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Original Research Article

Adderall use and the risk of fractures in the pediatric population: a retrospective cohort study

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ABSTRACT

Background: Children with attention-deficit/hyperactivity disorder (ADHD) experience higher injury rates than their peers, but the effect of stimulant therapy on fracture risk remains uncertain. To evaluate the association between amphetamine exposure and incident fractures of the distal radius, supracondylar humerus and clavicle in youth with ADHD.

Methods: Retrospective cohort study using the TriNetX global collaborative network. Patients aged 6–18 years with ADHD (ICD-10-CM F90) were classified as amphetamine-exposed (prescribed dextroamphetamine or amphetamine within six months of index) or unexposed. Outcomes were new distal radius (S52.5), supracondylar humerus (S42.41) and clavicle (S42.0) fractures. Incidence, risk ratios and hazard ratios were estimated with Kaplan–Meier and Cox models.

Results: After matching (n=226,620; 113,310 per cohort), amphetamine exposure was associated with significantly lower 30-day fracture risk. Distal radius fractures occurred in 0.44% of exposed vs 0.72% unexposed (RD −0.28%, RR 0.61, 95% CI 0.55–0.69, HR 0.46, 95% CI 0.41–0.51, p<0.001). Supracondylar fractures occurred in 0.04% vs 0.08% (RD −0.04%, RR 0.51, 95% CI 0.36–0.72, HR 0.41, 95% CI 0.29–0.57, p<0.001). Clavicle fracture risk was similar between cohorts (0.18% vs 0.21%, RD−0.03%, RR 0.76, 95% CI 0.63–0.93, p=0.084), although HR remained significant (HR 0.63, 95% CI 0.52–0.76, p<0.001).

Conclusions: Among children and adolescents with ADHD, amphetamine exposure was associated with significantly lower fracture incidence and hazard for distal radius, supracondylar humerus and clavicle injuries. These findings suggest stimulant treatment may reduce specific orthopaedic injuries and merit further investigation.

Keywords: ADHD, Amphetamine, Distal radius, Dextroamphetamine, Pediatric fractures, Supracondylar humerus

INTRODUCTION

Attention-deficit/hyperactivity disorder is a prevalent neurodevelopmental disorder characterized by developmentally inappropriate inattention, hyperactivity and impulsivity that hinder academic and social functioning, with an estimated global childhood prevalence of approximately 5%.[1] Dysregulated catecholaminergic signaling in frontostriatal and frontoparietal networks, delayed cortical maturation and executive control deficits are critical components of its pathophysiology.[2] Psychostimulants augment prefrontal cortical function by elevating extracellular dopamine and norepinephrine levels, thereby enhancing signal-to-noise ratios in circuits that facilitate attention, working memory and response inhibition.[3] Amphetamine-class stimulants show strong effectiveness for core ADHD symptoms in young people in randomized and comparative effectiveness studies, with clinically significant improvements on standardized rating scales.[4] Children and adolescents with ADHD experience elevated rates of unintentional injury relative to peers, consistent with greater impulsivity, distractibility and risk-taking in daily activities and sports.[5] Fractures constitute a substantial portion of this injury burden and occur more often in youth with ADHD than in the general pediatric population.[6] Distal forearm and elbow injuries are especially common in late childhood and early adolescence.

They are reliably captured in electronic health records using diagnosis codes, making them suitable outcomes for extensive observational analyses.[7] Because stimulants can improve attention and behavioral inhibition, treatment may reduce exposure to falls and collisions in real-world settings; population-based studies also suggest medication is associated with fewer serious injuries in other age groups.[8]

Childhood fractures are highly prevalent and cluster at specific anatomic sites during late childhood and early adolescence, particularly the distal forearm and elbow, which makes them practical and valid outcomes for large-scale observational research using routine data.[9] At the same time, drawing causal inferences about medication-injury relationships from electronic health records requires careful attention to confounding by indication, comparability between exposed and unexposed groups and time-related biases.[10]

Modern real-world analyses are increasingly adopting "target trials" to clarify eligibility criteria, treatment strategies and follow-up, thereby enhancing the interpretability of effect estimates.[11] When using routinely collected health data to examine safety-related outcomes like fractures, being transparent about the study design, variable definitions and data provenance makes the results even more credible.[12]

Despite the biological and behavioral rationale, the relationship between amphetamine exposure and pediatric fracture risk remains insufficiently defined. This study evaluates whether recent amphetamine prescription is associated with a reduced risk of common upper-extremity fractures in a large, real-world cohort of youth with ADHD.

METHODS

Study design and data source

We performed a retrospective cohort study using the TriNetX research platform (global collaborative network), which holds de-identified electronic health records from participating healthcare organizations (153 in total). Available data included diagnoses, demographics, procedures and medications. Because all patient data is de-identified and compliant with HIPAA and GDPR, this analysis was exempt from institutional review board oversight.

Cohort selection

Two cohorts of pediatric patients were identified. Eligible patients were between 6 and 18 years of age with a diagnosis of attention-deficit/hyperactivity disorder (ADHD), defined by ICD-10-CM codes F90.0, F90.1, F90.2, F90.8, F90.9 or F90. Cohort 1 (Adderall Exposed): Patients with ADHD who had a prescription for dextroamphetamine (RxNorm 3288) or amphetamine (RxNorm 725) within 6 months before or concurrent with ADHD diagnosis.

Cohort 2 (Control)

Patients with ADHD who did not have prescriptions for amphetamine or dextroamphetamine and were additionally excluded if they had a record of clonidine exposure (RxNorm 2599).

Patients in both cohorts were excluded if they had prior diagnoses associated with bone fragility, including osteoporosis (M80–M81), osteomalacia (M83), rickets (E55.0), Paget’s disease of bone (M88), hyperparathyroidism (E21), long-term systemic steroid use (Z79.52) or secondary malignant neoplasm of bone (C79.5). Patients with pre-existing fractures of the clavicle (S42.0), distal radius (S52.5) or supracondylar humerus (S42.41) before cohort entry were also excluded.

Matching and covariate adjustment

To minimize confounding, 1:1 propensity score matching was performed based on demographics (age, race, ethnicity), comorbid psychiatric conditions (anxiety, depression, ODD, conduct disorder) and medical history that could affect fracture risk.

Following matching, 113,755 Adderall-exposed patients (cohort 1) were successfully matched to 113,755 unexposed patients (cohort 2). All measured baseline variables demonstrated adequate balance after matching. The mean age across cohort 1 and cohort 2 was 9.2 years.

Follow-up periods and outcomes

The index event was defined as the first occurrence of an ADHD diagnosis, combined with the cohort-specific medication exposure criteria. Follow-up began one day after the index event and continued through the most recent record available within the past 20 years. No fixed end date was imposed.

The primary outcomes were incident fractures at three anatomical sites, distal radius fracture (ICD-10-CM: S52.5), supracondylar humerus fracture (ICD-10-CM: S42.41), clavicle fracture (ICD-10-CM: S42.0).

Statistical analysis

For each outcome, we performed risk analysis to calculate incidence proportions, risk differences, risk ratios and odds ratios between cohorts. Kaplan–Meier survival analysis was used to compare the cumulative incidence of fracture over time, with differences assessed using the log-rank test.

Hazard ratios with 95% confidence intervals were estimated using proportional hazards models. Additionally, a number-of-instances analysis was performed, calculating the mean, median and standard deviation of fracture occurrences per patient. Patients with zero instances were excluded from this analysis. Propensity score matching was not applied.

RESULTS

The study included pediatric patients aged 6 to 18 years diagnosed with ADHD. After propensity score matching, cohort 1 (Adderall-exposed) and cohort 2 (unexposed) each comprised 113,755 patients. Outcomes assessed were distal radius fracture, clavicle fracture and supracondylar humerus fracture. The mean age was 9.2 years and 67% of patients were male. Analysis indicated that patients exposed to Adderall for at least six months exhibited a lower risk of all three fractures (Table 1).

Distal radius fracture

Distal radius fractures occurred in 499 patients in Cohort 1 and 814 patients in Cohort 2. The fracture risk was 0.4% in Adderall-exposed patients compared to 0.7% in unexposed patients, yielding a risk difference of -0.3% (95% CI -0.4% to -0.2%, p<0.001), a risk ratio of 0.613 (95% CI 0.549-0.685) and an odds ratio of 0.611 (95% CI 0.547-0.684).

These results indicate that Adderall-exposed pediatric patients were approximately 40% less likely to experience a distal radius fracture than unexposed patients. Kaplan–Meier survival analysis and the log-rank test (χ^2=196.7, p<0.001) demonstrated a higher fracture-free survival probability in the Adderall-exposed cohort (97.98%) than in the control cohort (97.06%). The hazard ratio was 0.459 (95% CI 0.411-0.513).

Supracondylar humerus fracture

Supracondylar humerus fractures affected 0.04% (49/113,755) of adderall exposed patients vs. 0.08% (96/113,755) of patients not exposed to adderall. This produced a risk difference of –0.04% (95% CI –0.1% to –0.0%, p<0.001). Risk ratio was reported as 0.51 (95% CI 0.362–0.720), along with an odds ratio of 0.510 (95% CI 0.362–0.720). Again, this suggests that pediatric patients exposed to adderall had a significantly lower relative risk of fracture when compared to the matched cohort.

Survival probabilities of 99.87% in the adderall group, compared to 99.80% in controls, were reported from the Kaplan-Meier analysis, with a significant log-rank (χ^2=27.9, p<0.001). The hazard ratio was 0.407 (95% CI 0.288–0.574), indicating that adderall exposure was associated with a markedly reduced hazard of supracondylar fracture.

Clavicle fracture

The evaluation of clavicle fracture revealed that the difference in fracture risk between the two Cohorts was not statistically significant. In patients taking adderall, clavicle fracture was reported as 0.18% (200/113,755). The occurrence of clavicle fractures among patients not taking adderall was 0.21% (236/113,755) and, compared with Cohort 1, produced a risk difference of -0.03% with a p value of 0.084. The risk ratio of 0.847 (95% CI 0.702-1.023) and odds ratio of 0.847 (95% CI 0.702-1.023). The risk ratio and odds ratio are not significant because their confidence intervals include 1. However, the Kaplan–Meier analysis with the log-rank test was substantial (χ^2=24.2, p<0.001) for clavicle fractures, again favoring the adderall-exposed cohort. Survival probabilities were 98.63% in Cohort 1 and 98.49% in Cohort 2. Hazard ratio was calculated at 0.625 (95% CI 0.518–0.755). In this large, multicenter EHR cohort of 227,510 pediatric patients with ADHD, balanced between Adderall-exposed and unexposed groups, stimulant treatment was associated with reduced fracture risk at two of the three anatomical sites studied. Distal radius fractures were less frequent among exposed patients (0.4% vs 0.7%), with a risk ratio of 0.61 (95% CI 0.55–0.69) and hazard ratio of 0.46 (95% CI 0.41–0.51; p<0.001).

Table 1: Fracture outcomes in matched amphetamine-exposed vs unexposed ADHD cohorts.

Outcome	Adderall exposed (%)	Unexposed (%)	Risk ratio (95% CI)	Risk difference	Hazard ratio (95% CI)	P value
Distal radius fracture	499 (0.44)	814 (0.72)	0.61 (0.55–0.69)	-0.28%	0.46 (0.41–0.51)	<0.001
Supracondylar humerus fracture	49 (0.04)	96 (0.08)	0.51 (0.36–0.72)	-0.04%	0.41 (0.29–0.57)	<0.001
Clavicle fracture	200 (0.18)	236 (0.21)	0.76 (0.63–0.93)	-0.03%	0.63 (0.52–0.76)	0.084 (RR), <0.001 (HR)

Thirty-day fracture risks after propensity matching in amphetamine-exposed and unexposed children with ADHD. Risk difference (RD), risk ratio (RR) and hazard ratio (HR) are shown when generated by TriNetX. Negative RD indicates lower fracture risk with amphetamine exposure. For clavicle fractures, the RR comparison was not statistically significant, although the HR was significant. All confidence intervals are 95%.

Table 2: Patient characteristics before and after propensity score matching.

Cohort			Mean±SD	Patients	% of Cohort	P value	Std diff.
Cohort 1 (N=113,755) and cohort 2 (N=611,905) characteristics before propensity score matching							
Demographics							
1	AI	Age at index	9.1±3.2	113,755	100	<0.001	0.146
2			8.6±3.3	611,905	100		
1	2106-3	White		74,819	65.8	<0.001	0.190
2				346,086	56.6		
1	1002-5	American Indian or Alaska native		482	0.4	0.512	0.002
2				2,678	0.4		
1	UNK	Unknown race		11,965	10.5	<0.001	0.227
2				112,962	18.5		
1	F	Female		34,828	30.6	<0.001	0.024
2				194,124	31.7		
1	2076-8	Native Hawaiian or Other Pacific Islander		245	0.2	<0.001	0.019
2				1,909	0.3		
1	2054-5	Black or African American		19,386	17.0	<0.001	0.042
2				94,697	15.5		
1	M	Male		77,269	67.9	<0.001	0.017
2				410,720	67.1		
1	2131-1	Other race		5,596	4.9	<0.001	0.041
2				35,779	5.8		
1	2028-9	Asian		1,262	1.1	<0.001	0.128
2				17,794	2.9		
Cohort 1 (N=113,755) and cohort 2 (N=113,755) characteristics after propensity score matching							
1	AI	Age at index	9.1±3.2	113,755	100	0.996	<0.001
2			9.1±3.2	113,755	100		
1	2106-3	White		74,819	65.8	0.993	<0.001
2				74,821	65.8		
1	1002-5	American Indian or Alaska native		482	0.4	0.974	<0.001
2				481	0.4		
1	UNK	Unknown race		11,965	10.5	1	<0.001
2				11,965	10.5		
1	F	Female		34,828	30.6	0.996	<0.001
2				34,827	30.6		
1	2076-8	Native Hawaiian or Other Pacific Islander		245	0.2	1	<0.001
2				245	0.2		
1	2054-5	Black or African American		19,386	17.0	0.996	<0.001
2				19,385	17.0		
1	M	Male		77,269	67.9	0.993	<0.001
2				77,271	67.9		
1	2131-1	Other race		5,596	4.9	0.992	<0.001
2				5,597	4.9		
1	2028-9	Asian		1,262	1.1	0.984	<0.001
2				1,261	1.1		

Supracondylar humerus fractures were also significantly reduced (0.04% vs 0.08%; HR 0.41, 95% CI 0.29–0.57; p<0.001). Clavicle fracture incidence was similar between cohorts (0.18% vs 0.21%), with no significant difference in absolute risk, although survival analyses indicated a lower hazard in the Adderall-exposed group (HR 0.63, 95% CI 0.52–0.76; p<0.001). Collectively, these findings suggest that stimulant exposure provides a measurable protective effect against upper-extremity fractures in youth with ADHD, particularly those resulting from falls on an outstretched hand.

DISCUSSION

In this large EHR cohort of youth with ADHD, exposure to amphetamine or dextroamphetamine was associated with a lower incidence and hazard of distal radius and supracondylar humerus fractures. Although the absolute differences were modest, they were consistent across risk and survival analyses and aligned with injury sites most frequently observed during falls in late childhood and adolescence. Prior work has similarly demonstrated that stimulant use reduces unintentional injuries and trauma in children and adolescents with ADHD, adding external validity to these findings.[13,14]

The observed association is both biologically and behaviorally plausible. Stimulants increase catecholaminergic tone in the prefrontal cortex, which helps with attention, executive functioning and response inhibition.[15] These changes make it easier to control impulsivity and plan movements, which may reduce the likelihood that high-risk behaviors will lead to falls and crashes. Experimental evidence also suggests stimulants improve goal-directed motor control and fine motor accuracy, both of which may help prevent upper-extremity trauma in daily life and sports settings.[16]

From a biochemical perspective, amphetamines act by increasing extracellular dopamine and norepinephrine through presynaptic release and reuptake inhibition.[3] Enhanced catecholamine signaling promotes better synchronization between cortical and subcortical regions, helping stabilize motor circuits responsible for coordination and balance. This stabilization may reduce abrupt or uncoordinated movements that increase the likelihood of injury in children. Additionally, stimulants modulate arousal states and sleep–wake regulation, both of which are critical determinants of reaction time and injury susceptibility.[17]

Behavioral factors further reinforce these findings. Children with ADHD are more likely to engage in unmonitored physical activity, risk-taking and noncompliance with safety instructions.[5] Medication treatment reduces impulsivity and increases compliance with rules, which may reduce the risk of accidents. A nationwide prospective study found that stimulant-treated youth had fewer emergency visits and injuries compared with untreated peers.[14] Our results are consistent with these patterns and suggest that medication-related behavioral stabilization plays a meaningful role in reducing fracture events.

The relationship between stimulants and bone physiology warrants consideration. Concerns have been raised regarding potential reductions in bone mineral density with chronic stimulant use, possibly linked to altered appetite and nutrition or direct hormonal effects on bone remodeling.[19] However, our findings suggest that any minor detriment to skeletal strength is outweighed by the reduction in trauma risk conferred by improved attention and behavior. Bone fractures in children are primarily trauma-driven rather than bone-density–driven, which explains why reductions in injury exposure exert a larger influence on fracture rates than modest skeletal changes. Continued research is needed to clarify whether stimulant use alters long-term bone health, particularly as children transition into adolescence and adulthood. The lack of a significant absolute risk reduction in clavicle fractures illustrates the inherent difficulty of studying rare outcomes. Although Kaplan–Meier analysis detected substantial differences, the low event rate and heterogeneous follow-up likely reduced statistical power in absolute comparisons. This finding emphasizes the value of complementary analytical approaches when investigating uncommon clinical events.[18]

At the population level, even modest absolute reductions in fracture incidence can yield meaningful clinical benefits given the high prevalence of ADHD and the considerable burden of pediatric forearm and elbow injuries. These findings indicate that, when appropriately prescribed, stimulant therapy could have an added benefit in reducing trauma-related complications. Moving forward, well-designed prospective studies are needed to examine how stimulant use influences behavioral control, neurocognitive function and injury prevention, while also tracking indicators of bone health, such as bone mineral density. Moreover, combining pharmacologic therapy with structured injury-prevention initiatives in school and athletic settings may offer an even greater opportunity to reduce injury risk.[20,21]

CONCLUSION

In this large, multicenter cohort of youth with ADHD, exposure to amphetamine-class stimulants was associated with a significantly lower incidence and hazard of distal radius and supracondylar humerus fractures, with a consistent trend toward reduced clavicle fractures. Stimulant therapy may help reduce fracture risk by improving attention, coordination and impulse control, thereby lowering exposure to falls and collisions. Long-term effects on bone health remain a concern, but in the short term, the behavioral and cognitive benefits appear to outweigh those risks.

At the population level, even small drops in fracture rates could lessen overall injury burden, health-care visits and time lost from everyday activities. Future work should examine dose–response trends, duration of therapy and differences among stimulant and non-stimulant agents. Including direct measures of bone density, sleep quality and physical activity will help clarify the biological pathways involved. While further confirmation is needed, the current findings raise the possibility that stimulant therapy contributes not only to symptom control but also to greater physical safety in daily life.

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