 14.6 months; and 22.6% were taking atomoxetine for a mean of 7.0 months (Table 1). Methylphenidate and mixed amphetamine salts/dextroamphetamine were generally prescribed at the time of diagnosis, but some patients were switched to atomoxetine about 1 year later.

Multivariable Analyses

As shown in the logistic regression modeling the individual differences and comorbid conditions (Table 2), several predictor variables were significantly associated with increased odds of a child or adolescent being diagnosed with more than 1 of the traumatic musculoskeletal injuries. The risk of sustaining a fracture was significantly related to being female (aOR = 1.15) and having a comorbid substance use diagnosis (aOR = 1.42). The risk of sustaining a sprain was significantly related to being black (aOR = 1.14) and being diagnosed with comorbid hypertension (aOR = 1.60), thyroid disorder (aOR = 1.44), or a substance use disorder (aOR = 1.58). The risk of sustaining a concussion was significantly related to being diagnosed with comorbid hypertension (aOR = 2.00) and a thyroid disorder (aOR = 2.05).

For the overuse injuries, an increased risk of incident arthropathies and connective tissue disorders was associated with comorbid diagnoses of hypertension (aOR = 2.09) and substance use disorder (aOR = 1.38). An increased risk of incident muscle and joint disorders was also associated with comorbid diagnoses of hypertension (aOR = 1.46) and substance use disorder (aOR = 1.28). Incident dorso/spinal disorders were more likely in individuals diagnosed with an anxiety disorder (aOR = 1.71) and a substance use disorder (aOR = 1.21). Finally, bone and cartilage disorders were more likely to occur in individuals diagnosed with comorbid diabetes (aOR = 1.61).

Comorbid CD/ODD (1 severity indicator) was not associated with a differential impact on risk for any of the musculoskeletal injury categories, nor was there a significant or direct differential medication effect for either type of psychostimulant or atomoxetine.

DISCUSSION

ADHD is a major health concern in youth, and its association with musculoskeletal injuries among children and adolescents has been incompletely examined. Our results confirm and add to the existing knowledge base in several respects.

Consistent with previous studies[17–23] in which ADHD was closely associated with an increased risk of sports-related concussion and with upper extremity bone fractures, diagnosed fractures (21.2%) in this cohort were most frequent in the upper extremities, particularly the radius and ulna, hand, and humerus, but were also present in the lower extremities, particularly the ankle and foot. Fracture frequency was somewhat higher than those reported from a tertiary care sports medicine clinic (13.4%), the only comparable statistics in this age group reported over a similar period of time for a non-ADHD cohort.[25] In our ADHD cohort, 27.2% sustained sprains versus 3.2% in the specialty clinic, and dislocations were diagnosed in 2.8% of this ADHD cohort versus 2.5% in the specialty clinic.[25] Furthermore, an estimated 36.2% of our ADHD cohort had multiple fractures, 22.6% had multiple sprains, and 4.1% had multiple concussions; no comparable statistics were reported in the tertiary care clinic. Also consonant with our results, the increased intensity of recreational or competitive sports activities combined with a decrease in daily physical activity is making overuse injuries in youth more common, generally involving the lower limbs, especially the knees, ankle, and feet.[1]

Comorbid hypertension, thyroid disorder, and substance use disorder were associated with an increased risk of more than 1 category of traumatic and overuse musculoskeletal injury. Each of these comorbid disorders can, independently, exacerbate the inattention and hyperactivity symptoms of ADHD, which have been linked to resulting musculoskeletal injury.[17–22] Although we identified no direct, differential risk of incident musculoskeletal injury by type of prescribed medication, an indirect effect of these medications on musculoskeletal injury via their impact on hypertension and thyroid disorder cannot be ruled out. That is, cardiovascular (hypertension and arrhythmias) and neuromuscular and skeletal (tremors, arthralgia, and dyskinesia) adverse effects have been reported in ≤ 10% of ADHD patients exposed to adrenergic stimulants.[10–16] Other investigators have reported an association between ADHD symptoms of inattention, anxiety and depression, aggressiveness, and lower cognitive function and elevated serum thyroid-stimulating hormone levels, despite these levels appearing to be in the "normal" range.[26–28] Moreover, adrenergic stimulant medications may increase the amount of dopamine and norepinephrine in the neural synapse, which may inhibit the secretion of growth hormone and growth-related hormones such as prolactin, thyroid hormones, sex hormones, and insulin.[16] This effect on growth-related hormone activity might also explain the low incidence of untreated diabetes in the cohort and its significant association with bone and cartilage disorders. However, using an observational data set, we cannot speculate beyond these previously identified associations. In some susceptible individuals, the effects of psychostimulant agents on the endocrine system may be more comprehensive or pronounced than previously thought.[5–16] Practitioners need to be aware of this possibility and share relevant information.[16]

While all athletes should have their blood pressure measured before beginning competition or training, many youths engaging in routine physical education or recreational sport activities may not be screened or thoroughly monitored as closely for cardiovascular risk factors (tobacco use, diabetes, and dyslipidemia), end-organ damage, or the secondary causes of hypertension or the medical information available to a primary care physician may not be conveyed to school athletic program authorities and health care staff. Moreover, not all cases of diagnosed hypertension are treated with antihypertensive medications (only 23% in this cohort), because children and adolescents may appear asymptomatic or the medications may incur additional side effects, but practitioners should note the possible noncardiovascular, musculoskeletal injury outcomes related to this decision, especially in youths being treated with adrenergic stimulants.[1,4]

Substance use disorders of tobacco, alcohol, or street drugs are not only considered an important and independent cardiovascular disease risk factor, but also negatively impact effective metabolism of the psychostimulant medications and further impair cognitive functioning and behavioral controls. Among adolescent and young adult athletes, sports involvement is clearly a risk factor for substance use disorder, specifically, consuming significantly more drinks per week, binge drinking, and using illegal drugs more frequently than nonathletes or younger athletes in team, individual, or intramural sports.[29–33] Moreover, previous studies in children and young adults have indicated that those with ADHD are more vulnerable to substance use disorder and its negative consequences than those without ADHD.[34,35] Again, early detection and management is an ongoing clinical issue.

Demographic differences were weaker predictors of incident musculoskeletal injury but should be noted. The risk of sustaining a fracture was also significantly higher for females (15%) compared to males being at a higher risk of sustaining fractures in the specialty clinic analysis.[25] The risk of sustaining a sprain was significantly related to being black (13%) in our cohort, but we found no recent comparable data on race and ethnic differences in previous pediatric studies.

The perspective provided by this longitudinal database has several strengths. The cohort represents a large, heterogeneous group of children and adolescents being treated for diagnosed ADHD and varying periods of exposure to the ADHD medications examined. Generally, there is sufficient power in the treated cohort to detect low-incidence comorbid psychiatric or medical conditions. Previous studies have found that although observational (Medicaid) databases provide much less detailed information on individuals than would a structured research interview, the medical and psychiatric diagnoses coded and the utilization data are more reliable than patient or family self-reports,[36] and administrative claims data have been used to accurately identify positive predictive values for outcomes such as cardiovascular events in children.[37,38] The cohort is also representative of pediatric patients in routine care settings in the southeastern states and other small states with predominantly small-city and rural populations in terms of age, sex, racial demographics, and Medicaid eligibility, but these results may not be generalizable to other patient groups.[39–41]

Furthermore, these results need to be interpreted with several limitations in mind. Secondary administrative data sets and observational techniques were used, and no structured research or clinical interviews were employed to confirm any of the diagnoses assigned by the physician. Identification of psychiatric and nonpsychiatric medical conditions was based on spontaneous reporting to or observation by a primary care physician or psychiatrist and their designation of each diagnosis in the Medicaid billing system; consequently, the incidence of these conditions (especially concussions) may be an underestimate, which we cannot quantify. Moreover, the methods employed in this study focus exclusively on diagnosed cases seeking treatment, not to the prevalence of musculoskeletal injury in an epidemiologic or community sample of cases that may include those not seeking or receiving treatment through Medicaid. Data regarding key risk factors such as family history of obesity or related cardiometabolic or endocrine disorders were not available to the investigators and are not modeled in these analyses. Children and adolescents who dropped out of treatment or who were periodically ineligible for Medicaid are not represented in this data set. These results report associations and, as a result, directions of causality cannot be inferred. Finally, although many significant covariates have been controlled for, other unmeasured differences in patients or their treatment, including nonpharmacologic treatments, may explain the findings.

In certain susceptible individuals with ADHD and comorbid disorders (especially hypertension, thyroid dysfunction, and substance use disorder) that can impact cognitive functioning and behavioral controls without the benefit of attenuating medications, exposure to certain athletic situations may be associated with amplification of the risk of injury. Increased clinical attention to these intrinsic factors and their management is, therefore, warranted to minimize repeated musculoskeletal injuries in these individuals over time. In conclusion, the important clinical implication of our findings is that increased surveillance of youths participating in both competitive and recreational athletic activities is warranted, as well as increased attention to ensuring appropriate treatment and monitoring of their comorbid disorders as they age. Increasing the clinical knowledge base regarding intrinsic clinical factors associated with sustaining musculoskeletal injuries among youth with ADHD should broaden the focus of treating primary care physician and pediatricians, sports medicine physicians, and athletic health staff toward earlier recognition of the complexities of ADHD and its treatment, as well as adjustment of the screening, monitoring, and treatment criteria for children and adolescents with ADHD and comorbid medical disorders who are involved in recreational or competitive sports.

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Additional information: The Medicaid data set used in these analyses is not available to other investigators due to the confidentiality restrictions imposed by the South Carolina Department of Health and Human Services.

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