



Mental Health And Developmental Consequences Of Ophthalmologic Disease In Nonsyndromic Craniosynostosis

Robin T. Wu, MD; Olubunmi A. Fariyike, BS; Aura S. Eguizabal, BS; Payton Grande, BS; Brian F. Sweeney Jr., MD; Shannon J. Beres, MD; Laura M. Prolo, MD, PhD; Kelly B. Mahaney, MD; Rohit K. Khosla, MD; H. Peter Lorenz, MD



Introduction

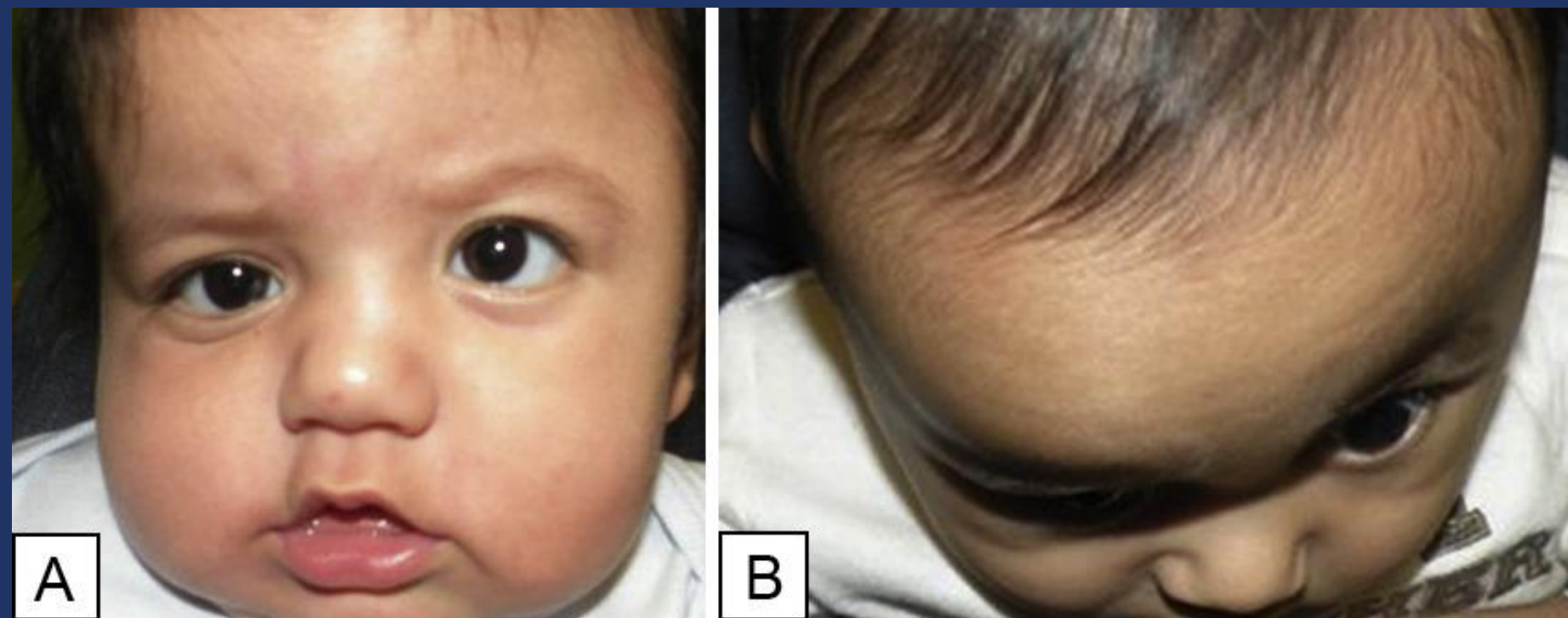
Ocular complications of craniosynostosis are both common and varied, including optic neuropathies, strabismus, exposure keratopathy, refractive errors, ptosis, and, in many cases, resultant amblyopia. Among non-syndromic patients, longitudinal and retrospective studies have reported notable rates of strabismus, amblyopia, and refractive errors following surgical intervention, highlighting the persistent burden of ophthalmologic disease in this population.

In nonsyndromic craniosynostosis, abnormal orbital morphology can disrupt extraocular muscle function, contributing to strabismus. Shallow orbits are also implicated in the development of refractive errors, including astigmatism, as well as exposure keratopathy. Collectively, these ocular abnormalities increase the risk of amblyopia, a form of cortical visual impairment resulting from inadequate visual stimulation during development. If the underlying causes are not addressed in a timely manner, these deficits may become permanent, emphasizing the importance of early craniofacial and ophthalmologic evaluation and intervention.

Purpose

Current literature investigating the associations and underlying mechanisms of ocular disease in craniosynostosis is sparse. Further, the true prevalence of ophthalmologic disease in this population is difficult to estimate as reported rates vary widely between different studies. While ophthalmologic comorbidities are present in synchrony with developmental and mental health disorders, the interplay of these factors is unknown. Further study of craniosynostosis is thus needed in order to develop evidence-based guidelines for ophthalmologic screening and treatment as part of the multidisciplinary care required for these patients.

Methods



- Retrospective review of patients from the Stanford Cleft and Craniofacial Clinic (2014–2021)
- Included all patients diagnosed with nonsyndromic craniosynostosis (NSC)
- Excluded: syndromic craniosynostosis, suspected genetic cases under workup, ophthalmology evaluations or ≥ 1 -year postoperative follow-up
- Ophthalmologic outcomes obtained from standardized annual neuro-ophthalmology visits and adjunct optometry visits
- All patients underwent dilated eye exams and cycloplegic refraction
- Age-appropriate refractive errors (e.g., mild hyperopia, astigmatism) were excluded
- Developmental delay assessed via two measures: subjective mention and formal diagnosis
- Developmental delays categorized as global, motor, speech, or academic
- Mental health disorders included ASD, ADHD, anxiety, OCD, PTSD, depression, and other psychiatric conditions
- Categorical variables analyzed with chi-square testing; continuous variables with two-tailed t-tests
- Linear mixed-effects models used to evaluate associations with ophthalmologic outcomes
- Models accounted for both fixed and random effects and included significant univariate predictors

Results

Demographics		Average	SD
Age at Surgery	Months	10.22	4.49
Weight at Surgery	Kg	8.41	4.49
EBL per weight	mL/kg	18.77	16.40
Intraoperative Transfusion per Weight	mL/kg	16.91	14.84
Drop in Hg per Weight	Hg/kg	0.70	1.12
		Number	%
Sex	Male	111	66.47
	Female	55	33.13
Race	White	0	0.00
	Asian	0	0.00
	Black	0	0.00
	Hispanic/White	0	0.00
	Hispanic/Other	0	0.00
	Other	0	0.00
Comorbidities	Neurologic	7	4.19
	Renal	5	2.99
	Respiratory	3	1.80
	Cardiac	1	0.60
Surgical Intervention	Open CVR	107	64.07
	Endoscopic strip craniectomy	59	35.33
	Sagittal	91	54.82
	Metopic	31	18.67
Craniosynostosis	Coronal	24	14.46
	Lambdoid	10	6.02
	Multiple	10	5.99
Reoperation	Total	20	11.98
	Frontal Orbital Advancement	13	7.78
	Posterior Vault Remodeling	3	2.99
	Bone Grafting for Persistent Cranial Defect	3	1.80
	Chiari I Decompression	1	0.60
	Scar Revision	1	0.60
	Infection Debridement	1	0.60

Figure 1. Demographic and perioperative variables

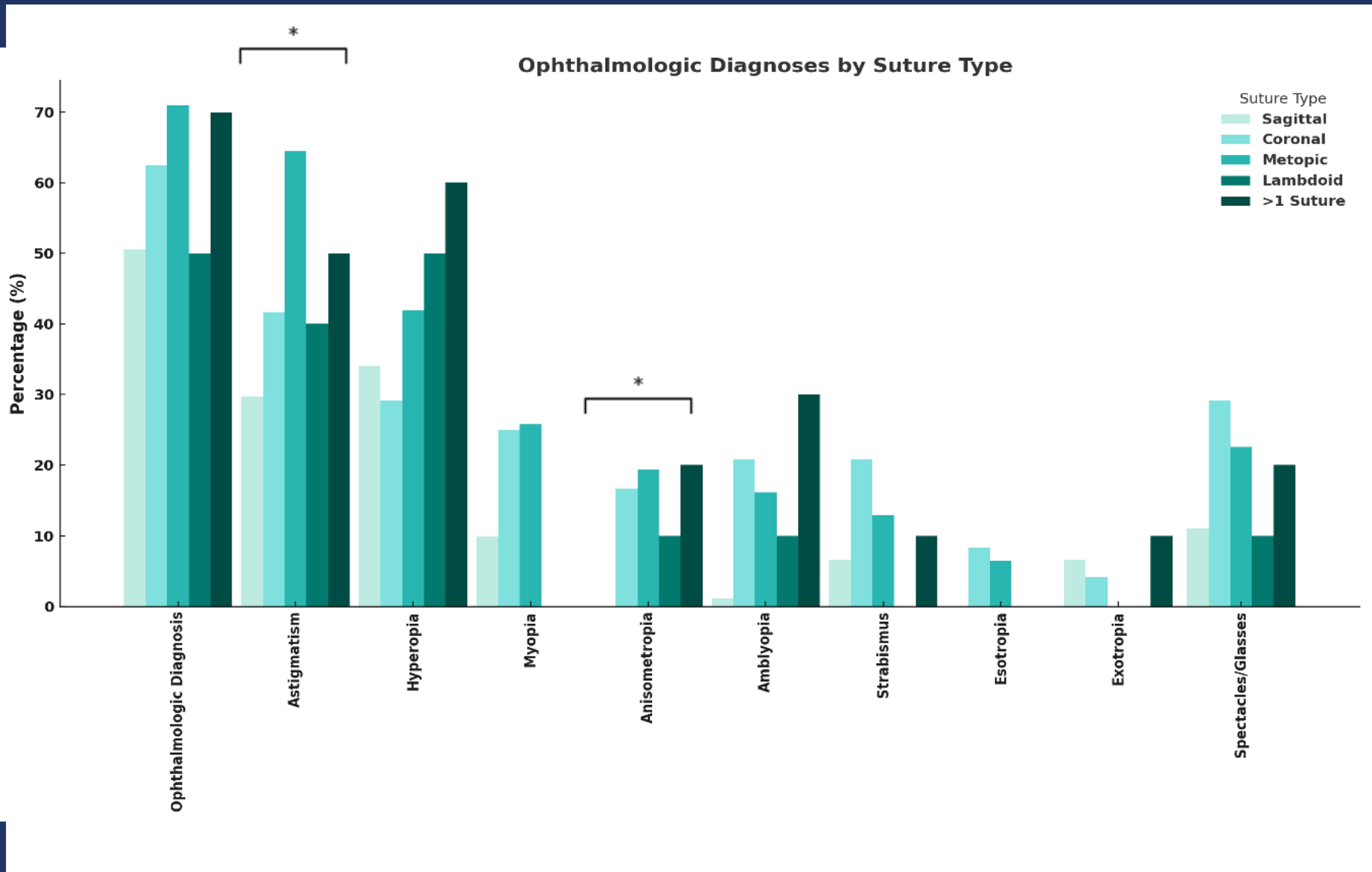


Figure 2. Multivariate regressions were run to control for all significant variables determined in univariate regression in addition to surgery type.

Metopic synostosis was associated with astigmatism (OR 1.47; $p=0.002$) and both metopic and >1 suture fusion were associated with anisometropia (OR 5.64, OR 2.72; $p=0.036$).

* $p<0.05$

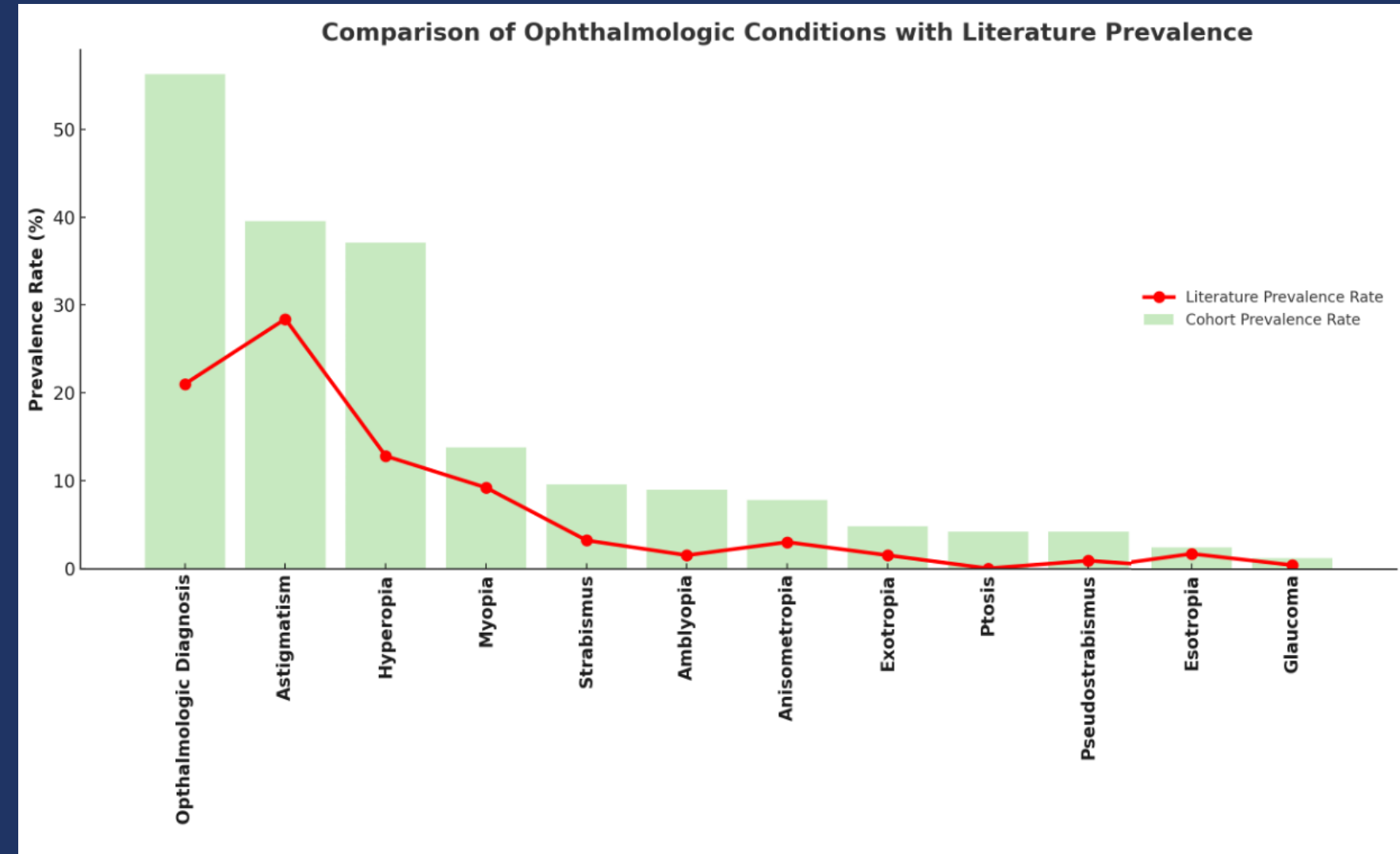
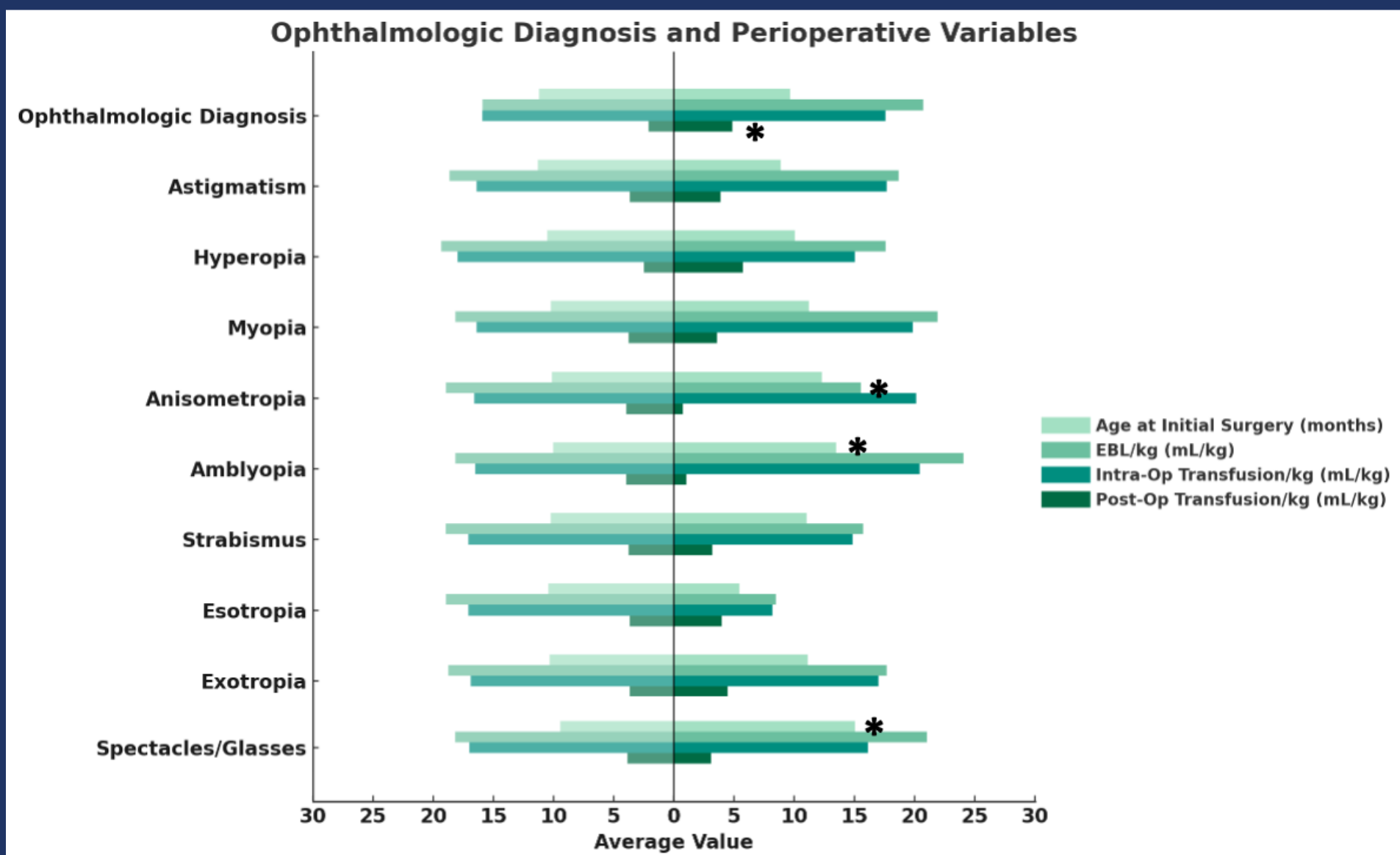


Figure 1. Prevalence of ophthalmologic diagnoses in the study cohort with literature prevalence.

Overall, 57.2% of patients received at least one ophthalmologic diagnosis. The average age of ocular diagnosis was 3.0 years, with the latest diagnosis at 8.7 years of age. Refractive errors were most common (51.8%), with astigmatism occurring in 39.8%, hyperopia in 37.4%, myopia in 13.86%, and anisometropia in 7.8%. Strabismus occurred in 9.6%, with exotropia making up 4.8% and esotropia comprising 2.4%. Other diagnoses included amblyopia (9.0%), ptosis (4.2%), and glaucoma (1.2%). 16.3% of patients required glasses. Prevalence is presented in comparison to normal population prevalence as determined in previous literature in Figure 1.24–31 Distribution of developmental and mental health disorders is presented in Table 3.



Older age at surgery was seen to lead to amblyopia (13.5 vs 10.2 mo; $p=0.049$) and future glasses use (16.1 vs 9.4 months, $p=0.007$). A lower intraoperative blood loss was associated with anisometropia (15.6 vs 18.9 unit/kg; 0.021). Higher post-operative transfusion was associated with overall ophthalmologic diagnosis (4.5 vs 2.9 mL/kg; $p=0.009$). * $p<0.05$

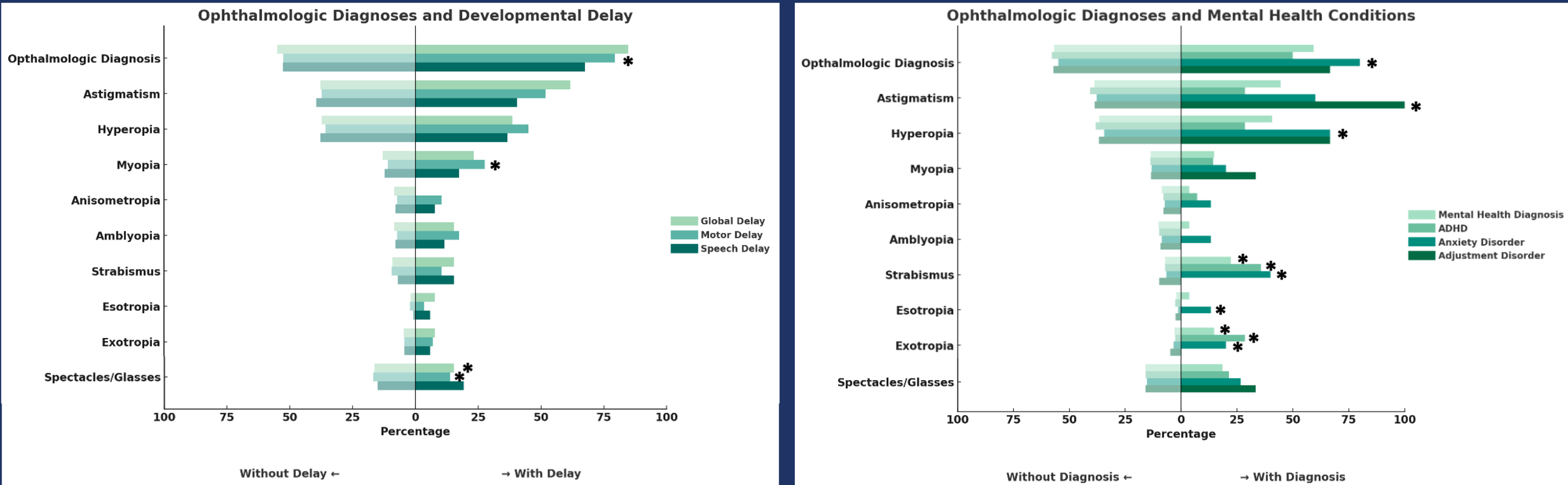


Figure 4. Future global delay was associated with no use of glasses (OR 0.93; $p=0.033$). Motor delay was associated with overall ophthalmologic diagnosis (OR 3.46; $p=0.049$), myopia (OR 3.10; $p=0.014$), EOM palsy (OR 5.00; $p=0.013$), and lack of glasses (OR 0.79; $p=0.012$). * $p<0.05$

Mental health diagnoses were more common with strabismus (OR 3.69; $p<0.001$) and exotropia (OR 5.87; $p=0.025$). ADHD was associated similarly with strabismus (OR 7.12; $p<0.001$), and exotropia (OR 14.8; $p<0.001$). Anxiety disorders were associated with overall ophthalmologic diagnoses (OR 3.28; $p=0.029$), hyperopia (OR 3.81; $p=0.012$), strabismus (OR 9.40; $p<0.001$), esotropia (OR 11.46; $p<0.001$), and exotropia (OR 7.30; $p=0.004$). Adjustment disorder was associated with astigmatism (OR >100 ; $p=0.006$) and glaucoma (OR 8.10; $p<0.001$). * $p<0.05$

Conclusions

NSC patients have higher prevalence of all ophthalmologic diagnoses compared to the general population. Ocular diagnoses, particularly myopia, can lead to motor delay. Multiple connections existed between eye diseases and mental health diagnoses. Among the strongest relationships, ADHD was associated with both strabismus and exotropia, anxiety was associated with strabismus, esotropia, and exotropia, and adjustment disorder was associated with astigmatism and glaucoma. Yearly neuro-ophthalmologic surveillance with systematic evaluation of all pathologies is imperative for all patients with NSC. Patients identified with eye diseases may benefit from further developmental and mental health screening.

Citations

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