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Researching Eyesight Trends IN ADHD (RETINA)

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Abstract

Background: There has been limited exploration of the relationship between ADHD and vision impairment, especially in relation to ADHD medication regimens and age. This study aims to examine trends in visual disorders in young patients with ADHD. **Methods:** We analyzed deidentified patient records from TriNetX database. Patients under 22 years old were divided into cohorts based on ADHD status and medication regimen. We compared prevalence of vision disorders between cohorts. **Results:** We studied over 1 million patients. The ADHD cohort had higher rates of all visual disorders than their non-ADHD peers. Medication usage was found to have a slight impact, with non-stimulants associating with higher rates for all outcomes. **Discussion:** Our findings suggest that the higher occurrence of visual disorders in ADHD is not primarily due to misdiagnosis or medication effects. There is a need for regular eye care in ADHD patients and further investigation into the role of ADHD medications in eye health. (*J. of Att. Dis. XXXX; XX(X) XX-XX*)

Keywords

ADHD, ophthalmology, visual disorders, associated disorders, medication effects

Introduction

ADHD is one of the most common psychiatric neurodevelopmental disorders affecting children. One meta-analysis estimates that the prevalence of ADHD ranges from 5.9% to 7.1% depending on the method of diagnosis (Sayal et al., 2018). ADHD can have many impacts on patients' lives beyond a psychiatric diagnosis. Those with ADHD have been shown to have increased health risk behaviors that can interfere with routine care (Q. Chen et al., 2018). A relatively new and growing body of research is linking ADHD to an increased risk of many other health problems such as obesity, allergies and asthma, diabetes mellitus types 1 and 2, autoimmune diseases including ankylosing spondylitis, ulcerative colitis, and autoimmune thyroid disease, substance use disorder, unintentional physical injuries, and of particular interest to this study, eye disorders (Chen et al., 2017; M. H. Chen et al., 2018; Q. Chen et al., 2018; Groenman et al., 2017; Ho et al., 2019; Kapellen et al., 2016; Lee et al., 2011; Ruiz-Goikoetxea et al., 2018). All these comorbidities can exacerbate the physical and economic burden of ADHD on patients, families, and the society.

Along with regular medical and dental check-ups, preventative routine eye care is very important to prevent, diagnose, and treat vision disorders sooner rather than later to mitigate the effects the disorder may have on the patient's vision, long term health, and economic burden. We sought to examine the trends in ophthalmologic disorders in young patients with ADHD. Disorders examined in this study are strabismus, astigmatism, myopia, hypermetropia, anisometropia & aniseikonia, presbyopia, amblyopia ex anopsia, subjective visual disturbances, diplopia, visual field defects, color deficiencies, legal blindness, optic nerve disorders, glaucoma, non-age-related cataracts, and nystagmus. A short description each disorder is presented in Table 1. While this list of vision impairment is not exhaustive, it covers many of the most common vision abnormalities encountered in children and adolescents or that develop in adulthood as the result of undiagnosed vision disturbances through inadequate routine eye care.

There has been limited research into the intersection between ophthalmology and psychiatry with only a few studies exploring the association between ADHD and vision (Bellato et al., 2022; Ho et al., 2019). Often these studies have been limited in size and patient diversity, yet they have offered evidence that ADHD has a substantial impact on

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Table 1. Descriptions of Studied Visual Disorders.[AQ: 3]

Condition	Description
Strabismus	Colloquially termed "crossed eyes"—misalignment of the eyes due to muscular or nerve dysfunction
Astigmatism	A common disorder that involves incorrect curvature of the cornea or lens resulting in blurry vision
Myopia	A condition in which light is focused in front of the retina, making objects in the distance appear blurry
Hypermetropia	A condition in which light is focused behind the retina, making close objects appear blurry
Anisometropia & Aniseikonia	Anisometropia is a disorder in which the refractive error differs between a patient's eyes and can lead to aniseikonia where there is a difference in perceived size of images between eyes
Presbyopia	Age-related gradual loss of ability to focus on objects nearby as the eye's ability to appropriately accommodate declines
Amblyopia Ex Anopsia	Decreased vision in one eye due to abnormal visual development in early childhood
Subjective visual disturbances	A broad category of transient or permanent visual changes including diplopia, partial or total blindness, color blindness, halos, spots, or blurred vision
Diplopia	Colloquially termed "double vision,"—when a person sees two images of a single object
Visual field defects	Part of the pathway from the eye to the visual processing center of the brain is damaged, resulting in loss of vision in one or more fields of vision
Color deficiencies	A reduced or absent ability to distinguish between certain colors, most commonly red and green
Legal blindness	Visual acuity of less than 20/200 in the better eye with correction and/or a visual field of 20 degrees or less
Optic nerve disorders	A large category of disorders that affect the optic nerve itself, resulting in vision loss or impairment
Glaucoma	An elevated intraocular pressure which in turn damages the optic nerve, leading to blindness
Non-age-related cataracts	Accumulation of opacity or loss of transparency of the lens from protein or fiber breakdown, causing vision to become hazy and cloudy
Nystagmus	Involuntary oscillation of one or both eyes in one or more axes that can result in reduced vision and depth perception

vision. To our knowledge, no study has investigated ADHD medication regimens, age, and vision impairment across a large data set of over one million patients under the age of 220 years. The objective of our study is to quantify the differences in precedence of vision disorders between children and adolescents with ADHD compared to their non-ADHD peers to discover further avenues of research and better inform providers, making them aware of common visual disorders comorbid with ADHD and ultimately help lower these patients' disease burden and contribute to reducing the economic impact ADHD has on patients, their families, and society.

Methods

We analyzed deidentified aggregate data from electronic health records maintained by TriNetX. TriNetX contains electronic medical records from large healthcare organizations (HCOs). TriNetX, LLC is compliant with the Health Insurance Portability and Accountability Act (HIPAA), the US federal law which protects the privacy and security of healthcare data, and any additional data privacy regulations applicable to the contributing HCO (TriNetX, n.d.). TriNetX is certified to the ISO 27001:2013 standard and maintains an Information Security Management System (ISMS) to ensure the protection of the healthcare data it has access to and to meet the requirements of the HIPAA Security Rule. Any data displayed on the TriNetX Platform in aggregate form, or any patient level data provided in a data set generated by the TriNetX Platform only contains de-identified data as per the de-identification standard defined in Section §164.514(a) of the HIPAA Privacy Rule (TriNetX, n.d.).

Within this database, we identified all patients under the age of 22 years old and separated them into two cohorts based on attention deficit hyperactivity disorder (ADHD) status. Within the ADHD cohort, we further identified four sub-groups based on ADHD medication regimen: no medications used (cohort labeled as: "No Meds"), only stimulant medications ("Stims"), only non-stimulant medications ("Non-Stim"), and any individual medication ("Any Meds"). To provide clarity, a patient on amphetamine would be analyzed both in the "Stims" category and the "Any Meds" category. A patient on guanfacine would be analyzed both in the "Non-Stim" category and the "Any Meds" category. This method of dual analysis provides some perspective on the impact of medication type versus prescriptions themselves, as all prescriptions require access to a physician, which is impacted by socioeconomic factors. Studied disorders included strabismus, astigmatism, myopia, hypermetropia, anisometropia & aniseikonia, presbyopia, amblyopia ex anopsia, subjective visual disturbances, diplopia, visual field defects, color deficiencies, legal blindness,

Table 2. Cohort Size, Absolute Risk, Odds Ratio With Confidence Interval, and *t*-Test *p*-Value by Outcome. Bolded Values Indicate $p < .05$.

Event	Total *N*	Event *N*	Risk	Odds ratio [95% CI]	*p* Value	Event	Total *N*	Event *N*	Risk	Odds ratio [95% CI]	*p* Value
Any visual disorder						Subjective visual disturbances					
ADHD	684,131	90,326	13.2%	2.630	**.001**	ADHD	684,131	11,823	1.7%	2.872	**.001**
No ADHD	684,131	37,401	5.5%	[2.6, 2.66]		No ADHD	684,131	4,164	0.6%	[2.77, 2.98]	
Strabismus						Diplopia					
ADHD	684,131	23,236	3.4%	2.315	**.001**	ADHD	684,131	6,797	1.0%	3.603	**.001**
No ADHD	684,131	10,233	1.5%	[2.26, 2.37]		No ADHD	684,131	1,900	0.3%	[3.42, 3.79]	
Astigmatism						Color vision deficiencies					
ADHD	684,131	25,330	3.7%	2.730	**.001**	ADHD	684,131	853	0.1%	2.358	**.001**
No ADHD	684,131	9,501	1.4%	[2.67, 2.8]		No ADHD	684,131	362	0.1%	[2.1, 2.53]	
Myopia						Legal blindness					
ADHD	684,131	21,994	3.2%	2.352	**.001**	ADHD	684,131	19,057	2.8%	3.387	**.001**
No ADHD	684,131	9,528	1.4%	[2.3, 2.41]		No ADHD	684,131	5,739	0.8%	[2.09, 2.67]	
Hypermetropia						Optic nerve/pathway disorder					
ADHD	684,131	21,815	3.2%	2.782	**.001**	ADHD	684,131	4,800	0.7%	1.911	**.001**
No ADHD	684,131	8,006	1.2%	[2.71, 2.85]		No ADHD	684,131	2,520	0.4%	[1.82, 2.01]	
Anisometropia & Aniseikonia						Glaucoma					
ADHD	684,131	3,496	0.5%	2.082	**.001**	ADHD	684,131	2,224	0.3%	1.741	**.001**
No ADHD	684,131	1,684	0.3%	[1.96, 2.21]		No ADHD	684,131	1,279	0.2%	[1.63, 1.87]	
Presbyopia						Non-age-related cataract					
ADHD	684,131	531	0.1%	3.300	**.001**	ADHD	684,131	1,757	0.3%	1.988	**.001**
No ADHD	684,131	161	0.0%	[2.77, 3.94]		No ADHD	684,131	885	0.1%	[1.83, 2.16]	
Amblyopia ex anopsia						Nystagmus					
ADHD	684,131	12,611	1.8%	2.228	**.001**	ADHD	684,131	8,378	1.2%	3.361	**.001**
No ADHD	684,131	5,718	0.8%	[2.16, 2.3]		No ADHD	684,131	2,514	0.4%	[3.22, 3.52]	

optic nerve disorder, glaucoma, non-age-related cataract, nystagmus, and any visual disorders.

Once the cohorts and sub-groups were identified, we performed statistical analysis based on the occurrence rate of visual disorders within each cohort. Prior to comparison, cohorts were balanced on age, sex, race, and ethnicity using nearest-neighbor matching to a difference in propensity scores <0.1. There were no significant differences in age, sex, race, or ethnicity after cohort matching. Further demographic and matching information are available on request. Event rates between cohorts were compared using a *t*-test. Odds ratios with a 95% confidence interval were also calculated, and the results are presented in Table 1. Significance for this study was set at $p < .05$. As this study contained only deidentified aggregate data, the Colorado Multiple Institutional Review Board (COMIRB) designated it as non-human research not in need of approval.

Results

We found 684,131 patients with ADHD under 22 years old and matched these patients to peers without ADHD based on age, sex, race, and ethnicity, for a total of 1,368,262 studied records. The general ADHD cohort had an average age was 15 years old, was approximately 60% white, 33% female, and only 12% of patients identified as Hispanic or Latino. Of this cohort, 218,070 used medications for ADHD, with 179,330 using stimulant medications and 48,402 using non-stimulant medications. These were compared to peers with ADHD and without medication use, again matched to non-significant differences in age, sex, race, and ethnicity. For all visual disorders studied, patients with ADHD were more likely than those without ADHD to be diagnosed with that visual disorder. Detailed information is presented in Table 2 and depicted in Figure 1.

For 13 out of 16 outcomes, individuals with ADHD medication use were more likely than those without medication use to be diagnosed, with the remaining 3 events (non-age-related cataract, diplopia, and subjective visual disturbances) lacking statistical significance. Similarly, individuals on stimulant medications had a significantly increased risk in 7 of 16 outcomes and significantly decreased risk for diplopia only. Finally, individuals on non-stimulant medications had significantly higher rates in all outcomes. Compared to individuals on stimulant medications, individuals on non-stimulant medications had a statistically higher odds ratio for 11 of 16 outcomes. Detailed information is presented in Table 3.

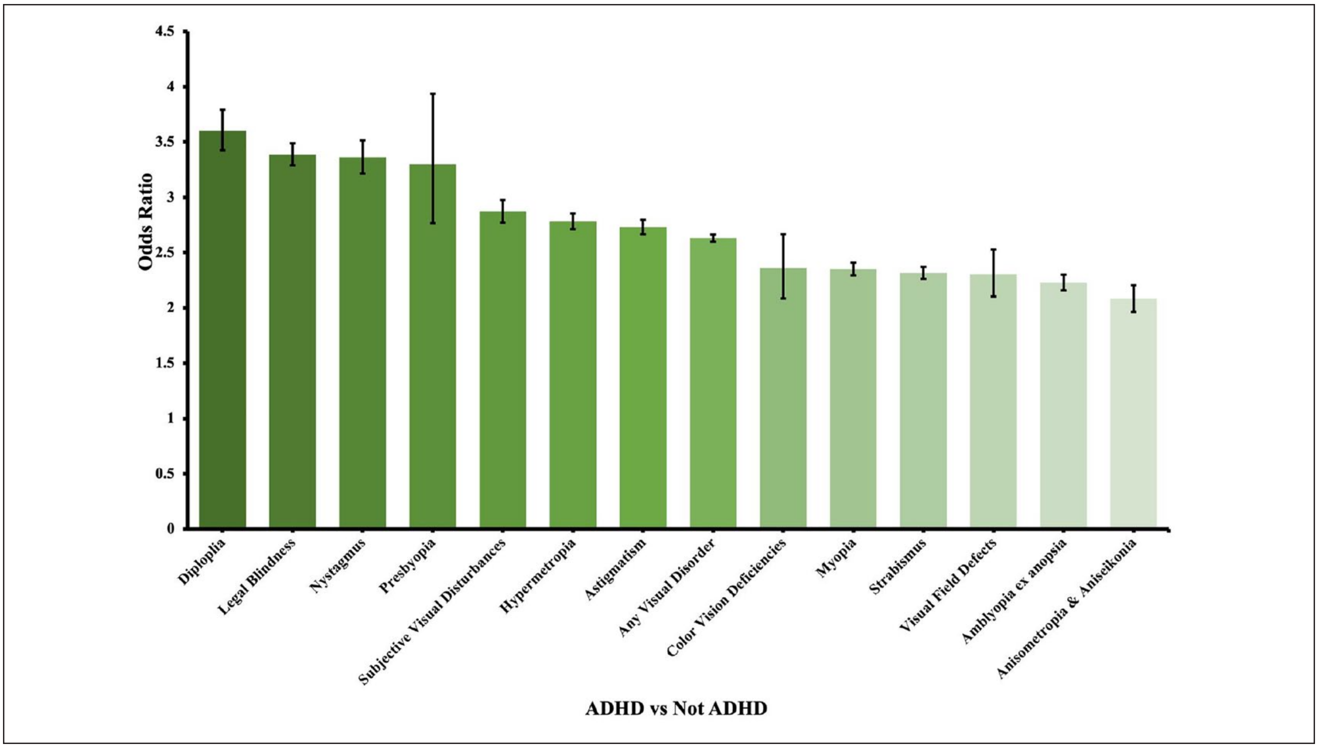

Figure 1. Odds ratio by outcome between patients without ADHD and with ADHD. Confidence bars represent 95% interval.

Discussion

Compared to those without ADHD, the cohort with ADHD had higher rates of every visual disorder studied and a 2.6 times higher rate of occurrence of any visual disorder. The odds ratio ranged from 1.7 times higher for glaucoma to 3.6 times higher for diplopia. The rates of occurrence in the ADHD cohort ranged from 0.1% for presbyopia to 3.7% for astigmatism. Some of these events have been examined in prior ophthalmologic-ADHD studies, but certain diagnoses like glaucoma are less commonly studied (Bellato et al., 2022). To our knowledge, our data provides the largest sample to date of individuals under 22 with ADHD and visual disorders and is largely in line with established findings of the field.

Many hypotheses have been suggested for the rationale behind the substantial association noted in our study and others, including medication adverse effects and misdiagnosis (Borsting et al., 2005). Our findings offer strong evidence to contradict the misdiagnosis hypothesis, which suggests that some individuals with ADHD and visual disorders do not truly have ADHD, but rather experience some of the symptoms like inattention due to an inability to adequately see the object of attention (Borsting et al., 2005; Decarlo et al., 2014). Although the hypothesis may hold true in isolated cases, there were 50,000 more individuals with ADHD diagnosed with visual disorders than matched peers in our study. While we cannot definitively disprove the misdiagnosis hypothesis with our data, it would be concerning if psychiatrists, psychologists, and other ADHD providers incorrectly diagnosed such a large group of individuals with a neurodevelopmental disorder without considering the possibility of an underlying vision problem.

Similarly, our data suggests that medications are not a reasonable explanation for the association. While individual case reports have suggested certain ophthalmologic effects may occur, there is not much data to support any eye-specific detrimental effect of ADHD medications, and ADHD medications are largely considered safe with regards to ophthalmologic health (Guvenmez et al., 2020). Our data supports the view that medications are likely safe. In our medication sub-analysis, the presence of any ADHD medication only mildly increased the likelihood of disorders compared to the absence of medication; ratios ranged from 1.09 for strabismus to 1.55 for presbyopia. Furthermore, the associations were far weaker than the comparison between ADHD individuals and neurotypical peers. After matching for age, sex, race, and ethnicity, presence of ADHD medications was not associated with a statistically significant increase in likelihood of subjective visual disturbances, diplopia, or non-age-related cataract.

The separation of stimulant and non-stimulant medications provides novel insight into visual disorders in ADHD. Compared to individuals with ADHD and no history of medication use, those with stimulant prescriptions had statistically

Table 3. Cohort Size, Absolute Risk, Odds Ratio With Confidence Interval, and t-Test p-Value by Outcome. Stimulants Abbreviated as "Stims." Non-Stimulants Abbreviated as "Non-Stim." Bolded Values Indicate $p < .05$.

Med type	Cohort *N*	Event *N*	Risk	Odds ratio	95% CI	*p* Value	Med type	Cohort *N*	Event *N*	Risk	Odds ratio	95% CI	*p* Value
Any visual disorder							Subjective visual disturbances						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	27,782	12.7%	1.22	[1.20, 1.24]	**.001**	Any meds	218,070	3,432	1.6%	1.01	[0.96, 1.06]	.634
Stims	179,330	21,979	12.3%	1.17	[1.15, 1.20]	**.001**	Stims	179,330	2,633	1.5%	0.95	[0.90, 1.01]	.077
Non-Stim	48,402	7,542	15.6%	1.51	[1.45, 1.57]	**.001**	Non-Stim	48,402	1,039	2.1%	1.41	[1.28, 1.55]	**.001**
Strabismus							Diplopia						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	6,793	3.1%	1.09	[1.05, 1.13]	**.001**	Any meds	218,070	2,014	0.9%	1.05	[0.99, 1.12]	.109
Stims	179,330	5,080	2.8%	1.00	[0.97, 1.04]	.848	Stims	179,330	1,398	0.8%	0.90	[0.84, 0.97]	**.004**
Non-Stim	48,402	2,194	4.5%	1.48	[1.38, 1.58]	**.001**	Non-Stim	48,402	800	1.7%	1.79	[1.59, 2.01]	**.001**
Astigmatism							Color vision deficiencies						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	7,766	3.6%	1.41	[1.36, 1.46]	**.001**	Any meds	218,070	296	0.1%	1.54	[1.29, 1.85]	**.001**
Stims	179,330	6,322	3.5%	1.38	[1.33, 1.44]	**.001**	Stims	179,330	235	0.1%	1.47	[1.20, 1.80]	**.001**
Non-Stim	48,402	1,898	3.9%	1.50	[1.40, 1.61]	**.001**	Non-Stim	48,402	73	0.2%	1.59	[1.10, 2.30]	**.013**
Myopia							Legal blindness						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	7,095	3.3%	1.39	[1.34, 1.44]	**.001**	Any meds	218,070	5,755	2.6%	1.09	[1.05, 1.13]	**.001**
Stims	179,330	5,840	3.3%	1.38	[1.32, 1.43]	**.001**	Stims	179,330	4,490	2.5%	1.04	[1, 1.09]	.052
Non-Stim	48,402	1,620	3.3%	1.44	[1.34, 1.56]	**.001**	Non-Stim	48,402	1,667	3.4%	1.41	[1.31, 1.52]	**.001**
Hypermetropia							Optic nerve/pathway disorder						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	6,663	3.1%	1.40	[1.35, 1.46]	**.001**	Any meds	218,070	1,460	0.7%	1.11	[1.03, 1.19]	**.007**
Stims	179,330	5,446	3.0%	1.39	[1.33, 1.45]	**.001**	Stims	179,330	998	0.6%	0.92	[0.85, 1.01]	.068
Non-Stim	48,402	1,583	3.3%	1.44	[1.33, 1.55]	**.001**	Non-Stim	48,402	597	1.2%	2.08	[1.81, 2.40]	**.001**
Anisometropia & Aniseikonia							Glaucoma						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	1,043	0.5%	1.21	[1.12, 1.32]	**.001**	Any meds	218,070	695	0.3%	1.18	[1.06, 1.32]	**.003**
Stims	179,330	801	0.4%	1.12	[1.01, 1.24]	**.001**	Stims	179,330	553	0.3%	1.10	[0.98, 1.24]	.116
Non-Stim	48,402	305	0.6%	1.54	[1.29, 1.85]	**.001**	Non-Stim	48,402	186	0.4%	1.58	[1.25, 1.99]	**.001**
Presbyopia							Non-age-related cataract						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	170	0.1%	1.55	[1.22, 1.97]	**.001**	Any meds	218,070	564	0.3%	1.13	[0.99, 1.27]	.053
Stims	179,330	134	0.1%	1.49	[1.14, 1.95]	**.003**	Stims	179,330	417	0.2%	1.01	[0.88, 1.157]	.889
Non-Stim	48,402	46	0.1%	1.92	[1.17, 3.14]	**.009**	Non-Stim	48,402	190	0.4%	1.87	[1.47, 2.38]	**.001**
Amblyopia ex anopsia							Nystagmus						
No meds			Reference cohort				No meds			Reference cohort			
Any meds	218,070	3,725	1.7%	1.10	[1.05, 1.15]	**.001**	Any meds	218,070	2,427	1.1%	1.17	[1.10, 1.24]	**.001**
Stims	179,330	2,920	1.6%	1.05	[0.99, 1.11]	.072	Stims	179,330	1,644	0.9%	0.98	[0.92, 1.06]	.663
Non-Stim	48,402	1,018	2.1%	1.34	[1.22, 1.48]	**.001**	Non-Stim	48,402	1,027	2.1%	2.14	[1.92, 2.39]	**.001**

equivalent rates of occurrence for 7 of 16 measured outcomes. This supports other medication-based ADHD research into medical comorbidities, which suggest that stimulant medications tend to mitigate the impact of ADHD on certain disorders (Chen et al., 2017; Evans et al., 2022; Walsh et al., 2022). Interestingly, non-stimulant medications had significantly increased rates for every disorder. Particularly in the field of pediatrics, stimulant medications are the subject of frequent discussions on safety, substance use, prescription stewardship, and patient advocacy (Banaschewski et al., 2004; Evans et al., 2022). In contrast, non-stimulant medications tend to be less commonly discussed, as they are seen as "safer" alternatives to stimulant medications (Banaschewski et al., 2004). Within the specific intersection of ADHD care and ophthalmology, our findings support the appropriate use of stimulant medication and indicate the need for further discussion into the comparative use of stimulant and non-stimulant medications for ADHD.

Our findings hold significance for a wide variety of health care professionals, including psychiatrists, psychologists, primary care providers (PCPs), optometrists, and of course, ophthalmologists. The data in our study present both the opportunity for further investigation and for intervention. Providers treating or diagnosing visual disorders may consider the following question raised by our study: are individuals with ADHD without medication use truly experiencing lower rates of visual disorders, or being diagnosed less frequently? In other words, investigation is needed into this disparity to ascertain if there is a difference in presence or formal diagnosis. As it is unlikely that the medications themselves are causally responsible for the visual disorders, which suggests two alternative hypotheses. Firstly, as individuals not requiring ADHD medications commonly experience less severe symptoms (Mowlem et al., 2019), it could be that their visual disorders are subclinical and less obvious than individuals requiring stimulant medications. Alternatively, the prescription of medications for ADHD requires regular contact with physicians and other providers, which may lead to an increased rate of visual disorder diagnosis even if the underlying prevalence is the same.

In either case, our findings support a low-cost intervention: intentional review of vision in ADHD patients. While the link between ADHD and visual disorders is well established (Bellato et al., 2022), it is a relatively new finding, and providers may not have a sufficiently elevated index of suspicion for visual disorders when treating patients for ADHD. As a review of systems is standard of care during a medical visit, it is important that providers in psychiatry or primary care intentionally spend time asking their patient about their vision. While consideration of vision impairment is common in the initial evaluation for ADHD, it is not frequently discussed in psychiatry. In the case of ophthalmologists and optometrists, it may be worth asking the patient specifically about ADHD and associated medications, as individuals may leave such diagnoses off health history forms when it does not seem relevant to their chief concern. However, the substantial association suggests that ADHD is relevant for ophthalmologic care and should be included in the related records. Our results highlight the significance of considering ADHD as a potential factor in the presentation of various visual disorders, and vice versa. Incorporating both questions about ADHD and vision during patient assessments could aid in accurate diagnosis and tailored treatment approaches.

Limitations exist in every study, and ours is no exception. As is common with deidentified aggregate data, we experienced limitations pertaining to the individual record. We were unable to identify patients in any way, so it is possible that patients were present in multiple events, such as both presbyopia and legal blindness. Similarly, we were unable to verify that prescribed medications were obtained and administered. Finally, we are unable to identify the providers involved in diagnosis, so visual disorders may have been diagnosed by ophthalmologists, primary care physicians, psychiatrists, optometrists, or any other medical professional empowered to diagnose such disorders. The absence of provider specialty information prevents the study from accounting for potential variations in diagnostic practices across different healthcare professionals, potentially affecting the interpretation of the study's findings. However, the large size of our study mitigates much of the potential confounding effect of these limitations.

Our study presents a novel investigation of ADHD medications and visual disorders. While prior research has explored the association between ADHD and vision, medications are commonly not investigated, and age is disregarded. Our analysis of over 1 million individuals offers important significance for many providers, and shows the potential insights yet to be gained from future research such as prospective longitudinal studies that follow individuals with ADHD and compare their visual outcomes over time. As the intersection of ophthalmology and psychiatry expands, it is important that all facets of ADHD and visual disorders are fully explored to provide this unique patient population with the best care possible.

Declaration of Conflicting Interests

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IRB Approval Status

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Author Biographies

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