What's New in Pediatric Ophthalmology Literature?

A semi-annual publication of the Professional Education Committee of the American Association of Pediatric Ophthalmology and Strabismus

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All-Star Nominees

Amblyopia, Refractive error, and Vision Screening

Retinal microvascular changes in unilateral functional amblyopia detected by oct-angiography and follow-up during treatment
Errera C, Romann J, Solecki L, et al
European Journal of Ophthalmology 2024;34(2):399-407
This study was designed to evaluate the macular microvascular changes using optical coherence tomographic angiography (OCT-A) in children with unilateral amblyopia and their reversibility during treatment. Patients with unilateral strabismic or anisometropic amblyopia or amblyopia status post congenital cataract surgery, examined between October 2019 and March 2021, were included. OCT-A parameters such as vessel density and perfusion density in the superficial capillary plexus and area, perimeter and circularity of the foveal avascular zone (FAZ) were analyzed. Analyses between the microvascular parameters and the visual acuity were also performed. A total of 128 eyes of 64 patients were included: 32 amblyopic eyes compared with 32 contralateral eyes and 64 control eyes. Vessel density and perfusion density in the superficial capillary plexus were significantly lower in amblyopic eyes compared to control eyes in 6 × 6 mm ($p < 0.02$) and 3 × 3 mm ($p < 0.01$) scans. Correlation analyses showed a linear decrease in vessel density and perfusion density with decreasing visual acuity. The microvascular changes observed were reversible with the occlusion treatment of amblyopia ($p < 0.001$). Based on these findings, OCT-A appears to be an additional clinical tool for diagnosing and monitoring functional amblyopia. The study findings are limited by the small patient sample size as well lack of robust longitudinal patient data.

Extended optical treatment versus early patching with an intensive patching regimen in children with amblyopia in Europe (EuPatch): a multicentre, randomized controlled trial
Proudlock FA, Hisaund M, Maconachie G, et al
Lancet 2024;403(10438):1766-1778
An extended period of optical treatment before patching is recommended by the clinical guidelines of several countries. The aim of this study was to compare an intensive patching regimen, with and without extended optical treatment (EOT) first, in a randomized controlled trial. 334 children, from 30 hospitals in Europe, aged 3-8 years old, with newly detected or untreated amblyopia (interocular difference > 0.30 logMAR BCVA) due to anisometropia, amblyopia, or both were randomly assigned to either receive 18 or 3 weeks of optical treatment prior to starting an intensive patching regimen (10 hours/day, 6 days/week) for up to 24 weeks. Primary outcome was successful treatment (< 0.20 logMAR interocular difference in BCVA) after 12 weeks of patching. 317 participants were analyzed for the primary outcome. 14% of the EOT group and 6% of the early patching group were excluded or dropped out. 67% of the early patching group had successful treatment at 12 weeks compared to 54% of the EOT group. This study involved multiple centers across Europe to ensure a diverse participant pool and robust results. Intensive patching is more effective at improving visual acuity quickly, but extended optical treatment can be a viable alternative, particularly for families seeking a less intensive approach with fewer complications such as discomfort and psychosocial impact.

Long-term effect of orthokeratology on choroidal thickness and choroidal contour in myopic children
Xu S, Wang M, Lin S, et al
Br J Ophthalmol 2024;108(8):1067-1074
Subjects from the Atropine Combined Orthokeratology (ACO) study, a previously conducted 2-year RCT, who completed the OCT scanning in the control and the ortho-k group, were included in this analysis to investigate the long-term effect of ortho-k on the choroid. Patients were 8-12 years old, had spherical equivalent refraction (SER) of −1.00 to −6.00 D in both eyes, astigmatism of no more than 1.50 D and anisometropia of no more than 1.50 D; a best-corrected visual acuity of no worse than 20/25 in both eyes; and no other ocular pathology. 64/80 patients (80%) successfully completed all the followup visits. The control group demonstrated more choroidal thinning and more prolate contour over the study period compared to the ortho-k group. The 2-year change in choroidal thickness was significantly associated with the 2-yearAL change in the control group, but this trend was not significant in the ortho-k group. The effect was seen to diminish in the long-term, however. The question remains regarding treatment duration, long-term effects vs rebound, and best patient populations for this myopia control intervention, but this study does contribute to knowledge on what role choroidal thickness and contour plays in myopia progression.

A pilot study of axial length changes associated with myopia control spectacles in subjects reading under mesopic conditions
Szeps A, Dankert S, Saracco G, Iribarren R
J AAPOS 2024 Apr;28(2):103857
Myopia control is an area of significant concern. One modality for trying to halt myopia progression is using plus lens defocus. Prior studies looking at people watching movies or reading on computers in dark rooms showed that plus lens defocus led to shortening of the axial length in emmetropes but did not lead to any difference in myopes. This paper aimed to see if a pair of novel defocus glasses that led to shortening of the axial length in myopes in photopic conditions would also lead to shortening of the AL in myopes in mesopic conditions. Patients read on a computer in a dark room, first in their normal monofocal correction then in the defocus glasses. The axial length increased by a significant amount after reading in the monofocal glasses and by an insignificant amount int eh defocus glasses. Most importantly, the defocus glasses did NOT lead to any shortening of the eye like they did in photopic conditions. Limitations of this study include that they only used one type of defocus lens and did not compare myopes to emmetropes. This study is important in that it highlights the possible role of lighting conditions on the progression of myopia, even in the setting of treatment. These results should make us consider recommending that patients do not spend time reading or doing other visual activities in mesopic conditions.

Choroidal Changes During and After Discontinuing Long-Term 0.01% Atropine Treatment for Myopia Control
Lee SS, Lingham G, Clark A, Read SA, Alonso-Caneiro D, Mackey DA
Invest Ophthalmol Vis Sci 2024;65(10):21

Low-dose atropine has emerged as a treatment for myopia control, with recent studies showing choroidal thickening with low-dose atropine which were sustained during the study period. There is also a documented “rebound” effect with cessation of low-dose atropine. This study analysis was conducted as part of a double-blind randomized control trial that compared 0.01% atropine to placebo. SD-OCT was used to obtain images which were analyzed for choroidal thickness. A total of 148 children were included in the analysis. During the treatment phase, the subfoveal choroid in both treatment and control groups thickened by 12–14 μm. During the washout phase, the subfoveal choroids in the placebo group continued to thicken by 6.6 μm, but those in the atropine group did not change. Participants with good axial eye growth control had greater choroidal thickening than the fast-progressors during the treatment phase regardless of the treatment group ($P < 0.001$), but choroidal thickening in the atropine group’s fast-progressors was not sustained after stopping eye drops. Overall, 0.01% atropine did not cause a difference in choroidal thickness, but abrupt cessation of long term atropine may disrupt normal choroidal thickening in children. Overall, this study challenges the positive data on low-dose atropine and suggests caution with sudden cessation of atropine for myopia control.

Effectiveness of the Spot tm Vision Screener With Variations in Ocular Pigments
Pophal CJ, Trivedi RH, Bowsher JD, et al
Am J Ophthalmol 2024;264:99-103
The study aimed to assess the effectiveness of the Spot Vision Screener in detecting Amblyopia Risk Factors (ARF) and refractive errors (myopia and hyperopia) in children, considering variations in ocular pigmentation. Involving 1,040 children from a pediatric clinic, the study categorized participants into three groups based on ocular pigment—darkly pigmented, medium pigmented, and lightly pigmented—and used the Spot Vision Screener prior to a complete eye examination by a blinded pediatric ophthalmologist. Results indicated that the Spot Vision Screener demonstrated excellent accuracy for myopia detection across all pigment groups, with sensitivities varying from 0.49 to 0.78, and good accuracy for hyperopia, with sensitivities ranging from 0.23 to 0.46. Specificities for both myopia and hyperopia were high across groups. The study's strengths include its large and diverse sample and robust diagnostic methods. However, its limitations include varying sensitivity based on ocular pigmentation, which could impact accuracy across different ethnic groups, and the lack of consideration for additional factors such as accommodation and pupil size. The findings endorse the use of the Spot Vision Screener but suggest that future advancements should address variations in sensitivity related to ocular pigmentation to enhance screening accuracy for diverse populations.

Strabismus and Strabismus Surgery

Mental Health Conditions Associated With Strabismus in a Diverse Cohort of US Adults
Jin K, Aboobakar IF, Whitman MC, Oke I
JAMA Ophthalmol 2024;142(5):472-475
Strabismus affects 2 to 3% of individual in the US and may negatively affect psychosocial well-being and predispose individuals to mental health conditions. This cross-sectional study used data from the National Institutes of Health’s All of Us Research programs to investigate the association between strabismus and mental health. 3,646 adults with a code for strabismus

(median age 67, 55% female) and 3,646 1:1 propensity score-matched controls (age, gender, race and ethnicity, income, educational level, and health insurance) were included. Compared with controls without strabismus, those with strabismus had a higher prevalence of anxiety (32% vs 14%, P<0.001), depression (33% vs 14%, P<0.001), substance use and addiction (3% vs 1%, P<0.001), bipolar disorder (7% vs 3%, P<0.001), and schizophrenia spectrum disorder (3% vs 1%, P<0.001). Among those with strabismus, higher odds of mental health conditions were associated with younger age, female gender, Black or African American race and ethnicity, low income, and high school education or less. Overall, in this study, adults with strabismus were about 2 to 3 times more likely to have mental health conditions compared to adults without strabismus. Limitations of this study include the use of diagnostic codes susceptible to coding errors, potential barriers to receiving a diagnosis of a mental health condition, and potential confounding factors.

Prematurity May Affect the Postoperative Sensory Results in Children With Strabismus
Niyaz L, Kocak N, Subası M, et al
J Pediatr Ophthalmol Strabismus 2024;61(4):267-272
Significant prematurity has effects on many systems, including the eyes. Here, the authors hypothesize that prematurity may affect surgical outcomes in strabismus. They set out to test this hypothesis by retrospectively reviewing all children undergoing strabismus surgery at a single institution over an 8 year period. This included 70 patients in the premature group (defined as born prior to 37 weeks gestation) and 242 patients in the control (non-premature) group. They then collected both motor (alignment) and sensory (stereopsis) outcomes for these patients. The amount of preoperative deviation and postoperative deviations was similar between the premature and non-premature groups. There were also similar rates of overcorrection and undercorrection between the groups. However, the premature group showed significantly less improvement in stereopsis post-surgery than the control group (560 to 300 arc/sec postoperatively in the premature group and 1,156 to 685 arc/sec in the control group). Thus, despite similar improvements in motor outcomes, children born premature showed less improvement in stereopsis. This suggests that prematurity may serve, as the authors state, as a “barrier for normal development of sensory function.” This is important for pre-operative counseling of any premature patient undergoing strabismus surgery.

Comparison of anterior segment optical coherence tomography and ultrasound biomicroscopy in localizing horizontal rectus muscle insertions
Duan R, Yang J
European Journal of Ophthalmology 2024;34(3):656-665
The authors aimed to evaluate the reliability of measuring the distance from the limbus to extraocular muscle insertion using anterior segment optical coherence tomography (AS-OCT) and panoramic ultrasound biomicroscopy (UBM) before and after strabismus surgery. Patients with strabismus underwent evaluation with AS-OCT and UBM preoperatively, 2 weeks, an 1,3 and 6 months post-operatively, specifically looking at the distance between limbus to muscle insertion. These measurements were also manually obtained using calipers in the operating room at the start and end of the surgical procedure. Preoperative AS-OCT and UBM values were compared to intraoperative caliper measurements as the gold standard. Postoperative

AS-OCT and UBM values were compared to the new postoperative limbus-insertion distance. The limit of agreement deemed clinically acceptable was defined as 1 mm. A total of 85 horizontal muscles of 40 patients, including 48 lateral rectus muscles and 37 medial rectus muscles, were analyzed. The rectus muscles were successfully detected by preoperative AS-OCT (95%) and UBM (100%). At 2 weeks and 1, 3, and 6 months postoperatively, the new rectus muscle attachment site detection rate by AS-OCT was 6%, 32%, 80%, and 89%, respectively, and that by UBM was 24%, 60%, 85%, and 93%, respectively. The accuracy of UBM measurements of preoperative muscles was 81%, and this decreased to 59% at 6 months postoperatively (P = 0.001). The findings in this study suggest that AS-OCT and UBM performed well in terms of imaging horizontal rectus muscles prior to surgery, but showed decreased accuracy and reproducibility in measuring the positions of rectus muscles postoperatively. The study is limited by its small sample size and single center design.

Long-term comparison of horizontal rectus surgery with vertical tendon transposition and combined vertical tendon transposition and inferior oblique-weakening in V-pattern exotropia
Tellioğlu A, Yilmaz T, İnal A, et al.
J AAPOS 2024;28(4):103958
This study compared the effectiveness of two surgical approaches for treating V-pattern exotropia: bilateral lateral rectus recession with vertical tendon transposition (LRVT) and LRVT combined with inferior oblique disinsertion (IO disinsertion). A retrospective chart review was conducted on patients with V-pattern exotropia and +1 or +2 inferior oblique overaction (IOOA) who underwent these surgeries and were followed for at least 3 years. Data collected included pre-operative, 6-month, and 3-year post-operative assessments, with surgical success defined as achieving less than 10 prism diopters of distance deviation in primary gaze. The results showed similar surgical success rates between the two groups (77.3% for LRVT alone and 73.9% for LRVT with IO disinsertion). Both groups had a reduction in the V-pattern, but the combination surgery achieved a statistically significant greater decrease of 5 prism diopters compared to LRVT alone. The study's strengths include its long follow-up period and comparison of two techniques, though limitations involve its retrospective nature and lack of pre- and post-operative torsion data. Clinically, this study highlights that combining LRVT with IO disinsertion may provide a more significant reduction in V-pattern exotropia than LRVT alone.

Novel superior oblique anterior fiber plication with or without adjustable sliding knot for extorsion
Anderson M, Bothun ED
J AAPOS 2024 Jun;28(3):103927
To report a novel surgical technique for correcting excyclotropia, a superior oblique anterior fibers plication (SOAFP) with or without a hemi hangback anterior knot was introduced, allowing for postoperative adjustment. A retrospective interventional case series was conducted on patients undergoing SOAFP between January 1, 2019, and March 1, 2023, with at least one month of postoperative follow-up. Exclusion criteria included concurrent vertical or torsional strabismus surgery or evidence of preoperative orbital restriction. Ocular alignment was assessed using prism and alternate cover and double Maddox rod tests preoperatively, and at initial (1-5 days) and final (closest to 6-8 weeks) postoperative visits. Fourteen patients, aged 21-92 years, underwent SOAFP, with 18 eyes treated and 14 eyes receiving adjustable

plications of 2-30 mm (mean, 8.93 ± 5.63 mm). SOAFP was the sole procedure in 12 eyes, while in 6 eyes it was combined with up to four horizontal rectus muscle recession, resection, or plication procedures. Preoperatively, the mean extorsion was 10.14° ± 7.01° (range, 2° to 30°). At the initial postoperative examination (1-5 days), the mean intorsional shift was 11.18° ± 7.37°, corresponding to 1.86° ± 1.04° of correction per millimeter of plication. Three eyes were adjusted after the initial visit to achieve a stronger plication effect targeting 5° intorsion. At the final visit, 61 ± 23 days postoperatively, the mean extorsion was 1.21° ± 2.29°, ranging from 5° of extorsion to 3° of intorsion. The mean final intorsional shift was 9.14° ± 7.53°, representing 1.16° ± 0.50° of correction per millimeter of plication. Of the 14 patients, 13 experienced improvement in diplopia. Limitations of the study include its retrospective design, small sample size, and short follow-up period. SOAFP allowed for targeted and easily adjustable correction of extorsion. Although no significant vertical or horizontal deviation was induced, there was an initial ipsilateral hyposhift and esoshift at distance and near. Therefore, it is recommended that SOAFP be performed on the ipsilateral eye of any small hypertropia (<4 PD).

Associations of strabismus surgery timing in childhood with mental health: a retrospective cohort study

Hidinger I, Kong L, Ely A

J AAPOS 2024 Jun;28(3):103929

To investigate the incidence of psychiatric diagnoses in relation to strabismus surgery timing among children with an early strabismus diagnosis who underwent surgery in childhood, a retrospective cohort study using TriNetX network data from 2003-2023 was conducted. Patients diagnosed with strabismus at ≤5 years of age and who had strabismus surgery before 18 years of age were included. Cohort 1 comprised patients who underwent initial strabismus surgery at ≤6 years of age, while cohort 2 included those with initial surgical intervention at ≥7 years of age. The incidence of mental health diagnoses from ages 7 to 18 was compared between cohorts. Results indicated that more patients in cohort 2 (123 of 693 patients, or 17.7%) were diagnosed with at least one mental health disorder compared to cohort 1 (59 of 688 patients, or 8.6%), with a risk ratio (RR) of 2.07 (95% CI, 1.546 to 2.77; P < 0.0001). Increased risk for specific psychiatric diagnoses was observed in cohort 2 versus cohort 1, including anxiety disorders (RR = 2.19; 95% CI, 1.225-3.922; P = 0.0065), attention-deficit/hyperactivity disorder (RR = 2.18; 95% CI, 1.499-3.175; P < 0.0001), conduct disorders (RR = 2.81; 95% CI, 1.425-5.556; P = 0.0018), and adjustment disorders (RR = 2.07; 95% CI, 1.103-3.876; P = 0.0204). However, no statistically significant difference was found between cohorts in depressive disorders (RR = 1.00; 95% CI, 0.419-2.392; P = 0.9974). Gender analysis showed that only males had a statistically significant increased rate of mental health diagnoses in cohort 2 versus cohort 1 (RR = 1.82; 95% CI, 1.284 to 2.577; P = 0.006). The strengths of the study include the use of a large database, while limitations include the retrospective nature of the study, which cannot assign causality, and the limited data available in the TriNetX database, such as race information. The impact on clinical practice suggests that children who undergo strabismus surgery at a later age after an early diagnosis may be more likely to experience mental health disorders during childhood, although it remains unclear whether these disorders result from delayed surgery or influence the decision to pursue surgery rather than continued conservative management.

Outcomes of Strabismus Surgery Following Teprotumumab Therapy
Hilliard G, Pruett J, Donahue SP, et al
Am J Ophthalmol 2024;262:186-191
The study assessed the outcomes of surgical treatment for strabismic diplopia in patients with Thyroid Eye Disease (TED) who had previously received teprotumumab. Conducted as a multicenter, retrospective case series involving 28 patients from seven academic centers, the research examined variables such as time since the last teprotumumab dose, prior orbital decompression, preoperative deviations, and postoperative outcomes. Results indicated that 57% of patients were diplopia-free after one surgery, with an overall success rate of 79% and 89% after additional surgery. For patients who had undergone prior orbital decompression, success rates were 64% after one surgery and 82% after a second. The study, notable for being the first to evaluate TED-related strabismus surgery outcomes following teprotumumab treatment, revealed that teprotumumab does not negatively impact surgical results. Despite its strengths, including data from multiple centers, the study has limitations such as its retrospective design, lack of long-term follow-up, and variability in surgical protocols. The findings support the continued use of teprotumumab and suggest that surgical approaches for TED-related strabismus remain effective.

Retinopathy of Prematurity, Practice Systems, and Education

The Incidence and Timing of Treatment-Requiring Retinopathy of Prematurity in Nanopremature and Micropremature Infants in the United States: A National Multicenter Retrospective Cohort Study
Scarboro SD, Harper CA 3rd, Karsaliya G, et al
Ophthalmol Retina 2024;8(3):279-287
With advances in neonatology, premature babies with younger gestational ages and lower birth weight are surviving. This unique population of extremely premature infants was not well included in landmark ROP trials evaluating prevalence and treatment of ROP. This is a multicenter retrospective cohort study from five sites across the United States focused on ROP in micropremature (<800g BW and/or <26 weeks GA) and nanopremature (<600g BW and/or <24 weeks GA). Primary data collected were number of patients treated for ROP, type of initial treatment pursued, and post-menstrual age at development of treatment-requiring ROP. A total of 7293 patients were screened for ROP across all sites, and 8.52% required treatment with an average PMA of 37.2 weeks. Infants defined as nanopremature had a 63% chance of requiring treatment at an average postmenstrual age (PMA) of 36.6 weeks, whereas those defined as micropremature had a 30% chance of requiring treatment at an average PMA of 36.3 weeks. Those with the highest risk are nanopremature infants by both weight and gestational age, being 26.2 times more likely to require treatment than the entire group of infants screened, Interestingly, the average postmenstrual age at treatment did not differ between groups. Overall, this is an important study highlighting the increased risk of ROP in mricopremature and nanopremature infants and assists in screening and counseling for these extremely premature infants.

Lack of racial and ethnic diversity in pediatric ophthalmology clinical trials from 2000 to 2022
Kuo A, Yazji I, Abbass N, Chong DD, Fane L, Örge FH
J AAPOS 2024 Apr;28(2):103870
Randomized control trials (RCTs) are important in both informing clinical care decisions and policy decisions. Lack of diversity in RTCs is problematic for several reasons, including less generalizable results. This study aims to look at this issue specifically in pediatric ophthalmology as there is a lack of knowledge regarding the prevalence of reporting racial/ethnic data and whether each race/ethnicity is under- or over-represented in peds ophtho RCTs. An extensive literature search was done to identify peds ophtho RCTs from 2000-2022. Once the trials were identified, reviewers collected data on racial/ethnic breakdown. Just over half of the articles reported race or ethnicity. This increased in trials published after 2010. In the studies that reported race, the majority of pts were White (88.6%) followed by Black (9.7%) and Asian (1.6%). In those reporting ethnicity, the majority of pts were non-Hispanic (87.5%). The major strengths of this study is the extensive literature search to find a good representation of RCTs over the years. Limitations include the observational design and discrepancies in how this data was labelled/defined between studies. This information is important for all pediatric ophthalmologists to be aware of as RCTs have a major impact on how we treat patients. It is imperative that we know that the results from these studies might not apply to all of our patients. It is also important that we are aware of this problem and work to identify ways to try to remedy it.

Access to Pediatric Eye Care by Practitioner Type, Geographic Distribution, and US Population Demographics
Siegler NE, Walsh HL, Cavuoto KM
JAMA Ophthalmol 2024;142(5):454-461
Vision disorders such as amblyopia can be prevented if detected and addressed early in childhood, yet problems with access to care may limit the ability for children to receive necessary care. The shortage of pediatric ophthalmologists, especially in lower-income and rural communities, is well documented, but there is limited evidence on the distribution of pediatric optometrists. The purpose of this study was to evaluate the geographic distribution of pediatric optometrists and pediatric ophthalmologists and correlate the locations with population demographics from the 2020 US census. 586 pediatric optometrists (51.5% female) and 1060 pediatric ophthalmologists (44.3% female) were identified using 4 online public databases in April 2023 (American Optometric Association, American Academy of Optometry, American Academy of Ophthalmology, and AAPOS). Among US counties, 6.5% had at least 1 pediatric optometrist and 9.7% had at least 1 pediatric ophthalmologist with substantial geographic overlap ($P<0.001$). Of the counties without pediatric ophthalmologists, 96.4% also lacked pediatric optometrists. Counties with pediatric ophthalmologists had higher mean household incomes compared to counties with pediatric optometrists ($P=0.003$) and higher mean population with bachelor's degrees ($P<0.001$). Counties without pediatric optometrists or pediatric ophthalmologists had lower median household incomes, smaller populations with bachelor's degrees, lower home internet access, and a great population younger than 19 years than counties with both practitioners. This study is limited due to the dynamic nature of

databases used to collect practitioner information and US census data that may omit certain demographics such as undocumented immigrants.

Anterior Segment, Cataract, and Glaucoma

Ten-year outcomes of congenital cataract surgery performed within the first six months of life
Oshika T, Nishina S, Unoki N, et al
J Cataract Refract Surg 2024;50(7):707-712
This study evaluates the 10-year post-operative outcomes of congenital cataracts that received surgical treatment within the first six months of life. It is a retrospective study examining outcome differences between aphakic versus pseudophakic, unilateral versus bilateral cases, and surgeries performed within the critical period of visual development (before 10 weeks of age for bilateral cases and 6 weeks of age for unilateral cases) versus those performed outside of this window. This study included 216 eyes of 121 patients, with 190 bilateral and 26 unilateral cases. Of these eyes, an intraocular lens (IOL) was inserted in 30, while 186 were left aphakic. Surgery performed during the critical period of visual development resulted in significantly better final visual acuity. However, these patients also showed a higher risk of visual axis opacification compared to those whose surgery was done after the critical period. Pseudophakic patients had better final visual acuities but also higher rates of visual axis opacification. The most dramatic finding was the comparative rates of glaucoma: 38 eyes in the aphakic group developed glaucoma (20%), compared with none (0%) in the pseudophakic group. The study boasts an impressive 10-year follow-up and is sufficiently powered to yield several statistically significant comparisons. Its limitations include the retrospective nature and the lack of analysis on amblyopia therapy. Nonetheless, it reinforces the importance of intervening within the critical period of visual development and provides further evidence supporting the efficacy of employing an IOL in this young age range.

External Validation of a Model to Predict Postoperative Globe Axial Length in Children After Bilateral Cataract Surgery
Lottelli AC, Trivedi RH, Jorge EC, Wilson ME
Am J Ophthalmol 2024;264:162-167
The study aimed to externally validate a mathematical model designed to predict postoperative axial length (AL) growth in children over 2 years of age who underwent bilateral cataract surgery with primary intraocular lens (IOL) implantation. This retrospective validation used a case series from a different population with similar characteristics to the original model cohort. It included 55 eyes from 30 children, with follow-up AL measurements taken at various intervals. The model's predicted AL was compared with actual measured values, showing a median measured AL of 22.37 mm and a median estimated AL of 22.16 mm. Statistical analyses demonstrated a strong correlation between estimated and actual AL values (Pearson correlation coefficient of 0.9534 and Lin correlation coefficient of 0.9258), with 95% of measurements falling within a range of 0.71 mm to -1.19 mm from the estimates, though some outliers exceeded these limits. Strengths of the study include its effective validation of the model across different populations and robust statistical analysis, while limitations include the retrospective design, variable follow-up times, small sample size, and regional specificity. Clinically, the validation of the model supports its use

in predicting postoperative AL growth, aiding in the accurate selection of IOL power and potentially improving refractive outcomes and reducing the need for future corrective procedures in pediatric cataract patients.

Outcomes and Complications 5 Years After Surgery for Pediatric Cataract Associated With Persistent Fetal Vasculature
Haider KM, Repka MX, Sutherland DR, et al
Am J Ophthalmol 2024;260:30-36
This study evaluated the 5-year outcomes of cataract surgery in children with cataract associated with persistent fetal vasculature (PFV). Conducted as a clinical cohort study, it analyzed data from 64 children under 13 years old who underwent surgery for unilateral, non-traumatic cataract associated with PFV, comparing visual acuity (VA) outcomes and complications between PFV and non-PFV cataracts. Of the 64 eyes, 48 were aphakic (median age at surgery: 2 months) and 16 were pseudophakic (median age at surgery: 29 months). Only 10% of eyes achieved age-normal VA, with 59% of aphakic PFV eyes achieving VA better than 20/200 compared to 43% of aphakic non-PFV eyes. The median VA for aphakic PFV eyes was 20/100, while for non-PFV aphakic eyes it was 20/200. Pseudophakic PFV eyes had a median VA of 20/400 compared to 20/63 for non-PFV pseudophakic eyes. Glaucoma-related adverse events were the most common complication in aphakic PFV eyes, occurring in 24% of cases, with no significant difference between PFV and non-PFV eyes. VA outcomes were better for anterior PFV compared to posterior PFV, though not statistically significant. The study highlighted a wide range of visual outcomes and ongoing risk for glaucoma-related complications in PFV eyes post-surgery, underscoring the need for careful monitoring and management. Limitations included nonstandardized treatment protocols, variable optotype testing, loss to follow-up, and a small number of pseudophakic eyes.

Systemic Diseases and Syndromes, Infections, Uveitides, and Oculoplastics

Long-term Ocular Outcomes in Congenital Toxoplasmosis Treated Perinatally
Journé A, Garweg J, Ksiazek E, et al.
Pediatrics 2024;153(4):e2023064114
Congenital toxoplasmosis (CT) can be accompanied by serious organ manifestations, particularly retinochoroiditis, and may occur throughout life. Patients with CT diagnosed between 1987 and 2021 were prospectively included and followed for up to 35 years. A total of 646 infected live born children were followed for a median of 12 years (range, 0.5–35); 187 patients (29%) had at least 1 ocular lesion (first at a median age of 5 years; range, 0–26 years) with peaks at 7 and 12 years. Early maternal infection and the presence of nonocular signs at birth were associated with a higher risk of retinochoroiditis, whereas delayed diagnosis of CT (after birth versus before or at birth) was associated with a lower risk (13% decrease for each additional month after birth; P = .01). A period effect for the risk of developing retinochoroiditis in patients born after 2008 was not detected. Despite prenatal screening and prolonged perinatal treatment, retinochoroiditis is not a rare event in French patients with CT and can occur well into adulthood, with peak incidences at 7 and 12 years of age. It rarely causes severe damage but warrants regular follow-up into adulthood. This article reinforces that congenitally infected

children with Toxoplasmosis, can present with lesions throughout their life, even when no lesions are found perinatally.

Sensitivity, Specificity, and Cutoff Identifying Optic Atrophy by Macular Ganglion Cell Layer Volume in Syndromic Craniosynostosis
Chang YH, Staffa SJ, Yavuz Saricay L, et al.
Ophthalmology 2024;131(3):341-348
This retrospective cross-sectional study evaluated patients with syndromic craniosynostosis over 12 years, focusing on the association between macular ganglion cell layer (GCL) volume and optic atrophy. The study aimed to determine if GCL volume, as measured by optical coherence tomography (OCT), is independently affected by obstructive sleep apnea (OSA), Chiari malformation, or a history of elevated intracranial pressure (ICP) and its relation to optic atrophy. Findings revealed that a GCL volume of less than 1.02 mm^3 is a reliable indicator of optic atrophy, with a sensitivity of 83% and specificity of 77%. OSA was independently linked to lower GCL volume. While factors such as type of craniosynostosis, Chiari malformation, and history of elevated ICP were considered risk factors in univariate analysis, they were not significant in multivariate analysis. The study highlights that reduced GCL volume can predict optic atrophy and that OSA further reduces GCL volume, offering a useful method for assessing vision risk in patients with craniosynostosis, especially given their often limited cognitive abilities and challenges in obtaining visual field measurements.

Retinoblastoma, Intraocular Tumors, and Trauma

Consensus Guidelines for Ocular Surveillance of von Hippel-Lindau Disease
Daniels AB, Chang EY, Chew EY, et al
Ophthalmology 2024;131(5):622-633
This paper was written as recommendations for screening and early treatment of retinal hemangioblastomas in patient with VHL as part of the effort by the International VHL Surveillance Guidelines Consortium to develop a comprehensive evidence-based set of guidelines for patients with VHL disease to help promote universal and standardized care. The ophthalmology task force performed a retrospective study with de-identified subject details and a comprehensive literature review within the committee. The papers were reviewed and based on the type and strength of evidence the group made recommendations. 1) individuals with known of suspected VHL should undergo periodic ocular screening. This was recommended as the detection and treatment of small asymptomatic lesions may lead to better visual outcomes. 2) patients at risk for VHL or those with single or multifocal RHs should undergo genetic testing for the VHL gene. This could lead to earlier surveillance and detection of life threatening manifestations of the disease and may lead to increased life expectancy. 3) ocular screening should begin within 12 months of birth and continue throughout life. 4) screening should occur every 6-12 months until 30 and then yearly thereafter. 5) ocular screening should be performed before a planned pregnancy and every 6-12 months during pregnancy. 6)Ultra-widefield fundus photos and IVFA may be useful to monitor RHs and detect small RHs but should be used as adjuncts to detailed dilated fundus exam. 7)Patients should be managed in a setting with subspecialists experienced with VHL or RHs. 8) Extramacular or extrapappilary RHs should be treated promptly especially in places with poor follow-up or in patients with whom poor reporting

of symptoms is concerned. This paper is significant as it sets out a clear set of guidelines for the surveillance and possible management of RHs in VHLdisease. Overall the early detection and treatment of the RHs seems to indicate an improvement in vision preservation and thus the recommendations could provide a framework to better improve outcomes.

Pediatric and Adolescent Traumatic Macular Hole: A Systematic Review
Helmy YAH, ElNahry AG, Zein OE, et al
Am J Ophthalmol 2024;265:165-175
The study is a systematic review aimed at evaluating the optimal management strategies for pediatric traumatic macular holes (TMH), given the lack of prospective randomized trials. It compares three approaches: early pars plana vitrectomy (PPV) within one month of trauma, delayed PPV beyond one month, and observation. The review analyzed data from multiple databases up to July 31, 2023, assessing visual acuity (VA), visual gain, and time to hole closure, while categorizing holes by size (small, medium, large). Findings indicate that for small TMH, final VA and visual gain were similar between PPV and observation groups. For medium TMH, observation led to better visual gain, although final VA was comparable. Large TMH showed similar outcomes between early and delayed PPV. Closure times were similar for small TMH in both approaches, with PPV generally having longer follow-up periods but similar or slightly better outcomes. The review highlights that PPV is effective in closing TMH and improving vision, especially for large holes, while the timing of surgery (early vs. delayed) may be flexible based on clinical judgment. Observation remains a viable option for smaller to medium-sized holes, particularly when immediate surgery is not feasible. The review underscores the need for more rigorous studies to clarify the optimal management and natural history of pediatric TMH.

Neuro-ophthalmology, Nystagmus, and Visual Impairment

Prevalence, time course, and visual impact of peripapillary hyperreflective ovoid mass-like structures (PHOMS) in pediatric patients with optic nerve pathologies
Jeon-Chapman J, Estrela T, Heidary G, Gise R
J AAPOS 2024;28(4):103966
The presence of peripapillary hyperreflective ovoid mass-like structures (PHOMS) are reported to have a higher prevalence in optic nerve pathology, but this has not been well studied in the pediatric population. The prevalence of PHOMS in pediatric patients with optic nerve pathologies compared to normal control subjects, the natural history of PHOMS, and visual function related to PHOMS were evaluated in this study. This is a retrospective study of a cohort of pediatric patients (<18 years of age) with diagnoses of optic nerve head drusen, optic neuritis, papilledema, papillitis, and neuroretinitis who were examined at the Boston Children's Hospital between October 2011 and April 2022. Normal subjects age 4-18 years were included for a control group. OCT images were examined for presence of PHOMS by two graders and the relationship between PHOMS and diagnosis compared to the normative group as well as associations to visual acuity, RNFL thickness, and visual fields were analyzed. PHOMS were identified in 2.7% of healthy eyes and 54.9% of eyes with optic nerve diagnosis. Compared to the control group, prevalence of PHOMS was statistically significant in patients with papilledema, optic neuritis, and optic nerve head drusen. There was no difference between the

groups in RNFL thickness, GCL volume, visual field mean deviation, or visual function. Strengths include large cohort of pediatric patients with a control group and cross-sectional analysis of factors that are clinically relevant. Limitations are due to retrospective nature which leads to variability of evaluation and follow-up as well as selection bias. Tests in young children have known limitations and may result in incomplete testing. PHOMS have an increased prevalence in pediatric patients with papilledema, optic neuritis, and optic nerve head drusen but were not associated with RNFL thickness, GCL volume, or visual function in this study.

Modernizing the evaluation of infantile nystagmus: the role of handheld optical coherence tomography
Joseph S, Naithani R, Alvarez S, et al.
J AAPOS 2024 Jun;28(3):103924
Infantile nystagmus syndrome, an eye movement disorder diagnosed within the first six months of life, can be associated with afferent problems, either in the anterior or posterior segments, or may present as an isolated idiopathic condition. Current clinical guidelines recommend ancillary testing, such as electroretinography (ERG) or magnetic resonance imaging (MRI), based on specific historical and examination findings. The aim of this study was to assess the role of handheld optical coherence tomography (HH-OCT) in the initial diagnostic evaluation of infantile nystagmus. In this cross-sectional case series, the medical records of all children with infantile nystagmus who underwent HH-OCT imaging at Duke Eye Center between August 2016 and July 2021 were retrospectively reviewed. Children with anterior segment disorders, evident retina or optic nerve pathology, bilateral ophthalmoplegia, or Down syndrome were excluded. The study compared the testing recommendations (MRI vs. ERG) made by a pediatric neuro-ophthalmologist based on clinical findings alone against those made using both clinical findings and HH-OCT for each patient. A total of 39 cases were included, with a mean presenting age of 1.3 years. Final diagnoses included retinal or foveal abnormalities (7 cases), optic nerve pathology (13 cases), idiopathic nystagmus (10 cases), and unknown etiology (9 cases). HH-OCT findings identified optic nerve hypoplasia (1 case), optic nerve elevation (3 cases), persistence of the inner retinal layers at the fovea (9 cases), thin ganglion cell layer (8 cases), ellipsoid zone abnormalities (3 cases), and thin choroid (1 case). In 41% of cases (16 children), HH-OCT findings led to changes in initial management, including avoiding MRI in 5 cases and ERG in 10 cases. One of the study's strengths was that all cases were reviewed by a pediatric neuro-ophthalmologist. However, limitations included its retrospective design, small sample size, and the uncertainty regarding the percentage of patients in whom good-quality HH-OCT images were obtained. HH-OCT has the potential to enhance and streamline the evaluation of infantile nystagmus, reducing the number of children who require diagnostically ambiguous and sedation-requiring procedures, thus potentially expediting the time to diagnosis.

Genetics

Characteristics of Eyes With CRB1-Associated EOSRD/LCA: Age-Related Changes
Ayash J, Woods RL, Akula JD, et al
Am J Ophthalmol 2024;263:168-178

Biallelic variants in CRB1 cause inherited retinal disorders, including early onset severe retinal dystrophy/Leber congenital amaurosis (EOSRD/LCA) and retinitis pigmentosa (RP). The purpose of this retrospective cohort study is to evaluate ocular and retinal features of CRB1-associated early onset severe retinal dystrophy/Leber congenital amaurosis (EOSRD/LCA) for age-related changes. Sixteen pediatric patients with biallelic CRB1 EOSRD/LCA who had been followed for up to 18 years were reviewed. Visual acuity dark-adapted visual sensitivity, and area of seeing visual field (all subnormal from the earliest ages recorded) declined with increasing age. Hyperopia was stable through childhood and adolescence. In CRB1 EOSRD/LCA, OCT extrafoveal inner and outer laminar thicknesses exceeded those in controls but varied little with age, and foveal metrics (depth, breadth, thickness at rim) differed significantly from those in controls, but variations in foveal metrics were not associated with declines in acuity. From the youngest ages, retinal and visual function is significantly subnormal and becomes progressively compromised. A goal of future therapies should be intervention at young ages, when there is more function to be rescued.

Genetic Characteristics and Clinical Manifestations of Foveal Hypoplasia in Familial Exudative Vitreoretinopathy
Ju Y, Zhang L, Gao F, et al
Am J Ophthalmol 2024;262:73-85
This retrospective cohort study aimed to ascertain the occurrence of foveal hypoplasia (FH) in individuals diagnosed with familial exudative vitreoretinopathy (FEVR). A total of 102 eyes from 58 patients were suitable for analysis. Forty-nine mutations in LRP5, FZD4, NDP, TSPAN12, KIF11, CTNNB1, and ZNF408 were examined and detected, with 26 of them being novel. Forty-seven eyes (46.1%) revealed FH. The majority (53.2%) were due to the typical grade 1 FH. Patients with mutations in LRP5 and KIF11 were found to exhibit a higher prevalence of FH ($P = .0088$). Group B displayed the lowest visual acuity compared with group A ($P = .048$) and the group without FH ($P < .001$). The retinal arteriolar angle in group B was significantly smaller than in group A ($P = .001$) and those without FH ($P < .001$). This study offers a new diagnostic approach and expands the spectrum of FEVR mutations. LRP5 and KIF11 were found to be more susceptible to causing FH in patients with FEVR. FEVR eyes with FH exhibited both greater visual impairment and reduced retinal arteriolar angles. The assessment of foveal status in patients with FEVR should be valued.

Neuroimaging changes in the pregeniculate visual pathway and chiasmal enlargement in Leber hereditary optic neuropathy
Xu X, Zhou H, Sun M, et al
Br J Ophthalmol 2024;108(9):1313-1317
Leber hereditary optic neuropathy (LHON) is characterised by bilateral severe visual loss in young adults resulting from primary degeneration of retinal ganglion cells accompanied by ascending optic atrophy. A few studies of MRI research have demonstrated atrophy and increased T2-weighted signal in visual pathway with Leber hereditary optic neuropathy (LHON) patients, but the imaging manifestations were non-specific. The purpose of this study was to describe the pattern of MRI changes in the pregeniculate visual pathway in Leber hereditary optic neuropathy (LHON). This retrospective observational study enrolled 60 patients with

LHON between January 2015 and December 2021. The cohort included 48 (80%) males and 53 (88%) had bilateral vision loss. The median age of onset was 17.0 years (range 4.0-58.0). 28 (47%) patients had the m.11778G>A mutation. 34 (57%) patients had T2 hyperintensity (HS) in the pregeniculate visual pathway and 13 (22%) patients with chiasmal enlargement. 20 patients (71%) carrying the m.11778G>A mutation had T2 HS, significantly more than the 14 patients (44%) with T2 HS in the other LHON mutation groups (p=0.039). Furthermore, significantly more patients in the m.11778G>A group (16 patients (57%)) had T2 HS in optic chiasm (OCh)/optic tract (OTr) than the other LHON mutation groups (7 patients (22%), p=0.005). Optic chiasmal enlargement was more common in patients with vision loss duration <3 months compared with those ≥3 months (p=0.028). T2 HS in the pregeniculate visual pathway is a frequent finding in LHON. Signal changes in the OCh/OTr and chiasmal enlargement, in particular within the first 3 months of visual loss, were more commonly seen in patients carrying the m.11778G>A mtDNA mutation, which may be of diagnostic significance. 4

Mitochondrial retinopathies and optic neuropathies: The impact of retinal imaging on modern understanding of pathogenesis, diagnosis, and management
Borrelli E, Bandello F, Boon CJF, et al.
Prog Retin Eye Res 2024 Jul;101:101264
This is an excellent review of clinic, pathology, and image modalities for mitochondrial retinopathies and optic neuropathies. The article provides a detailed overview of the crucial genetic and clinical features essential for correctly interpreting in vivo imaging. The article also discussed the limitations of imaging. Leber hereditary optic neuropathy (LHON), Neuropathy, ataxia, retinitis pigmentosa (NARP) or maternally inherited Leigh syndrome (MILS), Maternally inherited nonsyndromic deafness, with or without association with aminoglycoside use, Myoclonus, epilepsy, ragged-red-fibers syndrome (MERRF), Maternally inherited diabetes and deafness (MIDD), mitochondrial encephalopathy, lactic acidosis, stroke-like syndrome (MELAS), and the spectrum of chronic progressive external ophthalmoplegia (CPEO), Kearns–Sayre syndrome (KSS), and Pearson's syndrome are presented in detail. Highly recommend reading this article.

Genetic Analysis of 252 Index Cases with Inherited Retinal Diseases Using a Panel of 351 Retinal Genes
Abu Elasal M, Mousa S, Salameh M, et al.
Genes (Basel) 2024 Jul 16;15(7):926 This paper analyzes a cohort of 252 index cases with IRDs undergoing genetic testing using the Blueprint Genetics panel for “Retinal Dystrophy” that includes 351 genes. The cause of disease could be identified in 55% of cases. A clear difference was obtained between newly recruited cases (74% solved but also smaller cohort) and cases that were previously analyzed by panels or whole exome sequencing (26% solved). As for the mode of inheritance, 75% of solved cases were autosomal recessive (AR), 10% were X-linked, 8% were autosomal dominant, and 7% were mitochondrial. Interestingly, in 12% of solved cases, structural variants (SVs) were identified as the cause of disease. The most commonly identified genes were ABCA4, EYS and USH2A. Heterozygous AR mutations that were not the cause of disease were found in 36% of cases. In 11 cases the interpretation of the test was revised based on the clinical findings (VUS was reclassified as pathogenic). This study

underscores the importance of clinical findings and familial segregation when interpreting genetic testing results.

Amblyopia

Retinal microvascular changes in unilateral functional amblyopia detected by oct-angiography and follow-up during treatment
Errera C, Romann J, Solecki L, et al
European Journal of Ophthalmology 2024;34(2):399-407
This study was designed to evaluate the macular microvascular changes using optical coherence tomographic angiography (OCT-A) in children with unilateral amblyopia and their reversibility during treatment. Patients with unilateral strabismic or anisometropic amblyopia or amblyopia status post congenital cataract surgery, examined between October 2019 and March 2021, were included. OCT-A parameters such as vessel density and perfusion density in the superficial capillary plexus and area, perimeter and circularity of the foveal avascular zone (FAZ) were analyzed. Analyses between the microvascular parameters and the visual acuity were also performed. A total of 128 eyes of 64 patients were included: 32 amblyopic eyes compared with 32 contralateral eyes and 64 control eyes. Vessel density and perfusion density in the superficial capillary plexus were significantly lower in amblyopic eyes compared to control eyes in 6 × 6 mm ($p < 0.02$) and 3 × 3 mm ($p < 0.01$) scans. Correlation analyses showed a linear decrease in vessel density and perfusion density with decreasing visual acuity. The microvascular changes observed were reversible with the occlusion treatment of amblyopia ($p < 0.001$). Based on these findings, OCT-A appears to be an additional clinical tool for diagnosing and monitoring functional amblyopia. The study findings are limited by the small patient sample size as well lack of robust longitudinal patient data.

Binocular Home Treatment for Amblyopia: Gains Stable for One Year
Wygnanski-Jaffe T, Moshkovitz A, Kushner BJ, Belkin M, Yehezkel O;
CureSight Pivotal Trial Group
Am J Ophthalmol 2024;262:199-205
The study provides a long-term follow-up of an RCT evaluating CureSight, a binocular eye-tracking-based home treatment for amblyopia. This prospective, multicenter, nonrandomized observational follow-up involved 43 children aged 4 to under 9 years, who initially received 16 weeks of CureSight treatment. Follow-ups were conducted at 12 weeks and 1 year post-treatment. Results showed that while visual acuity (VA) in the amblyopic eye and gains in stereoacuity and binocular VA were generally maintained 12 weeks after treatment, there was a partial reduction in VA improvement by 1 year, with 20.4% of patients experiencing amblyopia recurrence. Strengths of the study include its long-term data on CureSight's efficacy and the sustained visual and stereoacuity improvements. However, limitations include its nonrandomized design, lack of control groups, and some missing follow-up data. The study suggests that CureSight is effective for maintaining amblyopia improvements and reducing recurrence, but further research with randomized controlled trials is needed to confirm these findings and evaluate its broader clinical application.

Extended optical treatment versus early patching with an intensive patching regimen in children with amblyopia in Europe (EuPatch): a multicentre, randomised controlled trial
Proudlock FA, Hisaund M, Maconachie G, et al

Lancet 2024;403(10438):1766-1778
An extended period of optical treatment before patching is recommended by the clinical guidelines of several countries. The aim of this study was to compare an intensive patching regimen, with and without extended optical treatment (EOT) first, in a randomized controlled trial. 334 children, from 30 hospitals in Europe, aged 3-8 years old, with newly detected or untreated amblyopia (interocular difference > 0.30 logMAR BCVA) due to anisometropia, amblyopia, or both were randomly assigned to either receive 18 or 3 weeks of optical treatment prior to starting an intensive patching regimen (10 hours/day, 6 days/week) for up to 24 weeks. Primary outcome was successful treatment (< 0.20 logMAR interocular difference in BCVA) after 12 weeks of patching. 317 participants were analyzed for the primary outcome. 14% of the EOT group and 6% of the early patching group were excluded or dropped out. 67% of the early patching group had successful treatment at 12 weeks compared to 54% of the EOT group. This study involved multiple centers across Europe to ensure a diverse participant pool and robust results. Intensive patching is more effective at improving visual acuity quickly, but extended optical treatment can be a viable alternative, particularly for families seeking a less intensive approach with fewer complications such as discomfort and psychosocial impact.

Motion-Defined Form Perception in Deprivation Amblyopia
Giaschi DE, Asare AK, Jost RM, Kelly KR, Birch EE
Invest Ophthalmol Vis Sci 2024;65(4):13
This paper investigates how deprivation amblyopia affects the ability to perceive shapes and forms that are defined by motion rather than static cues in children with unilateral cataract. Coherence thresholds for orientation discrimination of motion-defined form were measured using a staircase procedure in 30 children with deprivation amblyopia and 59 age-matched controls. Visual acuity, stereoacuity, fusion, and interocular suppression were also measured. Fixation stability and fellow-eye global motion thresholds were measured in a subset of children. Motion-defined form coherence thresholds were elevated in 90% of children with deprivation amblyopia when viewing with the amblyopic eye and in 40% when viewing with the fellow eye. The results show that individuals with deprivation amblyopia exhibit deficits in perceiving motion-defined forms. This impairment indicates that the visual system's ability to integrate motion cues into coherent shape perception is a binocular mechanism. Understanding the specific deficits in motion-defined form perception can inform the development of targeted interventions and therapies that address both static and dynamic visual processing challenges in individuals with amblyopia.

Novel Quantitative Contrast Sensitivity Function Enhances the Prediction of Treatment Outcome and Recurrence in Amblyopia
Liu J, Huang C, Cotter SA, et al
Invest Ophthalmol Vis Sci 2024;65(5):31
Amblyopia treatment outcome is often unpredictable with up to 25% recurrence rate. This paper aims to evaluate whether a large-scale quantitative contrast sensitivity function (CSF) data source, coupled with machine learning (ML) algorithms, can predict amblyopia treatment response and recurrence in individuals. Visual acuity and novel CSF assessments were used as the main predictive variables in the models. Information from 58 potential predictors was

extracted to predict treatment response and recurrence. Six ML methods were applied to construct models. Analysis of 643 patients with amblyopia was completed. Combining variables from VA and CSF assessments gave the highest accuracy for treatment response prediction, with an AUC of 0.863 and 0.815 for outcome predictions after 3 and 6 months, respectively. Variables from the VA assessment alone predicted the treatment response, with AUC values of 0.723 and 0.675 after 3 and 6 months, respectively. Variables from the CSF assessment gave rise to an AUC of 0.909 for recurrence prediction compared to 0.539 for VA assessment alone. The interocular differences in CSF features are significant contributors to recurrence risk. One limitation is that the novel CSF method may require additional resources, training, and technology not available in all clinical settings. This could limit its widespread adoption and practicality in various healthcare environments. Incorporating this advanced contrast sensitivity measurement can significantly enhance the management of amblyopia by improving predictions related to both treatment outcomes and the risk of recurrence. This improved prediction helps tailor treatments more effectively and may lead to better visual results.

Peripheral Binocular Imbalance in Anisometropic and Strabismic Amblyopia
Wiecek E, Kosovicheva A, Ahmed Z, et al
Invest Ophthalmol Vis Sci 2024;65(4):36
This study's purpose was to investigate how peripheral vision is affected in individuals with anisometropic and strabismic amblyopia. This prospective cohort study recruited 12 participants with anisometropic amblyopia, 10 with strabismic amblyopia, and 10 typically sighted controls (age range 5–18 years). Binocular imbalance was tested at 0°, 4°, and 8° eccentricities (4 angular locations each) using band-pass filtered Auckland optotypes (5 cycles per optotype) dichoptically presented with differing contrast to each eye. The interocular contrast ratio was adjusted until the participant reported each optotype with equal frequency. Participants with amblyopia had decreased binocular imbalance, at 4° and 8° eccentricities as compared with central vision. Participants with strabismic amblyopia had significantly more binocular imbalance in the periphery as compared with individuals with anisometropic amblyopia or controls. The authors conclude that it may be more important to dichoptically balance binocular information in central vision when utilizing dichoptic binocular therapies, with unaltering peripheral eccentric visual stimuli for individuals with anisometropic amblyopia. Conversely, individuals with strabismic amblyopia may benefit from stimuli that require binocular balancing across the entire visual field. These variations in binocularity across the visual field among different amblyopia subtypes may necessitate tailored approaches for dichoptic treatment.

Reduced Monocular Luminance Promotes Fusion But Not Mixed Perception in Amblyopia
Zhou S, Weng L, Zhou C, Zhou J, Min SH
Invest Ophthalmol Vis Sci 2024;65(4):15
The study investigates the impact of reducing luminance in the fellow eye in amblyopic patients. This approach is used to see how changes in brightness affect visual processing and integration, specifically fusion and mixed perception. Twenty-three normally sighted observers and 12 adults with amblyopia participated in this study. A novel binocular rivalry task was used to measure the phase duration of four perceptual responses (right- and left-tilts, fusion, and mixed perception) before and after a neutral density (ND) filter was applied at various levels to

the dominant eye (DE) of controls and the fellow eye (FE) of patients with amblyopia. Phase durations were analyzed to assess whether the duration of fusion or mixed perception shifted after monocular luminance reduction. Binocular balance shifted in favor of the brighter eye in both normal adults and patients with amblyopia. This study found that reduced luminance in the fellow eye of amblyopic participants promotes better visual fusion and that lowering luminance helps improve the integration of visual information from both eyes. Despite improvements in fusion, the reduction in monocular luminance does not enhance mixed perception. This has implications for developing targeted treatments that address both fusion and mixed perception issues in amblyopic patients.

Fine visuomotor skills in amblyopia: a systematic review and meta-analysis
Rakshit A, Schmid KL, Webber AL
Br J Ophthalmol 2024;108(5):633-645
This was a systematic review of 22 studies involving 835 amblyopes and 561 controls comparing fine visuomotor performance in children or adults with amblyopia and those with normal binocular vision. Results included in the various studies included patient reported outcome measures of self-perception, tests of motor proficiency, and video recorded reaching and grasping. Regardless of the cause of amblyopia, significant reduction in self-perception of physical competence and athletic competence, fine motor skills scores, speed of visually guided reaching and grasping movements, and precision of temporal eye-hand coordination occurred in amblyopes compared to normal controls. One important limitation of this and all systematic reviews is the difference in methodology to assess and report the visuomotor skills and outcome measures among the various studies, which would be important to consider when developing a future prospective study.

Deficits of the "Good" Eye in Amblyopia: Processing Geometric Properties
Zhu M, Liang J, Wang W, Deng H, Huang Y
Invest Ophthalmol Vis Sci Jul 1 2024;65(8):33
There is evidence that the visual function of the fellow eye in individuals with amblyopia shows reduced visual acuity and diminished grating sensitivity compared to eyes without amblyopia. Higher-level cognitive processes have also been shown to be impaired. The authors enrolled 153 participants, categorized into four groups: child amblyopia, child control, adult amblyopia, and adult control. There were five types of stimuli: Euclidean geometry, affine geometry, projective geometry, and topology geometry. The authors used a color discrimination task as a control. Performance on the discrimination tasks was recorded in terms of accuracy and response time (RT). They calculated an inverse efficiency score (IES) by dividing RT by accuracy. The main effects of discrimination type, amblyopia, and age on IES were all found to be significant. Three-way and two-way ANOVAs were used to assess the following interactions, which were found to be significant, with the exception of discrimination type*age. The authors concluded that children with amblyopia showed poorer performance than control children in discriminating three local geometries (Euclidean, affine, and projection) as well as in color discrimination, suggesting that fellow eyes are affected by amblyopia. Adults demonstrated slightly worse, but not statistically significant, performance compared to controls across all discrimination conditions.

Expression of early growth responsive gene-1 in the lateral geniculate body of kittens with amblyopia caused by monocular form deprivation
Wang Y, Fan H, Zou Y, et al
European Journal of Ophthalmology 2024;34(2):408-418
This study aimed to evaluate whether expression of early growth responsive gene-1 (Egr-1) in the lateral geniculate body in kittens with deprivation monocular amblyopia differed from that in fellow/control eyes. A total of 30 healthy kittens were randomly divided into the control (n = 15) and the deprivation groups (n = 15). The kittens were raised in natural light and the right eyes of the deprived kittens were covered with a black opaque covering. Pattern visual evoked potential (PVEP) was measured before and at 1, 3, and 5 weeks after covering. Expression of Egr-1 in the lateral geniculate body in the two groups was compared by performing immunohistochemistry and in situ hybridization. After three weeks of covering, PVEP detection indicated that the P100 wave latency in the deprivation group was significantly higher than that in the control group ($P < 0.05$), whereas the amplitude decreased markedly ($P < 0.05$). The number of the positive cells ($P < 0.05$) and mean optical density ($P < 0.05$) of Egr-1 protein expression in the lateral geniculate body of the deprivation group were found to be substantially lower in comparison to the normal group, as well as the number ($P < 0.05$) and mean optical density of Egr-1 mRNA-positive cells ($P < 0.05$). However, with increase in age, positive expression of Egr-1 in the control group showed an upward trend ($P < 0.05$), but this trend was not noted in the deprivation group ($P > 0.05$). The authors found that Egr-1 expression in kittens plays a significant role in visual development. During critical periods of visual development in kittens, deprivation of visual input in one eye can cause a significant decline in Egr-1 expression, delay neuronal development, disrupt synaptic plasticity, and thereby contribute to the pathogenesis of amblyopia.

Visual Tracking in Amblyopia: A Continuous Psychophysical Approach
Li C, Yang Y, Zhu J, et al
Invest Ophthalmol Vis Sci 2024;65(5):7
This study explores how amblyopia affects the ability to track moving visual stimuli, or the observed visuomotor deficit in amblyopia. 24 adult and children participants with amblyopia and 22 without were instructed to continuously track a randomly moving Gaussian target on a computer screen using a mouse. Six different target sizes were utilized. In subsequent tests the participants were asked to track a target with the contrast adjusted to the individual's threshold. At the smallest target size, the peak in the amblyopic group was significantly lower than that in the normal group ($P = 0.024$). Amblyopic individuals show reduced accuracy and slower responses when tracking moving objects. This study highlights an important visuomotor difference in amblyopic patients, however, does not fully replicate real-world conditions where visual tracking occurs in more complex and variable environments. Understanding the impact of amblyopia on dynamic visual tasks like tracking can inform treatment approaches. The findings suggest that therapies targeting tracking abilities might be beneficial in addition to traditional treatments focusing on static visual acuity.

Comparison of Cambridge vision stimulator (CAM) therapy with passive occlusion therapy in the management of unilateral amblyopia; a randomized clinical trial

Khorrami-Nejad M, Akbari MR, Abdulhussein R, Azizi E
Strabismus 2024;32(3):123-138
The main purpose of this study was to compare the effect of CAM therapy with passive occlusion therapy in the management of unilateral amblyopia. In this randomized clinical trial study, 110 cooperative amblyopic children, who had not been managed previously, were randomly divided into two groups of CAM therapy (n = 55) and passive occlusion therapy (n = 55). In the CAM procedure, five discs with different spatial frequencies (SF) (2, 6, 15, 20, 30 cycles/degree) were presented to the patient (30 minutes a day, twice a week). Plates with SF equal to the two lines better than the measured corrected distance visual acuity (CDVA) were chosen. During the training, the non-amblyopic eye was occluded. The standard occlusion therapy protocols were performed in the occlusion therapy group. The CDVA for all patients was measured at baseline and then at one, two, and three months after the treatment. The mean age of patients in CAM and occlusion therapy groups was 7.0 ± 2.1 and 6.9 ± 1.9 years, respectively ($p = .721$). There was no significant difference in the mean CDVA between CAM and occlusion therapy groups after one (0.30 ± 0.16 vs. 0.25 ± 0.14, $p = .079$), two (0.15 ± 0.10 vs. 0.15 ± 0.11, $p = .732$) and three months (0.05 ± 0.08 and 0.05 ± 0.06, $p = .919$) from baseline. However, the mean amount of CDVA increased significantly in each follow-up in both groups (all $p < .001$). Regarding the amblyopia type and severity, the mean improvement of CDVA from baseline in the anisometropic patients and in moderate amblyopia was significantly higher in the CAM group than the occlusion group after two and three months ($p < .05$). CAM and conventional occlusion therapies significantly improved CDVA in children with amblyopia, and the difference was not significant; therefore, they could be used as alternatives. CAM therapy requires cost and time for the amblyopic patient and parents. Thus, it can be considered as a second treatment option in amblyopic patients, especially anisometropic type and moderate amblyopia, with poor compliance to patching. The main limitation was not having a Sham control group to investigate the real cause of VA improvement following CAM therapy. The lack of a comparison group, including patients treated by other strategies, such as a sham group or active vision therapy or penalization, made it impossible to compare the effectiveness of CAM therapy with other amblyopia treatment modalities.

Landolt C-Tests With "Fixed" Arcmin Separations Detect Amblyopia But Underestimate Crowding in Moderate-to-Severe Amblyopic Children and Adults
Waugh SJ, Fronius M Invest Ophthalmol Vis Sci 2024;65(10):33
Crowding is a well-known phenomenon in strabismus amblyopia where excessive crowding occurs in the central vision. This study explored the use of Landolt C-test, a method of assessing acuity and crowding magnitude. The test consists of “C”s in various directions and with variable spacing. A total of 69 patients participated and were separated into three groups – normal controls, anisometropic amblyopia, and strabismic amblyopia. Crowding magnitudes were greater in strabismic than in anisometropic amblyopia and control/fellow eyes. They were higher in pediatric control/fellow eyes than in juvenile/adult eyes. In high severity strabismic amblyopia, crowding magnitudes progressively and significantly reduced with worsening acuity. C-tests were effective in detecting amblyopia but underestimates crowding in children and adults with high severity strabismus amblyopia. While this method was effective for mild

amblyopia, measuring isolated acuity and sizing limit separately may be a more accurate strategy.

Anterior Segment

Epidemiology of Pediatric Ocular Surface Inflammatory Diseases in the United States Using the Optum Labs Data Warehouse
Fung SSM, Boghosian T, Perez C, et al
Ophthalmology 2024;131(5):568-576
This was a retrospective study using data from the Optum Labs Data Warehouse (OLDW) to detail the epidemiologic features among children with blepharokeratoconjunctivitis(BKC), herpes simplex keratoconjunctivitis (HSK) and vernal keratoconjunctivitis (VKC). These pediatric ocular surface inflammatory diseases (POSID) have the ability to affect quality of life due to amblyopia and permanent visual issues. The primary outcome of the study was the overall prevalence of POSID between 2018-2019. Secondary outcomes include prevalence of each of the three subcategories studies, changes in the prevalence of POSID from 2008-09 to 2018-119 and changes in the subcategories as well. The overall prevalence of POSID was 3.32 per 10,000 children with VKC being most prevalent followed by HSK and BKC. The study found that POSID was the most prevalent in children between the ages of 5 and 9, males, Asian ethnicity and most affected regions were the Northeast and West. While there was no significant change in the overall prevalence of POSID from 2008-2019 there was a significant increase in VKC among Asian children. The authors posit that this may be due to an increase in ocular allergies in asian countries as well as changing environmental and lifestyle factors. However, prevalence of VKC decreased in older children and adolescents which may be due to possibly better disease recognition and treatment. The authors also discuss the other subgroups and the data noted about these cohorts as well. The study is limited due to the use of a claims database and the retrospective nature that may have errors in coding and diagnosis. The database reflects commercial health care and may not reflect uninsured or government insured patients. The authors conclude that the 3 types of POSID have distinct distributions based on race, sex, ethnicity, and geography. The study can help providers differentiate children with POSID and may facilitate proper management in a timely fashion.

Diagnosis and Treatment of Vernal Keratoconjunctivitis: A Qualitative Study of Caregiver, Patient, and Clinician Experience in the United States
Rose H, Bielory L
J Pediatr Ophthalmol Strabismus 2024;61(4):252-256
VKC can be a visually debilitating diagnosis in children, which can take a toll on all involved parties. In this study, the authors sought to better quantify that toll by performing structured interviews with caregivers of children with VKC (n=7) and clinicians who treat VKC (n=16). Caregivers answered 49 questions over a 60 minute interview, while providers answered 30 questions. Overall, providers were concerned that caregivers and primary care providers often underestimate the severity of VKC and frequently seek care too late. By the time the patient finds the care of a specialist, they have often been misdiagnosed, seen a number of doctors, and progressed to severe disease. Providers estimate that up to 90% of patients/caregivers do not continue appropriate dosing once initial symptoms are managed, which causes concern for long-term control and outcomes. Overall, this instructive paper details the urgent need for more

education, targeted to both primary care providers and caregivers, about the potential severity and importance of treatment adherence in VKC.

Surgical approach to and morphology of visually significant persistent pupillary membranes
Chen W, Chen K, Chen H, et al
J Cataract Refract Surg 2024;50(5):511-517
This study reported specific surgical approaches to visually significant persistent pupillary membranes (PPMs). It additionally categorized these PPMs into three types based on the thickness of the iris strands as well as their relationship and adherence to the anterior capsule of the lens. 31 eyes from 19 patients ages 3 to 14 with visually significant PPMs requiring surgery were included in the study. The study elaborated on different surgical approaches to the different types of PPMs. Visual acuity did indeed improve, including the patients who would be considered outside of the amblyopic age range. The visual acuity improved from 0.34 ± 0.18 to 0.17 ± 0.09 logMAR. No complications were observed during a 9.5 month follow-up.This study's strengths include a novel classification of PPMs with an individualized surgical approach outlined to each type. It has a small N but given this is a relatively rare condition it is an impressive cohort of patients with this condition. The follow-up period is reasonable but at 9.5 months could be missing late complications. For physicians encountering a patient with a visually significant PPM, this study would be a cornerstone guide on management.

Birth prevalence and characteristics of congenital corneal opacities
Borik K, Mohney BG, Hodge D, et al
European Journal of Ophthalmology 2024;34(3):734-738
The authors designed this study to report the birth prevalence and natural history of congenital corneal opacities among a population-based cohort of children. The medical records of patients <5 years diagnosed with a congenital onset corneal opacity while residing in Olmsted County, Minnesota, from January 1, 1977, through December 31, 2016, were retrospectively reviewed. Fourteen patients were diagnosed with a congenital corneal opacity during the 40-year study period for a birth prevalence of 1 in 5188 live births. The mean age at diagnosis was 7.5 months (range 0–48 months) and 9 (64.3%) were males. Four patients had congenital glaucoma, 4 had limbal dermoids, 2 had sclerocornea, and 1 patient each had Descemet's tear from birth trauma, herpes simplex virus type 1 keratitis, corneal leukoma, and an undiagnosed scar. Six (42.8%) patients required treatment for their underlying corneal opacity including the four patients with congenital glaucoma. The other 8 (57.1%) patients had a clear central axis. Four (28.6%) of 14 patients required amblyopia therapy, and 4 (28.6%) developed strabismus. Four (28.6%) patients had associated systemic conditions. During a mean follow up of 5.4 years (range 1.3–27.0 years), the median best corrected visual acuity (BCVA) was logmar 0.16 (20/25) (range 20/20-hand motion) with one patient with unilateral BCVA less than 20/60 and one patient with bilateral BCVA less than 20/60. In this 40-year cohort, congenital corneal opacities were relatively rare and the result of a variety of disorders. Although amblyopia and strabismus were also frequently associated, most patients had good visual outcomes. Limitations of this study include its retrospective design and population bias (conducted in a city that is 95% Caucasian).

Dramatic Reduction in Corneal Transplants for Keratoconus 15 Years After the Introduction of Corneal Collagen Crosslinking
Hagem AM, Thorsrud A, Sæthre M, et al
Cornea 2024;43(4):437-442
A retrospective look at the number of corneal transplants for Keratoconus (KC) being performed in Norway 15 years after the introduction of Corneal Collagen Crosslinking (CXL). This same question has been investigated in Norway at the 7-8 year mark, showing a 50% reduction in corneal transplants. The authors propose that 15 years is a better time frame to have allowed CXL to be more diffusely established in ophthalmology and optometry clinics throughout the country. Out of 352 keratoplasties performed in Norway in 2021-2022, 11 of them were for patients with KC (3.1%). This number was compared to 55 keratoplasties done during 2005-2006, an 80% reduction. Amazingly, the cornea surgeons in this particular hospital in Norway who did the corneal transplants in 2005-2006 are the same two surgeons who did the corneal transplants in 2021-2022 – so that variable is controlled. Advancements in scleral contact lenses also may have contributed to the decrease in corneal transplants for KC. But overall, CXL has unquestionably reduced the need for corneal transplants in the Keratoconus patient population, which this study nicely demonstrates.

Keratoconus Frequency and Associated Risk Factors Among Patients Younger Than 18 Years With Significant Refractive Errors
Sarria Calderón NA, Martínez Córdoba CJ, Pinedo Agudelo JA, et al
Cornea 2024;43(5):585-590
This is a retrospective observational cross-sectional study examining the frequency of keratoconus at a central referral center in Colombia. The patient population included children under the age of 18 who were referred for a high refractive error, specifically those with high myopia (> -5.00 Diopters), high or oblique astigmatism (> 2.00 Diopters). These patients all received pentacam scans which were analyzed, along with additional risk factors, for the prevalence and severity of keratoconus. The study identified 426 patients who met the inclusion/exclusion criteria. Of this group they found the prevalence rate of keratoconus to be 9.4%. The average age of those with keratoconus was 14.9 years old. This study additionally found that 85% of those patients with keratoconus had atopic disease (atopic dermatitis, rhinitis, allergic conjunctivitis or asthma) – which was the leading risk factor. Patients who had a family history of keratoconus carried a relative risk of only 7.5%. This study illuminates the higher-than-suspected risk of keratoconus in specific pediatric populations that have both high refractive errors and atopic disease.

Descemet Membrane Endothelial Keratoplasty in Corneal Endothelial Decompensation After a Forceps-Induced Corneal Birth Injury: Case Series and Technique
Igarashi A, Hayashi T, Shimizu T, et al
Cornea 2024;43(8):989-993
This retrospective study looked at a case series of 4 patients who sustained a forceps injury at birth and subsequent corneal decompensation. The age at which the surgery was performed ranged from 57 to 70. The mean best-corrected visual acuity was 0.52 preoperatively and 0.15 postoperatively. Central corneal thickness decreased from 640 preoperatively to 576

post-operatively. The study is the first of its kind to demonstrate the successful use of DMEK in patients who sustained a forceps injury at birth.

Cataract

Ten-year outcomes of congenital cataract surgery performed within the first six months of life
Oshika T, Nishina S, Unoki N, et al
J Cataract Refract Surg 2024;50(7):707-712
This study evaluates the 10-year post-operative outcomes of congenital cataracts that received surgical treatment within the first six months of life. It is a retrospective study examining outcome differences between aphakic versus pseudophakic, unilateral versus bilateral cases, and surgeries performed within the critical period of visual development (before 10 weeks of age for bilateral cases and 6 weeks of age for unilateral cases) versus those performed outside of this window. This study included 216 eyes of 121 patients, with 190 bilateral and 26 unilateral cases. Of these eyes, an intraocular lens (IOL) was inserted in 30, while 186 were left aphakic. Surgery performed during the critical period of visual development resulted in significantly better final visual acuity. However, these patients also showed a higher risk of visual axis opacification compared to those whose surgery was done after the critical period. Pseudophakic patients had better final visual acuities but also higher rates of visual axis opacification. The most dramatic finding was the comparative rates of glaucoma: 38 eyes in the aphakic group developed glaucoma (20%), compared with none (0%) in the pseudophakic group. The study boasts an impressive 10-year follow-up and is sufficiently powered to yield several statistically significant comparisons. Its limitations include the retrospective nature and the lack of analysis on amblyopia therapy. Nonetheless, it reinforces the importance of intervening within the critical period of visual development and provides further evidence supporting the efficacy of employing an IOL in this young age range.

Early Diagnosis of Syndromic Congenital Cataracts in a Large Cohort of Congenital Cataracts
Wang Q, Wang D, Qin T, et al
Am J Ophthalmol 2024;263:206-213
The study aimed to investigate factors affecting the genetic diagnostic yield in syndromic congenital cataracts and to analyze the correlation between phenotype and genotype in affected patients. This prospective cohort study involved 115 patients who underwent clinical examinations and whole-exome sequencing (WES) between 2021 and 2022. The research included detailed clinical data, including facial and anterior eye segment photographs, and family histories. The genetic diagnostic yield was 72.2%, with 34.8% of patients diagnosed with various syndromes through genetic testing. Phenotype-genotype correlations were found, linking specific cataract types to particular genetic variants. The study achieved a high diagnostic yield and identified 48 novel variants, supporting the use of genetic testing for early diagnosis of syndromic conditions associated with congenital cataracts. However, the study did not include patients with unilateral cataracts, which may limit generalizability, and some genetic variants had uncertain significance. Overall, the findings emphasize the value of genetic testing in congenital cataracts for detecting underlying syndromic conditions early, improving patient outcomes through accurate diagnosis and targeted treatments.

Functional Vision of Pseudophakic Children Attending a Pediatric Ophthalmology Clinic in Southwest Nigeria

Aremu OO, Ugalahi MO, Olusanya BA, Oluleye TS
J Pediatr Ophthalmol Strabismus 2024;61(2):138-146
Pediatric cataracts are an important cause of (potentially avoidable) visual impairment in the pediatric population. As we examine outcomes in cases of pediatric cataract, we often focus on metrics such as visual acuity. However, relying solely on these objective outcome measures may not capture the subjective visual experiences of these patients well, a metric that is, perhaps, the most important measure of outcome. In this paper, the authors recruited 196 pseudophakic patients, ages 2 to 16, at a single institution in Nigeria and administered the Pediatric Eye Questionnaire (PedEyeQ) to them. The mean age of participants was 9.6 years old. The most common type of cataract was developmental (44%), followed by traumatic (32%) and congenital (24%). The median functional vision score on the PedEyeQ was 90.0. Several factors were related to lower scores: presence of associated comorbidities such as nystagmus and amblyopia, presence of congenital cataract, more than one surgical intervention, bilateral disease, low average family income, and lower BCVA. This study reminds us of the importance of assessing the patient's subjective experience of their pathology, and suggests that the routine evaluation of functional vision in pediatric cataract patients – whether formal (like the PedEyeQ) or informal – should be considered in such cases.

Intraocular lens calculation using the ESCRS online calculator in pediatric eyes undergoing lens extraction
Lwowski C, Wenner Y, Kaiser KP, et al
J Cataract Refract Surg 2024;50(7):676-681
This is a retrospective case reviewing the accuracy of several different intraocular lens (IOL) formulas in the pediatric population. The formulas selected were those utilized through the ESCRS online calculator and included BUII, EVO, Hoffer-QST, Kane, and Pearl DGS, with SRK/T added separately. All patients had pre-operative biometry measurements from an IOL Master, and their post-operative refractive outcomes were determined by retinoscopy 3-12 weeks after surgery. The study included 60 eyes from 47 patients, with a mean age of 6.5 ± 3.2 years (maximum age of 13). The mean and median prediction errors were calculated and compared. All formulas exhibited a tendency toward a myopic shift in their predictions. The SRK/T formula performed the best with the lowest mean prediction error, followed closely by BUII and Pearl DGS. The Kane formula had the highest prediction error. Notably, about two-thirds of the IOLs were positioned with posterior optic capture, which, when analyzed separately, reduced the prediction error. IOL calculations in the pediatric population are challenging and notoriously unpredictable. This study demonstrated that all seven formulas are predictive within 1.5 diopters for approximately 75% of patients, with all formulas having outliers. The study was sufficiently powered to compare these formulas but not enough to make definitive changes to A constants or to narrow the field to just one formula, although SRK/T did perform slightly better than the rest.

Patching in Children With Unilateral Congenital Cataract and Child Functioning and Parenting Stress
Drews-Botsch C, Cotsonis G, Celano M, et al
JAMA Ophthalmol 2024;142(6):503-510

Visually significant unilateral congenital cataracts (UCC) are treated with cataract extraction, refractive correction, and part-time occlusion therapy. Early patching after surgery has been associated with improved visual outcomes; however, many children born with a UCC never develop good vision in the affected eye. In the Infant Aphakia Treatment Study (IATS) 44% had VA of 20/200 or worse. The purpose of this study was to assess whether psychosocial and/or developmental outcomes were poorer in children treated for UCC with poor VA (20/200 or worse) who had extensive patching throughout the first 5 years of life compared to children with less patching. Data from the IATS study was used for this analysis. Amount of patching was categorized as minimal (mean minutes per day <15), moderate (15 to <120 min per day), or extensive (120 or more minutes per day). Stress associated with the parenting role, child behavior problems, gross and fine motor development, and self-perception were assessed. Among 47 children with patching data available and VA 20/200 or worse (42.5% female), 12 had minimal patching (10 of which were not patched at all), 11 had a moderate amount of patching, and 24 had extensive patching. Girls were less likely than boys to have been patching at least 120 min per day (P=0.03). The reported amount of patching time between ages 42 and 54 months was not associated with parenting stress, child behavior problems, or a child's self-perception at age 10.5 years. Motor skills did not differ between those patching at least 120 min per day and those patching <15 min per day. This study is limited by its small sample size and self-reporting of patching time. The results of this study suggest that patching children with UCC throughout the preschool years is not negatively associated with health-related quality of life or motor skills.

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Cataract Surgery

Predictors of early secondary IOL implantation after pediatric cataract surgery
Hayes WG, Wilson ME, Trivedi RH
J AAPOS 2024;28(4):103965
Congenital cataracts are removed early to prevent deprivation amblyopia, nystagmus, and strabismus, but refractive correction with contact lenses or aphakic spectacles is crucial to maximize visual potential. Both medical and nonmedical challenges can limit compliance with these corrections, often leading to early secondary IOL implantation. This study aimed to identify predictors of success and failure with aphakic glasses or contact lenses by examining rates of secondary IOL implantation in children under 4 years old. A retrospective chart review was conducted for children who had secondary IOL implantation due to aphakia from congenital cataracts between 2000 and 2022. Patients were grouped based on implantation age (under or over 4 years), and data on demographics, unilateral vs. bilateral cataract, operative notes, reasons for early implantation, and insurance type were collected and analyzed. Among 175 patients, 32 (18.3%) underwent secondary IOL implantation before age 4. Unilateral aphakia was significantly associated with an increased rate of early IOL implantation, and contact lens failure was the most common reason. Insurance type was not linked to early implantation rates. This study provides valuable data to help clinicians counsel families and assess risk factors for early IOL implantation. Limitations include the retrospective design and single-site bias, and the study did not assess visual acuity outcomes between groups. Unilateral cataracts were associated with a higher rate of secondary IOL implantation in children under 4, primarily due to contact lens failure.

Long-term results of anterior chamber iris claw intraocular lens implantation in children with ectopia lentis in Marfan syndrome
van Zeeburg EJT, Sminia ML, Schalij-Delfos NE
J AAPOS 2024 Jun;28(3):103922
This study reports on the long-term clinical and endothelial cell count (ECC) outcomes of lensectomy with primary anterior chamber iris claw lens implantation in patients ≤18 years old with ectopia lentis due to Marfan syndrome. Conducted as a retrospective review at a single institution from September 2007 to August 2020, the study analyzed data including sex, age at surgery, indication for surgery, lens position, ECC, complications, and visual acuity. A total of 42 eyes from 23 patients were included, with a median age at implantation of 6.1 years and a median follow-up of 6.2 years. Mean best-corrected visual acuity improved from 0.71 ± 0.38 logMAR before surgery to 0.02 ± 0.25 logMAR at final follow-up. ECC measurements, collected from 33 eyes, showed a median follow-up of 6.2 years and a mean annual decline of 0.71% ± 2.24, with a total cell loss of 150 ± 394 cells/mm² (4.81%). Pre- and postoperative ECC data for 17 eyes indicated a mean cell loss of 269 ± 268 cells (7.94%). Complications included iris bombé in 3 eyes and lens dislocation in 3 eyes. The study's limitations include its retrospective nature, small sample size, and single-surgeon context, potentially affecting generalizability. The findings suggest that anterior chamber iris claw IOL implantation after lensectomy in this population yields excellent visual outcomes and normal ECC loss compared to normative data. Recommendations include performing at least a 2 mm peripheral iridectomy to prevent

complications and advising patients and families on safety to avoid traumatic dislocation of IOLs.

Iris atrophy following intracameral dexamethasone injection: a report of two pediatric cases
Nguyen BM, Do CL, Boydstun IP, et al
J AAPOS 2024 Jun;28(3):103901
Dexycu (dexamethasone intraocular suspension 9%) received FDA approval on February 9, 2018, as a single-dose, sustained-release intracameral steroid aimed at simplifying postoperative anti-inflammatory treatment compared to standard topical regimens. Two case reports detail instances of iris atrophy occurring approximately one month after the use of Dexycu following unilateral goniotomy and unilateral juvenile cataract extraction. In both cases, a 2 mm aliquot of Dexycu was administered intracamerally at the end of the surgery. About one month post-operatively, iris atrophy was observed where the dexamethasone had settled, with findings including iris stromal thinning in one case and mild iris peaking towards the atrophic iris in the other. The study highlights the need for clinicians to be aware of the potential risk of iris atrophy associated with intracameral dexamethasone 9% injections.

Outcomes and Complications 5 Years After Surgery for Pediatric Cataract Associated With Persistent Fetal Vasculature
Haider KM, Repka MX, Sutherland DR, et al
Am J Ophthalmol 2024;260:30-36
This study evaluated the 5-year outcomes of cataract surgery in children with cataract associated with persistent fetal vasculature (PFV). Conducted as a clinical cohort study, it analyzed data from 64 children under 13 years old who underwent surgery for unilateral, non-traumatic cataract associated with PFV, comparing visual acuity (VA) outcomes and complications between PFV and non-PFV cataracts. Of the 64 eyes, 48 were aphakic (median age at surgery: 2 months) and 16 were pseudophakic (median age at surgery: 29 months). Only 10% of eyes achieved age-normal VA, with 59% of aphakic PFV eyes achieving VA better than 20/200 compared to 43% of aphakic non-PFV eyes. The median VA for aphakic PFV eyes was 20/100, while for non-PFV aphakic eyes it was 20/200. Pseudophakic PFV eyes had a median VA of 20/400 compared to 20/63 for non-PFV pseudophakic eyes. Glaucoma-related adverse events were the most common complication in aphakic PFV eyes, occurring in 24% of cases, with no significant difference between PFV and non-PFV eyes. VA outcomes were better for anterior PFV compared to posterior PFV, though not statistically significant. The study highlighted a wide range of visual outcomes and ongoing risk for glaucoma-related complications in PFV eyes post-surgery, underscoring the need for careful monitoring and management. Limitations included nonstandardized treatment protocols, variable optotype testing, loss to follow-up, and a small number of pseudophakic eyes.

External Validation of a Model to Predict Postoperative Globe Axial Length in Children After Bilateral Cataract Surgery
Lottelli AC, Trivedi RH, Jorge EC, et al
Am J Ophthalmol 2024;264:162-167

The study aimed to externally validate a mathematical model designed to predict postoperative axial length (AL) growth in children over 2 years of age who underwent bilateral cataract surgery with primary intraocular lens (IOL) implantation. This retrospective validation used a case series from a different population with similar characteristics to the original model cohort. It included 55 eyes from 30 children, with follow-up AL measurements taken at various intervals. The model's predicted AL was compared with actual measured values, showing a median measured AL of 22.37 mm and a median estimated AL of 22.16 mm. Statistical analyses demonstrated a strong correlation between estimated and actual AL values (Pearson correlation coefficient of 0.9534 and Lin correlation coefficient of 0.9258), with 95% of measurements falling within a range of 0.71 mm to -1.19 mm from the estimates, though some outliers exceeded these limits. Strengths of the study include its effective validation of the model across different populations and robust statistical analysis, while limitations include the retrospective design, variable follow-up times, small sample size, and regional specificity. Clinically, the validation of the model supports its use in predicting postoperative AL growth, aiding in the accurate selection of IOL power and potentially improving refractive outcomes and reducing the need for future corrective procedures in pediatric cataract patients.

Congenital Cataracts With Thin Lenses (Leptophakia) in Children: Morphology and Surgical Outcomes
Zhang MG, Gallo RA, Chang TC
Am J Ophthalmol 2024;265:1-5
The study aimed to evaluate the morphology and postoperative outcomes of pediatric cataracts associated with thin lenses, a condition known as leptophakia, to determine if these eyes experience higher complication rates. Conducted as a retrospective comparative clinical cohort study, it reviewed pediatric cataract surgeries performed between 2018 and 2023. Leptophakic eyes, defined as having lenses thinner than 2 standard deviations below age-specific norms, were compared with matched controls on various parameters including lens thickness, anterior chamber depth, axial length, and postoperative outcomes. The results revealed that leptophakic eyes had significantly thinner lenses compared to controls, but no significant differences were found in anterior chamber depth or axial length. Visual acuity improved postoperatively in both groups, with a notable improvement in leptophakic eyes within 2.5 months. However, 38% of leptophakic eyes experienced posterior capsular ruptures during surgery, compared to none in the control group. No significant differences in intraocular pressure changes were observed. The study's strengths include its detailed matched cohort design and significant sample size for the rare condition of leptophakia, while limitations include its retrospective nature, modest sample size, and short-term follow-up. The findings suggest that while cataract surgery in leptophakic eyes generally improves visual acuity, increased caution is needed to address the higher risk of posterior capsular ruptures, with further research recommended to assess long-term outcomes and refine surgical techniques.

Incidence Rate of Secondary Glaucoma Following Congenital Cataract Surgery: An In-Depth Systematic Review and Meta-Analysis
Li L, Wang X, Liu C, et al
Am J Ophthalmol 2024;265:176-188

This systematic review and meta-analysis aimed to evaluate the incidence of secondary glaucoma following congenital cataract surgery. The study reviewed 36 articles involving 3151 patients and 4717 eyes, identifying an overall incidence rate of 6.6% (95% CI: 3.9% to 9.9%). Incidence rates varied by surgical approach: 13.5% in the aphakia group, 3.3% with primary intraocular lens (IOL) implantation, and 3.5% with secondary IOL implantation. Additionally, secondary glaucoma was more common in Asian children (6.9%) compared to European children (0.9%). The study also found a correlation between the age at surgery and the risk of developing secondary glaucoma. Strengths of the study include its comprehensive inclusion of studies, large sample size, and detailed subgroup analyses. However, limitations include variability in definitions of glaucoma across studies, limited data on onset times, regional imbalances, and potential selection bias due to language constraints. The findings highlight the need for careful consideration of factors such as surgical timing and IOL choice to manage and mitigate secondary glaucoma risk, emphasizing the importance of further research to refine surgical strategies and follow-up protocols.

Cataract surgery outcomes in children and adolescents with type 1 diabetes mellitus
Agarkar S, Chandrasekaran A, Panicker GJ, Raman R
J AAPOS 2024 Jun;28(3):103926
The incidence of cataract in children and adolescents with type 1 diabetes mellitus is low. The purpose of this study was to report the visual outcomes of cataract surgery in children and adolescents with type 1 diabetes mellitus. The medical records of all pediatric patients (<18 years of age) with a diagnosis of type 1 diabetes mellitus who had undergone surgery for cataract between January 2000 and December 2019 at a tertiary care center were reviewed retrospectively. The study included 27 eyes of 15 patients. The median duration of type 1 diabetes before cataract onset was 3 (IQR, 1-4.5) years, the median age at cataract surgery was 13 (IQR, 9.5-16) years, and the median follow-up was 3.8 (IQR, 1.25-7.2) years. Visual acuity improved from a median preoperative value of 0.8 (IQR, 0.55-1.3) logMAR to 0.15 (IQR, 0-0.45) logMAR at final follow-up. However, 30% of children had poor visual outcomes, which were associated with optic atrophy, retinal dystrophy, glaucomatous optic neuropathy, or diabetic retinopathy. The most common complications requiring additional intervention included posterior capsular visual axis opacification in 40.7% and diabetic retinopathy in 14.8%, requiring laser capsulotomy and panretinal photocoagulation, respectively. Limitations of the study include its retrospective design and small sample size. Cataract surgery in children and adolescents with type 1 diabetes leads to improvement in visual acuity. Posterior capsular opacification commonly occurs at similar rates whether or not primary posterior capsulorhexis is performed.

Genetics

Progression, reliability, predicting parameters and sample size calculations for quantitative fundus autofluorescence measures in ABCA4-related retinopathy
Müller PL, Treis T, Tufail A, Holz FG
Br J Ophthalmol 2024;108(5):760-769
Biallelic mutations in ABCA4 are known to cause the most common form for juvenile macular degeneration namely ‘recessive Stargardt disease’ (STGD1, also called ‘ABCA4-related retinopathy’). This is the first study to analyse longitudinal data of qAF imaging in patients with ABCA4-related retinopathy. In this longitudinal monocentre study, 64 patients with ABCA4-related retinopathy (age (mean±SD), 34.84±16.36 years) underwent serial retinal imaging, including optical coherence tomography (OCT) and qAF (488 nm excitation) imaging using a modified confocal scanning laser ophthalmoscope with a mean (±SD) review period of 20.32±10.90 months. A group of 110 healthy subjects served as controls. Retest variability, changes of qAF measures over time and its association with genotype and phenotype were analysed. Furthermore, individual prognostic feature importance was assessed, and sample size calculations for future interventional trials were performed. Compared with controls, qAF levels of patients were significantly elevated. The test-retest reliability revealed a 95% coefficient of repeatability of 20.37. During the observation time, young patients, patients with a mild phenotype (morphological and functional) and patients with mild mutations showed an absolute and relative increase in qAF values, while patients with advanced disease manifestation (morphological and functional), and homozygous mutations at adulthood revealed a decrease in qAF. Considering these parameters, required sample size and study duration could significantly be reduced. Under standardised settings with elaborated conditions towards operators and analysis to counterbalance variability, qAF imaging might be reliable, suitable for quantifying disease progression and constitutes a potential clinical surrogate marker in ABCA4-related retinopathy. Trial design based on patients' baseline characteristics and genotype has the potential to provide benefits regarding required cohort size and absolute number of visits.

Genetic Analysis of 252 Index Cases with Inherited Retinal Diseases Using a Panel of 351 Retinal Genes
Abu Elasal M, Mousa S, Salameh M, et al.
Genes (Basel) 2024 Jul 16;15(7):926
This paper analyzes a cohort of 252 index cases with IRDs undergoing genetic testing using the Blueprint Genetics panel for “Retinal Dystrophy” that includes 351 genes. The cause of disease could be identified in 55% of cases. A clear difference was obtained between newly recruited cases (74% solved but also smaller cohort) and cases that were previously analyzed by panels or whole exome sequencing (26% solved). As for the mode of inheritance, 75% of solved cases were autosomal recessive (AR), 10% were X-linked, 8% were autosomal dominant, and 7% were mitochondrial. Interestingly, in 12% of solved cases, structural variants (SVs) were identified as the cause of disease. The most commonly identified genes were ABCA4, EYS and USH2A. Heterozygous AR mutations that were not the cause of disease were found in 36% of cases. In 11 cases the interpretation of the test was revised based on the clinical findings (VUS

was reclassified as pathogenic). This study underscores the importance of clinical findings and familial segregation when interpreting genetic testing results.

Frequency and Genetic Spectrum of Inherited Retinal Dystrophies in a Large Dutch Pediatric Cohort: The RD5000 Consortium
Heutinck PAT, van den Born LI, Vermeer M, et al.
Invest Ophthalmol Vis Sci 2024 Aug 1;65(10):40
This descriptive, retrospective study investigated the frequency of Various diseases in pediatric patients registered in the national retinal dystrophy 5000 database in Netherlands. Patients had the clinical diagnosis of IRD before the age of 20. The diagnostic process for IRD comprises ophthalmic examination, electroretinography, multimodal retinal imaging, and optionally electrooculography and visual field testing. Furthermore, with the consent of parents and/or patients, genetic testing was often conducted as part of the diagnostic process. A total of 473 patients were analyzed. Median age at registration was 13 years (interquartile range, 9–16). 30 different IRD phenotypes were present, of which 87% of the phenotypes were nonsyndromic IRD and 13% were syndromic IRD. Retinitis pigmentosa (RP; n = 123, 20%), Leber congenital amaurosis (LCA; n = 97, 16%), X-linked retinoschisis (n = 64, 10%), and achromatopsia (n = 63, 10%) were the most frequent phenotypes. The genetic cause was identified in 76% of the genetically examined patients (n = 473). The most frequently disease-causing genes were RS1 (n = 32, 9%), CEP290 (n = 28, 8%), CNGB3 (n = 21, 6%), and CRB1 (n = 17, 5%). Diagnostic yield after reanalysis of genetic data increased by 7%. Genetic analysis revealed a causative variant in 76% of patients. Variants in RS1, as a cause of XLRS, and variants in CEP290, as a cause of RP and LCA, were the overall most common disease-causing genes and the most common disease-causing genes in progressive retinal dystrophies. Variants in CNGB3, as a cause of achromatopsia, and variants in CACNA1F, as a cause of CSNB, were the most common disease-causing genes in stationary IRDs. Usher syndrome was most often caused by variants in USH2A and MYO7A.

Representation of Women Among Individuals With Mild Variants in ABCA4-Associated Retinopathy: A Meta-Analysis
Cornelis SS, IntHout J, Runhart EH, et al
JAMA Ophthalmol 2024;142(5):463-471
Stargardt disease is an inherited retinal dystrophy caused by biallelic mutations in ABCA4. It has a wide spectrum of phenotype severity and variably penetrance. Several studies have reports higher proportion of women with ABCA4 associated retinopathy (ABCA4-AR). This meta-analysis aims to investigate whether women are overrepresented among individuals with ABCA4-AR who are carrying at least 1 mild allele or carrying nonmild alleles. Further, data from two European centers were used for exploratory hypothesis testing to look at sex ratio comparison of ABCA4-AR individuals vs other autosomal retinopathies. Results show that women were significantly overrepresented in the mild variant group but not in the nonmild variant group. Subgroup analyses on mild variants showed differences in the proportions of women. In one of the databases used for exploratory hypothesis testing, the proportion of adult women among individuals with ABCA4-associated retinopathy was higher than among individuals with other retinopathies. This study supports the hypothesis that sex is a modifier in

developing ABCA4-AR for individuals with a mild ABCA4 allele. This finding may be relevant for prognosis predictions and recurrence risks for individuals with ABCA4-associated retinopathy. Future studies should further investigate whether the overrepresentation of women is caused by differences in the disease mechanism, by differences in health care–seeking behavior, or by health care discrimination between women and men with ABCA4-AR. These results may be helpful in counseling prognosis in ABCA4-AR patients.

ATXN7-Related Cone-Rod Dystrophy: The Integrated Functional Evaluation of the Cerebellum (CERMOI) Study
Nassisi M, Coarelli G, Blanchard B, et al
JAMA Ophthalmol 2024;142(4):301-308
Spinocerebellar ataxias (SCAs) are a group of inherited neurological disorders characterized by a progressive degeneration of the cerebellum, brainstem, and spinal cord. 50 subtypes and 39 associated genes have been identified. Oculomotor abnormalities are often present in patients with SCA even at preataxic and early disease. In some SCA subtypes, the optic nerve and the retina may be primarily involved. Spinocerebellar ataxia type 7 (SCA7) is the most known SCA form associated with retinal degeneration. This study aims to identify ophthalmological biomarkers in SCA7 carriers. This is a cross-sectional natural history study of 15 adult ATXN7 pathogenic expansion carriers (9 with preataxia and 6 with ataxia). Three visits over the course of 12 months were conducted with full neurologic and ophthalmologic examination. Results showed 12 displayed cone or cone-rod dystrophy, with the number of CAG repeats correlating with disease severity. Two patients with cone-rod dystrophy exhibited higher repeat numbers and greater ataxia scores compared to those with only cone dystrophy. Outer nuclear layer thickness on OCT was correlated with Scale for the Assessment and Rating of Ataxia (SARA) score and plasma neurofilament light chain (NfL) levels, therefore identifying it as a biomarker of disease severity. This study further characterizes the ocular findings in SCA7. The identification of outer nuclear thickness as a biomarker provides a potential easily accessible and noninvasive way to monitor disease progression and potential therapeutic interventions.

Presence of Copy Number Variants Associated With Esotropia in Patients With Exotropia
Martinez Sanchez M, Chan WM, MacKinnon SE, et al
JAMA Ophthalmol 2024;142(3):243-247
Strabismus is a common ocular disorder of childhood. While there is a clear hereditary component to strabismus, it is not clear if esotropia and exotropia share genetic risk factors. This study aims to determine whether genetic duplications associated with esotropia are also associated with exotropia. In this cross-sectional study, 234 individuals with history of exotropia were recruited from pediatric ophthalmic practices. The authors previously identified 3 rare and recurrent copy number variants (CNV) that are duplications on chromosomes 2, 4, and 10, associated with increased risk of esotropia. The presence of these genetic duplications were assessed in this cohort with exotropia. Results showed that all three duplications were present in patients with exotropia, at a similar proportion compared to previous esotropia cohorts, and higher than control group without strabismus. Individuals with a duplication had higher magnitudes of deviation and were more likely to have constant exotropia, and had a higher rate of strabismus surgery compared to those without a duplication. The findings in this study

suggest that the genetic duplications on chromosomes 2, 4, and 10 are a shared risk factor of both exotropia and esotropia. This is consistent with findings from other studies of other forms of genetic variants such as single nucleotide variations that are also shared risk factors of different forms of strabismus. The authors hypothesis that the form of strabismus (esotropia or exotropia) that develops in the presence of these duplications may be influenced by other shared or independent genetic variants or by environmental factors. This study helps further expand understanding of the complex genetic factors contributing to strabismus.

Gene Editing for CEP290-Associated Retinal Degeneration
Pierce EA, Aleman TS, Jayasundera KT, et al
N Engl J Med 2024;390(21):1972-1984
CEP290-associated inherited retinal degeneration, historically known as Leber's congenital amaurosis, causes severe early-onset vision loss. EDIT-101 is a clustered regularly interspaced short palindromic repeats (CRISPR)–CRISPR-associated protein 9 (Cas9) gene-editing complex designed to treat inherited retinal degeneration caused by a specific damaging variant in intron 26 of CEP290 (IVS26 variant). This study reports results from a phase 1–2, open-label, single-ascending-dose study in patients with CEP290-associated inherited retinal degeneration caused by a homozygous or compound heterozygous IVS26 variant received a subretinal injection of EDIT-101 in the worse (study) eye. The primary outcome was safety, which included adverse events and dose-limiting toxic effects. Key secondary efficacy outcomes were visual function changes. Twelve adults and 2 children (age 9 and 14) were included in this study. The most notable adverse events include a transient vitreous hemorrhage due to study procedure, two patients with subretinal hyperreflective mounds on OCT persisting at 6 months post injection, and two patients with retinal pigment epitheliopathy at the injection site. One patient required a second surgery to treat persistent subretinal fluids and a dislocated intraocular lens. The authors concluded that there were no serious adverse events related to the treatment or procedure and no dose-limiting toxic effect. Six participants had a meaningful improvement from baseline in cone-mediated vision as assessed with the use of FST, of whom 5 had improvement in at least one other key secondary outcome. Nine participants (64%) had a meaningful improvement from baseline in the best corrected visual acuity, the sensitivity to red light as measured with FST, or the score on the mobility test. Six participants had a meaningful improvement from baseline in the vision-related quality-of-life score. This study is an important proof of concept for a novel on-target gene editing therapy. Preliminary evaluations in this study in a small sample showed that the procedure is safe, and there is early evidence supporting improved cone photoreceptor function consistent with mechanism of the therapeutic. This supports further research into CIRSPR-Cas9 mediated therapy for inherited retinal diseases.

Mitochondrial retinopathies and optic neuropathies: The impact of retinal imaging on modern understanding of pathogenesis, diagnosis, and management
Borrelli E, Bandello F, Boon CJF, et al.
Prog Retin Eye Res 2024 Jul;101:101264 This is an excellent review of clinic, pathology, and image modalities for mitochondrial retinopathies and optic neuropathies. The article provides a detailed overview of the crucial genetic and clinical features essential for correctly interpreting in vivo imaging. The article also discussed the limitations of imaging. Leber hereditary optic

neuropathy (LHON), Neuropathy, ataxia, retinitis pigmentosa (NARP) or maternally inherited Leigh syndrome (MILS), Maternally inherited nonsyndromic deafness, with or without association with aminoglycoside use, Myoclonus, epilepsy, ragged-red-fibers syndrome (MERRF), Maternally inherited diabetes and deafness (MIDD), mitochondrial encephalopathy, lactic acidosis, stroke-like syndrome (MELAS), and the spectrum of chronic progressive external ophthalmoplegia (CPEO), Kearns–Sayre syndrome (KSS), and Pearson's syndrome are presented in detail. Highly recommend reading this article.

Ocular manifestations of CHARGE syndrome in a pediatric cohort with genotype/phenotype analysis
Kanwar K, Bashey S, Bohnsack BL, et al.
Am J Med Genet A 2024 Aug;194(8):e63618
CHARGE syndrome is a rare multi-system condition associated with CHD7 variants. Ocular manifestations and particularly ophthalmic genotype-phenotype associations Can be variable. This is a retrospective chart review of A cohort of 42 pediatric patients under 20 years-old with clinical diagnosis of CHARGE syndrome and documented ophthalmic examination. 93% had ophthalmic manifestations in at least one eye. Optic nerve/chorioretinal colobomas were most common (90%), followed by microphthalmia (30%), cataract (14%), and iris colobomas (9%). Extraocular findings included strabismus (76%), nasolacrimal duct obstructions (26%, 11% with punctal agenesis), and cranial nerve VII palsy (24%). Genotype-phenotype analyses (27 patients) showed variability in ocular phenotypes without association to location or variant types.

Towards Uncovering the Role of Incomplete Penetrance in Maculopathies through Sequencing of 105 Disease-Associated Genes
Hitti-Malin RJ, Panneman DM, Corradi Z, et al.
Biomolecules 2024 Mar 19;14(3):367
Inherited macular dystrophies (iMDs) are a group of genetic disorders, which affect the central region of the retina. To date 105 maculopathy-associated genes have been described. When analyzed they explain the disease in only approximately 40% of the patients. On a cohort of 1352 patients with inherited macular dystrophies the top five most frequent causative genes were ABCA4 (37.2%), PRPH2 (6.7%), CDHR1 (6.1%), PROM1 (4.3%) and RP1L1 (3.1%). Variance with incomplete penetrance were present on the third of the patients with positive genetic testing which suggests the proportion of those patients might not be explained solely by the variance reported. This study suggest strongly that many more genes are likely associated with the condition on the one hand and high percentage of variance with variable expressivity my act as potential disease modifiers in other conditions like age-related macular degeneration.

Bietti's crystalline dystrophy: genotyping and deep qualitative and quantitative phenotyping in preparation for clinical trials
Li Q, Wang C, Zhang S, et al
Br J Ophthalmol 2024;108(8):1145-1153
Bietti’s crystalline dystrophy (BCD) is a vision-threatening disease and remarkable phenotypic heterogeneity was shown. The goal of this cross-sectional and observational study is to qualitatively and quantitatively characterize the genotypes and phenotypes of Bietti's crystalline

dystrophy (BCD) in a cohort 74 clinically diagnosed BCD patients, c.802-8_810del17insGC was shown the predominant variant of the CYP4V2 gene (allele frequency 55.4%). Sixty-two cases (123 eyes) with full imaging data were classified according to a modified criterion into stages 1 (n=8, 6.50%), 2A (n=9, 7.32%), 2B (n=17, 13.82%), 3A (n=30, 24.39%) and 3B (n=59, 47.97%). The eyes of the stage 2B were particularly deemed 'high risk' due to atrophy near fovea, while in stage 3A, though with remarkable foveal atrophy, preserved retinal pigment epithelium/photoreceptor islands near the fovea were found in 14 eyes. A tendency of increase in PAFA with age was found (rs=0.31, p=0.014). Significant PAFA increase was shown through stages 1 to 3B, and best-corrected visual acuity (BCVA, Logarithm of the Minimum Angle of Resolution) was shown to moderately correlate with PAFA (rs=0.56, p<0.001). The PAFA might be an efficient biomarker for BCD severities correlating with BCVA. The highly heterogeneous chorioretinopathy and BCVA of BCD cases appear to be associated with disease stages, progression types and patients' ages. Foveal involvement should be of a major concern for consideration of potential therapeutic intervention.

Neuroimaging changes in the pregeniculate visual pathway and chiasmal enlargement in Leber hereditary optic neuropathy
Xu X, Zhou H, Sun M, et al
Br J Ophthalmol 2024;108(9):1313-1317
Leber hereditary optic neuropathy (LHON) is characterised by bilateral severe visual loss in young adults resulting from primary degeneration of retinal ganglion cells accompanied by ascending optic atrophy. A few studies of MRI research have demonstrated atrophy and increased T2-weighted signal in visual pathway with Leber hereditary optic neuropathy (LHON) patients, but the imaging manifestations were non-specific. The purpose of this study was to describe the pattern of MRI changes in the pregeniculate visual pathway in Leber hereditary optic neuropathy (LHON). This retrospective observational study enrolled 60 patients with LHON between January 2015 and December 2021. The cohort included 48 (80%) males and 53 (88%) had bilateral vision loss. The median age of onset was 17.0 years (range 4.0-58.0). 28 (47%) patients had the m.11778G>A mutation. 34 (57%) patients had T2 hyperintensity (HS) in the pregeniculate visual pathway and 13 (22%) patients with chiasmal enlargement. 20 patients (71%) carrying the m.11778G>A mutation had T2 HS, significantly more than the 14 patients (44%) with T2 HS in the other LHON mutation groups (p=0.039). Furthermore, significantly more patients in the m.11778G>A group (16 patients (57%)) had T2 HS in optic chiasm (OCh)/optic tract (OTr) than the other LHON mutation groups (7 patients (22%), p=0.005). Optic chiasmal enlargement was more common in patients with vision loss duration <3 months compared with those ≥3 months (p=0.028). T2 HS in the pregeniculate visual pathway is a frequent finding in LHON. Signal changes in the OCh/OTr and chiasmal enlargement, in particular within the first 3 months of visual loss, were more commonly seen in patients carrying the m.11778G>A mtDNA mutation, which may be of diagnostic significance.

Reclassification of Genetic Testing Results: A Case Report Demonstrating the Need for Structured Re-Evaluation of Genetic Findings
Schott C, Colaiacovo S, Baker C, et al.
Can J Kidney Health Dis 2024 Apr 14;11:20543581241242562

This is an interesting Report that uses the example of a patient with Allport syndrome which initially was reported to have a variant of unknown significance in the candidate gene. Patient proceeded to donate a kidney to a living relative however, It turned out that the VUS had been reclassified as a pathogenic variant which would have disqualified the patient from donating the kidney. This case demonstrates the importance of structured, periodic re-evaluation of genetic testing results. With the ever-changing landscape of genetics in medicine, the interpretation of a VUS can be dynamic and therefore warrant caution in living kidney donor evaluations. Studies have shown that about 10% of VUSs can be upgraded to a pathogenic classification after an 18- to 36-month interval. This is true for all diseases.

Voretigene neparvovec for inherited retinal dystrophy due to RPE65 mutations: a scoping review of eligibility and treatment challenges from clinical trials to real practice
Testa F, Bacci G, Falsini B, et al.
Eye (Lond) 2024 Sep;38(13):2504-2515
This is a review of relevant literature to explore whether recommendations on patient eligibility for Luxturna treatment can be extrapolated. 166 papers were reviewed to investigate: (1) the clinical and genetic features considered in VN treatment eligibility; (2) the psychophysical tests and imaging modalities used in the pre-treatment and follow-up; (3) the potential correlations between visual function and retinal structure that can be used to define treatment impact on disease progression; (4) retinal degeneration; (5) the most advanced testing modalities; and (6) the impact of surgical procedure on treatment outcomes. Patients' eligibility is undefined in clinical settings and not consistently reported across the studies. No upper limit of retinal degeneration can be defined as the univocal factor in patient eligibility, although evidence suggested that the potential for function rescue is related to the preservation of photoreceptors before treatment. In general, pediatric patients retain more viable cells, present a less severe disease stage and show the highest potential for improvements, making them the most suitable candidates for treatment.

Enhanced Learning and Memory in Patients with CRB1 Retinopathy
Wright GA, Rodriguez-Martinez AC, Conn H, et al.
Genes (Basel) 2024 May 22;15(6):660
Biallelic pathogenic variants in the crumbs cell polarity complex component 1 gene (CRB1, OMIM 604210) are associated with a diverse spectrum of retinopathies with phenotypic variability. The phenotypes reported are Leber congenital amaurosis, early onset severe retinal dystrophy (EOSRD), autosomal recessive retinitis pigmentosa (RP12), cone-rod dystrophy (CORD), and macular dystrophy (MD). CRB1 exhibits distinct expression patterns outside the eye specifically cerebellum, hippocampal dentate gyrus, olfactory bulbs, rostral migratory stream, and the subventricular area lining the telencephalic ventricles. 63 subjects 21 with CRB1 retinopathy and 42 with vision loss due to other inherited ocular conditions were included in this study. Cognitive function was assessed using standardized neuropsychological tests that did not involve visual processing and required only verbal interaction. No significant differences were observed between the two groups of retinopathy subjects in the story recall immediate ($p = 0.111$) and delayed ($p = 0.057$) memory tests or in the verbal fluency phonemic subtest ($p = 0.363$). CRB1 retinopathy subjects scored significantly higher than non-CRB1 retinopathy

subjects in the list learning tasks of immediate (p = 0.001) and delayed memory (p = 0.007), in the verbal fluency semantic subtest (p = 0.017), and in the Hayling test of mental processing speed (p = 0.068). Additionally, CRB1 retinopathy subjects scored higher in the cognitive estimation test of higher executive function (p = 0.020) and in the verbal IQ digit span subtest compared to the non-CRB1 group (p = 0.037). No significant differences were found in overall verbal IQ (p = 0.142) or in the verbal IQ vocabulary (p = 0.436) and similarities (p = 0.208) subtests. This led to the conclusion that subjects with CRB1 retinopathy may have enhanced cognitive function in areas of memory and learning. Further work is required to understand the role of CRB1 in cognition.

Genetic Characterization of 191 Probands with Inherited Retinal Dystrophy by Targeted NGS Analysis
Mihalich A, Cammarata G, Tremolada G, et al.
Genes (Basel) 2024 Jun 12;15(6):766
Inherited retinal diseases represent a frequent cause of blindness in children and adults. As a consequence of the phenotype and genotype heterogeneity of the disease, it is difficult to have a specific diagnosis without molecular testing. To date, over 340 genes and loci have been associated with IRDs.This study presents the molecular findings of a cohort of 191 individuals with IRDs who underwent next-generation sequencing broad testing. Genetic diagnostic yield was 41%. However, after stratifying the patients according to their clinical suspicion, diagnostic yield was higher for well-characterized diseases such as Stargardt disease (STGD), at 65%, and for congenital stationary night blindness 2 (CSNB2), at 64%. Diagnostic yield was higher in the patient group where family segregation analysis was possible (68%) and it was higher in younger (55%) than in older patients (33%). The results of this analysis demonstrated that targeted NGS is an effective method for establishing a molecular genetic diagnosis of IRDs, however when a broad test is performed out of a clear clinical context and without familial segregation the yield of positive testing is low, and the likelihood of ambiguous findings is high.

Whole-Exome Analysis for Polish Caucasian Patients with Retinal Dystrophies and the Creation of a Reference Genomic Database for the Polish Population
Matczyńska E, Szymańczak R, Stradomska K, et al.
Genes (Basel) 2024 Aug 1;15(8):1011
This paper presents the results of the first study of a large cohort of patients with inherited retinal disorders analyzed by whole exome sequencing in Poland. The diagnostic yield for the selected group of IRD patients reached 64.9%. The study uncovered the most common pathogenic variants in ABCA4 and USH2A in the European population.

Molecular Mechanisms Governing Sight Loss in Inherited Cone Disorders
Brotherton C, Megaw R
Genes (Basel) 2024 Jun 1;15(6):727
Inherited cone disorders affect approximately 1 in 10,000 individuals and are the result of dysfunction in our cone photoreceptors, responsible for the perception of color vision. This review is focused on known inherited cone disorders genes, their molecular function, and the diseases they cause, with a focus on the most common forms of ICDs, including achromatopsia,

progressive cone dystrophies (CODs), and cone–rod dystrophies (CORDs). This is an extensive review to distinguish between subsets clinically, though significant phenotypic overlap remains. Although 37 causal genes have been identified, over half of patients have no confirmed genetic diagnosis. Given the emergence of gene-based therapeutic approaches to target specific inherited cone disorders, achieving an improved understanding of the molecular mechanisms underpinning these diseases and an improved molecular diagnosis rate is paramount. Very good review.

Genetic profile of syndromic retinitis pigmentosa in Portugal
Cortinhal T, Santos C, Vaz-Pereira S, et al.
Graefes Arch Clin Exp Ophthalmol 2024 Jun;262(6):1883-1897
Retinitis pigmentosa (RP) comprises a genetically and clinically heterogeneous group of inherited retinal degenerations, where 20-30% of patients exhibit extra-ocular manifestations (syndromic RP). Understanding the genetic profile of RP has important implications for disease prognosis and genetic counseling. This study aimed to characterize the genetic profile of syndromic RP in Portugal. Thai is a multicenter, retrospective cohort study of 122 patients from 100 families. Usher syndrome was the most frequent diagnosis (62.0%), followed by Bardet-Biedl (19.0%) and Senior-Løken syndromes (7.0%). Deleterious variants were identified in 86/100 families for a diagnostic yield of 86.0% (87.1% for Usher and 94.7% for Bardet-Biedl). A total of 81 genetic variants were identified in 25 different genes, 22 of which are novel. USH2A and MYO7A were responsible for most type II and type I Usher syndrome cases, respectively. BBS1 variants were the cause of Bardet-Biedl syndrome in 52.6% of families. These findings are in line with general literature and apply to US patients as well.

Visual functions, ocular characteristics and visual quality of life in patients with homocystinuria
Koye A, Nilsson M, Epstein D, Oscarson M, Teär Fahnehjelm K
Ophthalmic Genet 2024;45(4):343-350
Homocystinuria (HCU) is a rare metabolic disease that affects many organs, including the eyes. Aims: to assess visual functions, ocular characteristics, visual quality of life and time from the onset of ocular manifestations to HCU-diagnosis in patients with HCU. Eighteen patients underwent ophthalmological examinations and visual quality of life questionnaires. Best corrected decimal visual acuity was median 1.0 (range amaurosis - 1.3) right eye and 1.0 (range amaurosis -1.3) left eye. Five patients presented with severe myopia as first HCU manifestation, duration to HCU diagnosis was mean 13.6 years (range 2-25). Two patients had suffered ectopia lentis as first HCU manifestation, HCU diagnosis was established mean 8.0 years (range 7-9) later. One patient had suffered both from thrombosis and ectopia lentis prior to diagnosis. Another four patients suffered thromboembolic events before diagnosis. Median VFQ-25 composite score was 93 (68-98). The prevalence of myopia, ectopia lentis and monocular blindness was high in HCU-patients, which was reflected in their visual quality of life. Diagnosis was often delayed after the first ocular manifestation, increasing the risk of other severe non-ocular complications.

Genotype-phenotype Correlations of Ocular Posterior Segment Abnormalities in Marfan Syndrome

Liu Y, Ju Y, Chen TH, Jiang YX
Ophthalmol Sci 2024 Apr 6;4(5):100526
Marfan syndrome (MFS) is a connective tissue disorder caused by mutations in the fibrillin-1 (FBN1). In addition to typical phenotypes such as ectopia lentis (EL) and aortic dilation, patients with MFS are prone to ocular posterior segment abnormalities, including retinal detachment (RD), maculopathy, and posterior staphyloma (PS). This study aims to investigate the correlations between FBN1 genotype and posterior segment abnormalities within a Chinese cohort of 212 patients with MFS. 60 eyes (49.59%) exhibited posterior segment abnormalities, including RD (4, 3.31%), maculopathy (47, 38.84%), and PS (54, 44.63%). The mean age was 11.53 ± 11.66 years, with 79.34% of patients <20 years old. The location and region of mutations were found to be associated with the incidence of maculopathy.

Familial Exudative Vitreoretinopathy With and Without Pathogenic Variants of Norrin/β-Catenin Signaling Genes
Kondo H, Tsukahara-Kawamura T, Matsushita I, et al.
Ophthalmol Sci 2024 Mar 15;4(5):100514
This is a multicenter, cross-sectional, observational and genetic study of 281 probands to determine the clinical characteristics of familial exudative vitreoretinopathy (FEVR) associated with or without pathogenic variants of the Norrin/β-catenin genes. FEVR is genetically heterogeneous, and the inheritance pattern is diverse. Autosomal dominant (AD), autosomal recessive (AR), and X-linked modes of inheritance are known to occur with AD the most common. Genes of the Norrin/β-catenin signaling pathway consisting of the FZD4, LRP5, TSPAN12, and NDP genes encode proteins of a ligand-receptor complex that are expressed in the retinal vascular endothelial cells. They play a role in the development of the retinal vasculature and mutations in these genes account for approximately 50% of all FEVR patients. Although FEVR has been thought to be a nonsyndromic disorder, more severe loss-of-function mutations of the same Norrin/β-catenin genes can cause syndromic disorders with severe vitreoretinopathy - Norrie disease. The osteoporosis-pseudoglioma syndrome is caused by mutations in the LRP5 gene, and it is associated with spontaneous skeletal fractures due to the osteoporosis. Variants in the KIF11 and CTNNB1 genes are known to be associated with a FEVR-like phenotype and systemic abnormalities like microcephaly. In this cohort, 38.5% of patients had positive genetic results. The features associated with the positive genetic results were positive family history (64%), progression during infancy (75%), nonsyndromic and asymmetric severity between the two eyes. The advanced stages of 3 to 5 in the more severe eye were found more frequently in probands with variants than in those without variants (83.3% vs. 58.4%, $P < 0.0001$). Genetic testing is recommended in cases with clinical suspicion of FEVR for diagnostic and prognostic purposes.

A Retrospective Longitudinal Study of 460 Patients with ABCA4-Associated Retinal Disease
Fenner BJ, Whitmore SS, DeLuca AP, et al
Ophthalmology 2024;131(8):985-997
This is a retrospective cohort study investigating the distribution of genotypes and natural history of ABCA4-associated retinal disease in cohort of 460 patients from the same institution. The median age of onset of uncorrectable vision loss for the cohort was 16 years of age. The

range of clinical features was very broad. Those with the most severe disease comprised >10% of the cohort and were characterized by loss of both cone and rod photoreceptor, and bone spicule-like retinal changes similar to retinitis pigmentosa. BCVA in this group was 20/200 or less before the age of 10. Stargardt disease was the most prominent phenotype, comprising >70% of the cohort and had vision loss starting between 7 and 40 yo. The mildest group, referred to as those with autosomal-recessive pattern dystrophy, made up about 10% of the cohort was characterized by large yellow pisciform or reticular flecks and relative preservation of the outer retina until late in the course of the disease. These patients were asymptomatic when the flecks were first seen and first visual symptoms occurred after 40yo. In regard to genotype evaluation of the entire cohort, 736 instances of 241 different alleles of the ABCA4 gene were observed. The investigators compared the patients' genotypes with their clinical phenotypes to see if any relationships could be identified that would be reproducible enough to be of value in stratifying patients during their enrollment in clinical trials. Their evaluation determined that, at present, it is not possible to control for the pathogenicity of a participant's genotype using DNA sequencing alone for 2 interdependent reasons: the extreme genetic heterogeneity of the ABCA4 gene and the magnitude of the genetic background effects. Based on these observations, the authors suggest that patients' clinical findings in most cases will be more useful for predicting their clinical course than their genotype.

Early-Onset of Familial Exudative Vitreoretinopathy: Clinical Characteristics, Management, and Outcomes
Kitic N, Chapron T, Metge-Galatoire F, et al.
Retina 2024;44(4):669-679
Familial exudative vitreoretinopathy cases with a diagnosis in early infancy have a severe stage at presentation, and a worse prognosis. The purpose of this retrospective study is to describe the clinical characteristics, management, and outcomes of toddlers (under the age of 3) diagnosed with familial exudative vitreoretinopathy. 54 patients (108 eyes) with a mean age at diagnosis of 10.9 ± 2.6 months were included. Poor visual behavior (33%) and strabismus (26%) were the most common presenting symptoms, whereas screening only represented 11%. About half of included patients had a severe disease (stages 4 and 5). Genetic testing was positive in 40.7% of patients with 24% having a family history of familial exudative vitreoretinopathy. LRP5 was the most prevalent mutation (54.5%).Surgery was performed in 44.4% of eyes and was successful in 69.8% of cases. Failure exclusively occurred in eyes with severe stages. Among eyes evaluated for visual acuity (72 eyes), most (76.4%) had a vision of hand motion or better. Familial exudative vitreoretinopathy tended to be worse with earlier age at diagnosis, subsequently affecting the prognosis. Surgical intervention was common and primarily included lens-sparing vitrectomy and combined lensectomy and vitrectomy. Surgical success hinged on the stage of the disease. Early examination of first-degree relatives with familial exudative vitreoretinopathy under general anesthesia is essential for a prompt screening and treatment of the disease, to avoid progression of the disease and complications.

Substitution of a single non-coding nucleotide upstream of TMEM216 causes non-syndromic retinitis pigmentosa and is associated with reduced TMEM216 expression
Malka S, Biswas P, Berry AM, et al

Am J Hum Genet 2024;111(9):2012-2030
Genome analysis of individuals affected by retinitis pigmentosa (RP) identified two rare nucleotide substitutions at the same genomic location on chromosome 11 (g.61392563 [GRCh38]), 69 base pairs upstream of the start codon of the ciliopathy gene TMEM216 (c.-69G>A, c.-69G>T [GenBank: NM_001173991.3]), in individuals of South Asian and African ancestry, respectively. Genotypes included 71 homozygotes and 3 mixed heterozygotes in trans with a predicted loss-of-function allele. Haplotype analysis showed single-nucleotide variants (SNVs) common across families, suggesting ancestral alleles within the two distinct ethnic populations. Clinical phenotype analysis of 62 available individuals from 49 families indicated a similar clinical presentation with night blindness in the first decade and progressive peripheral field loss thereafter. No evident systemic ciliopathy features were noted. Functional characterization of these variants by luciferase reporter gene assay showed reduced promotor activity. Nanopore sequencing confirmed the lower transcription of the TMEM216 c.-69G>T allele in blood-derived RNA from a heterozygous carrier, and reduced expression was further recapitulated by qPCR, using both leukocytes-derived RNA of c.-69G>T homozygotes and total RNA from genome-edited hTERT-RPE1 cells carrying homozygous TMEM216 c.-69G>A. In conclusion, these variants explain a significant proportion of unsolved cases, specifically in individuals of African ancestry, suggesting that reduced TMEM216 expression might lead to abnormal ciliogenesis and photoreceptor degeneration.

Novel heterozygous OPA3 variant in a family with congenital cataracts, sensorineural hearing loss and neuropathy, without optic atrophy and comparison of pathogenic and population variants
Penon-Portmann M, Naugle K, Brodie F, et al.
Am J Med Genet A 2024 Aug 21:e63846 Heterozygous mutations in the OPA3 gene are associated with autosomal dominant optic atrophy-3 (OPA3), whereas biallelic mutations cause autosomal recessive 3-methylglutaconic aciduria type III. Most cases with pathogenic variants in the gene OPA3 have presented with optic atrophy. This paper reports a large family with congenital cataracts, hearing loss and neuropathy, with a likely pathogenic novel missense variant in OPA3, c.30G>C; p.(Lys10Asn) that segregates with disease in the family pedigree. The family's clinical presentation has significant phenotypic overlap with previously reported cases of OPA3, except for a notable lack of optic atrophy.

Genetic Characteristics and Clinical Manifestations of Foveal Hypoplasia in Familial Exudative Vitreoretinopathy
Ju Y, Zhang L, Gao F, et al
Am J Ophthalmol 2024;262:73-85
The study aimed to assess the prevalence of foveal hypoplasia (FH) in individuals with familial exudative vitreoretinopathy (FEVR) and was conducted at the Eye and ENT Hospital, Fudan University, from 2017 to 2023. It included both familial and sporadic FEVR cases, using optical coherence tomography (OCT) to classify FH and genetic screening to identify mutations. Results revealed that 46.1% of eyes exhibited FH, with 53.2% classified as grade 1 FH. The study identified 49 mutations associated with FEVR, including 26 novel mutations, with mutations in LRP5 and KIF11 linked to a higher prevalence of FH. Eyes with FH had poorer

best-corrected visual acuity (BCVA), particularly those with Group B FH, which also had smaller retinal arteriolar angles compared to Group A and those without FH. Strengths of the study include the discovery of new mutations and detailed FH classification using OCT. Limitations include a small sample size and unclear pathogenicity of some novel variants. Clinically, genetic testing for mutations like those in LRP5 and KIF11 can inform the likelihood of FH in FEVR patients, while regular FH assessment is crucial for managing visual outcomes and guiding personalized treatments.

IQCB1 (NPHP5)-Retinopathy: Clinical and Genetic Characterization and Natural History
Sen S, Fabozzi L, Fujinami K, et al
Am J Ophthalmol 2024;264:205-215
The IQCB1 gene is associated with Senior-Loken syndrome (SLS), a rare autosomal recessive condition involving renal dysfunction and leber congenital amaurosis/early-onset severe retinal degeneration. The purpose of this retrospective cohort study at a single tertiary care referral center is to describe the clinical and genetic features, and explore the natural history of retinopathy associated with IQCB1 variants in children and adults with retinopathy. 19 patients with retinopathy, harboring likely disease-causing variants in IQCB1 were included. Ten patients had best corrected visual acuity better than 1.0 LogMAR, and BCVA remained stable till the last review. Seven patients had a vision of hand movements or worse in at least one eye at presentation. There was no correlation found between age of onset and severity of vision loss. Nine patients (47.4%) had a diagnosis of end-stage renal failure at presentation. The other 10 patients (52.6%) had a diagnosis of non-syndromic IQCB1-retinopathy and maintained normal renal function until the last follow-up. The mean age at diagnosis of renal failure was 26.3 ±19.8 years. OCT showed ellipsoid zone (EZ) disruption with foveal sparing in 8/13 patients. All patients had stable OCT findings. Full-field ERGs in four adults revealed a severe cone-rod dystrophy and three children had extinguished ERGs. We identified 17 IQCB1 variants, all predicted to cause loss of function. IQCB1-retinopathy is a severe early-onset cone-rod dystrophy. The dissociation between severely decreased retinal function and relative preservation of retinal structure over a wide age window makes the disease a candidate for gene therapy.

Genetics, Clinical Characteristics, and Natural History of PDE6B-Associated Retinal Dystrophy
Hashem SA, Georgiou M, Fujinami-Yokokawa Y, et al
Am J Ophthalmol 2024;263:1-10
This study outlines the clinical characteristics, natural history, and genetics of PDE6B-associated retinal dystrophy. It is a retrospective, observational cohort study including 40 patients (80 eyes); mean age (±SD, range) was 42.1 years (± 19.0, 10-86) at baseline, with a mean follow-up time of 5.2 years. Twenty-nine (72.5%) and 27 (67.5%) patients had no or mild visual acuity impairment at baseline and last visit, respectively. Best-corrected visual acuity (BCVA) was 0.56 ± 0.72 LogMAR (range -0.12 to 2.80) at baseline and 0.63 ± 0.73 LogMAR (range 0.0-2.80) at the last visit. BCVA was symmetrical in 87.5% of patients. A hyperautofluorescent ring was observed on FAF in 48 and 46 eyes at baseline and follow-up visit, respectively, with a mean area of 7.11 ± 4.13 mm2 at baseline and mean of 6.13 ± 3.62 mm2 at the follow-up visit. Mean horizontal ellipsoid zone width at baseline was 1946.1 ± 917.2

μm, which decreased to 1763.9 ± 827.9 μm at follow-up. Forty-four eyes had cystoid macular edema at baseline (55%), and 41 eyes (51.3%) at follow-up. There were statistically significant changes during the follow-up period in terms of BCVA and the ellipsoid zone width. Genetic analysis identified 43 variants in the PDE6B gene, including 16 novel variants. This study details the natural history of PDE6B-retinopathy in the largest cohort to date. Most patients had mild to no BCVA loss, with slowly progressive disease, based on FAF and OCT metrics. There is a high degree of disease symmetry and a wide window for intervention.

Characteristics of Eyes With CRB1-Associated EOSRD/LCA: Age-Related Changes
Ayash J, Woods RL, Akula JD, et al
Am J Ophthalmol 2024;263:168-178
Biallelic variants in CRB1 cause inherited retinal disorders, including early onset severe retinal dystrophy/Leber congenital amaurosis (EOSRD/LCA) and retinitis pigmentosa (RP). The purpose of this retrospective cohort study is to evaluate ocular and retinal features of CRB1-associated early onset severe retinal dystrophy/Leber congenital amaurosis (EOSRD/LCA) for age-related changes. Sixteen pediatric patients with biallelic CRB1 EOSRD/LCA who had been followed for up to 18 years were reviewed. Visual acuity dark-adapted visual sensitivity, and area of seeing visual field (all subnormal from the earliest ages recorded) declined with increasing age. Hyperopia was stable through childhood and adolescence. In CRB1 EOSRD/LCA, OCT extrafoveal inner and outer laminar thicknesses exceeded those in controls but varied little with age, and foveal metrics (depth, breadth, thickness at rim) differed significantly from those in controls, but variations in foveal metrics were not associated with declines in acuity. From the youngest ages, retinal and visual function is significantly subnormal and becomes progressively compromised. A goal of future therapies should be intervention at young ages, when there is more function to be rescued.

Genetic Characteristics and Clinical Manifestations of Foveal Hypoplasia in Familial Exudative Vitreoretinopathy
Ju Y, Zhang L, Gao F, et al
Am J Ophthalmol 2024;262:73-85
This retrospective cohort study aimed to ascertain the occurrence of foveal hypoplasia (FH) in individuals diagnosed with familial exudative vitreoretinopathy (FEVR). A total of 102 eyes from 58 patients were suitable for analysis. Forty-nine mutations in LRP5, FZD4, NDP, TSPAN12, KIF11, CTNNB1, and ZNF408 were examined and detected, with 26 of them being novel. Forty-seven eyes (46.1%) revealed FH. The majority (53.2%) were due to the typical grade 1 FH. Patients with mutations in LRP5 and KIF11 were found to exhibit a higher prevalence of FH ($P = .0088$). Group B displayed the lowest visual acuity compared with group A ($P = .048$) and the group without FH ($P < .001$). The retinal arteriolar angle in group B was significantly smaller than in group A ($P = .001$) and those without FH ($P < .001$). This study offers a new diagnostic approach and expands the spectrum of FEVR mutations. LRP5 and KIF11 were found to be more susceptible to causing FH in patients with FEVR. FEVR eyes with FH exhibited both greater visual impairment and reduced retinal arteriolar angles. The assessment of foveal status in patients with FEVR should be valued.

Functional Vision in Patients With Biallelic USH2A Variants
Heon E, Melia M, Bocchino LE, et al
Am J Ophthalmol 2024;260:200-211
Mutations in USH2A are the most common cause of autosomal recessive progressive rod and cone photoreceptor degeneration with or without hearing loss. The purpose of this multicenter, international, cross-sectional study is to describe functional vision (FV) and investigate the relationship between FV, visual acuity (VA), and hill of vision (VTOT) at baseline in patients with biallelic USH2A variants. In individuals with biallelic disease-causing variants in USH2A, clinical diagnosis of Usher syndrome type 2 (USH2) or autosomal recessive nonsyndromic retinitis pigmentosa (ARRP) was based on history of hearing loss and audiology examinations. The VALVVFQ-48 was administered verbally to participants ≥18 years old. VA was measured in both eyes; VTOT was determined from static perimetry in the study eye (better VA). FV scores were calculated using Rasch analysis. Median age of 121 participants (76 with USH2, 45 with ARRP) was 41 years (range: 19-80); 54% were female. FV scores varied from -2.0 to 7.6 logits (median [interquartile range (IQR)]: 2.8 [1.5-3.8]). ARRP and USH2 participants had similar FV scores, both before [mean (95% CI): 2.8 (2.3-3.4) and 2.7 (2.3-3.2), respectively], and after [mean (95% CI): 2.5 (2.1-3.0) and 2.9 (2.6-3.3), respectively; P = .24] adjusting for age, VA, disease duration, and VTOT. VA and VTOT accounted for 29% and 26% of the variance in FV scores, respectively (P < .001 for each). Together, they accounted for 36% of variance observed. Biallelic USH2A variants were associated with a large range of FV, yet similar in ARRP and USH2, despite hearing loss in USH2. The modified VALVVFQ-48 we evaluated is not ideal for detecting the impact of USH2A-associated retinal degenerations on activities of daily living.

Deep phenotyping of PROM1-associated retinal degeneration
Schließleder G, Kalitzeos A, Kasilian M, et al
Br J Ophthalmol 2024;108(4):558-565
The purpose of this study was to investigate retinal structure in detail of subjects with autosomal-dominant (AD) and autosomal-recessive (AR) PROM1-associated retinal degeneration (PROM1-RD), study design: institutional, cross-sectional study. Four eyes from four subjects (three with AD and one with AR) PROM1-RD were investigated by ophthalmic examination including best-corrected visual acuity (BCVA) and multimodal retinal imaging: fundus autofluorescence (FAF), spectral-domain optical coherence tomography (SD-OCT) and adaptive optics scanning light ophthalmoscopy. Quantitative assessment of atrophic lesions determined by FAF, thickness of individual retinal layers and cone photoreceptor quantification was performed. BCVA ranged from 20/16 to 20/200. Initial pathological changes included the presence of hyperautofluorescent spots on FAF imaging, while later stages demonstrated discrete areas of atrophy. In all patients, thinning of the outer retinal layers on SD-OCT with varying degrees of atrophy could be detected depending on disease-causing variants and age. Cone density was quantified both in central and/or at different eccentricities from the fovea. PROM1-RD comprises a wide range of clinical phenotypes. Depending on the stage of disease, the cone mosaic in PROM1-RD is relatively preserved and can potentially be targeted by cone-directed interventions.

KCNV2-associated retinopathy: genotype-phenotype correlations - KCNV2 study group report 3

de Guimaraes TAC, Georgiou M, Robson AG, et al Br J Ophthalmol 2024;108(8):1137-1144

KCNV2-associated retinopathy is a rare form of autosomal recessive inherited retinal dystrophy. The electrophysiology, retinal imaging and clinical course of the disease have been well described in the literature. Genotype–phenotype correlations have not been elucidated to date. The goal of this work is to investigate genotype-phenotype associations in patients with KCNV2 retinopathy. Review of clinical notes, best-corrected visual acuity (BCVA), molecular variants, electroretinography (ERG) and retinal imaging. Subjects were grouped according to the combination of KCNV2 variants-two loss-of-function (TLOF), two missense (TM) or one of each (MLOF)-and parameters were compared. Ninety-two patients were included. The mean age of onset (mean±SD) in TLOF (n=55), TM (n=23) and MLOF (n=14) groups was 3.51±0.58, 4.07±2.76 and 5.54±3.38 years, respectively. The mean LogMAR BCVA (±SD) at baseline in TLOF, TM and MLOF groups was 0.89±0.25, 0.67±0.38 and 0.81±0.35 for right, and 0.88±0.26, 0.69±0.33 and 0.78±0.33 for left eyes, respectively. The difference in BCVA between groups at baseline was significant in right (p=0.03) and left eyes (p=0.035). Mean outer nuclear layer thickness (±SD) at baseline in TLOF, MLOF and TM groups was 37.07±15.20 µm, 40.67±12.53 and 40.38±18.67, respectively, which was not significantly different (p=0.85). The mean ellipsoid zone width (EZW) loss (±SD) was 2051 µm (±1318) for patients in the TLOF, and 1314 µm (±965) for MLOF. Only one patient in the TM group had EZW loss at presentation. There was considerable overlap in ERG findings, although the largest DA 10 ERG b-waves were associated with TLOF and the smallest with TM variants. Patients with missense alterations had better BCVA and greater structural integrity. This is important for patient prognostication and counselling, as well as stratification for future gene therapy trials.

Relationship between genotype, phenotype, and refractive status in patients of inherited retinal degeneration

Tsai WC, Liu YL, Tsai TH, et al

Eye (Lond) 2024 Aug; EpublishedThis is a retrospective analysis of a cohort of 500 Taiwanese patients with inherited eye diseases. No significant differences were observed in visual acuity, refractive state and myopia rate between patients with IRD and the general population In this cohort. Patients with LCA had a higher incidence of high astigmatism. Patients with RPGR and PROM1-related Disorders had a higher incidence of myopia. Significantly poorer visual acuity was found in ABCA4, CRB1 and PROM1-related patients, and more preserved visual acuity was seen in patients with EYS, USH2A, and RDH12 mutations. One caveat that this study is that the number of patients for each disease was rather small and diseases like congenital stationary night blindness were severely underrepresented. The heterogeneity of disease-causing genes in Asian patients may lead to variable refractive state. Additionally, the high incidence of myopia in general population may affect the statistics.

Expanding the genetics and phenotypes of ocular congenital cranial dysinnervation disorders

Jurgens JA, Barry BJ, Chan WM, et al.

Genet Med 2024 Sept; Epublished

The genetic etiologies and genotype/phenotype associations of congenital cranial dysinnervation disorders (oCCDDs) is complex and genetically heterogeneous. The diagnostic

yelled of known genes that are known to be associated with oCCDD is less than 20%. Genetic testing is recommended to establish list of syndromic phenotypes and recurrence in families.

Myocilin Mutation N480K Leads to Early Onset Juvenile and Adult-onset Primary Open Angle Glaucoma in a Six Generation Family
Kader MA, Devarajan B, Vijayan S, et al.
J Glaucoma 2024 Mar 1;33(3):218-224
This is a report of a pathogenic autosomal dominant MYOC mutation N480K detected in 6 generations of an Indian family, primarily responsible for juvenile open angle glaucoma (JOAG) and adult-onset primary open angle glaucoma (POAG), emphasizing the importance of screening this mutation at a younger age. Among the unaffected carriers, 1 was less than 5 years old, and another was 25 years old. The earliest to develop the disease was a 10-year-old child. The penetrance of the mutation was 95% over 10 years of age. This report highlights the importance of genetic testing in juvenile and congenital glaucoma as well as the phenotypic variability of genetically associated glaucoma.

Systematic study of ophthalmological findings in 10 patients with PEX1-mediated Zellweger spectrum disorder
Karuntu JS, Klouwer FCC, Engelen M, Boon CJF
Ophthalmic Genet 2024;45(4):351-362
This cross-sectional study describes the ophthalmological and general phenotype of 10 patients from six different families with a comparatively mild form of Zellweger spectrum disorder (ZSD), a rare peroxisomal disorder. Nine patients were homozygous for c.2528 G > A (p.Gly843Asp) variants in PEX1 and one patient was compound heterozygous for c.2528 G>A (p.Gly843Asp) and c.2097_2098insT (p.Ile700TyrfsTer42) in PEX1. Median age was 22.6 years (interquartile range (IQR): 15.9 - 29.9 years) at the most recent examination, with a median symptom duration of 22.1 years. Symptom onset was variable with presentations of hearing loss (n = 7) or nyctalopia/reduced visual acuity (n = 3) at a median age of 6 months (IQR: 1.9-8.3 months). BCVA (median of 0.8 logMAR; IQR: 0.6-0.9 logMAR) remained stable over 10.8 years and all patients were hyperopic. Fundus examination revealed a variable retinitis pigmentosa (RP)-like phenotype with rounded hyperpigmentations as most prominent feature in six out of nine patients. Electroretinography, visual field measurements, and microperimetry further established the RP-like phenotype. Multimodal imaging revealed significant intraretinal fluid cavities on SD-OCT and a remarkable pattern of hyperautofluorescent abnormalities on FAF in all patients. This study highlights the ophthalmological phenotype resembling RP with moderate to severe visual impairment in patients with mild ZSD. These findings can aid ophthalmologists in diagnosing, counselling, and managing patients with mild ZSD.

Outer Retinal Microcavitations in Retinitis Pigmentosa: A Novel Optical Coherence Tomography Finding Common in RP1-Related Retinopathy
Dimopoulos IS, Huryn LA, Hufnagel RB, et al
Retina 2024;44(7):1260-1267
Pathogenic variants in the RP1 gene have historically been associated with autosomal dominant retinopathy, accounting for 5% to 10% of total patients with RP. The goal of this study is to

describe a novel optical coherence tomography (OCT) finding of outer retina microcavitations in RP1 -related retinopathy and other retinal degenerations. Medical charts and OCT images of 28 patients with either autosomal dominant retinitis pigmentosa or autosomal recessive retinitis pigmentosa RP1 -related retinopathy were reviewed. Outer retina microcavitations were defined as hyporeflective OCT structures of at least 30 μ m in diameter between the ellipsoid zone and retinal pigment epithelium. Comparison was made based on the following metrics: (1) functional measures including best-corrected visual acuity and color discrimination errors on D-15 test; and (2) structural measures, including central subfield, average macular thickness, and preserved transfoveal ellipsoid zone width. Mann-Whitney tests were used for comparisons with significance set at $P < 0.05$. The specificity of microcavitations for RP1 -related retinopathy was estimated against 26 patients with non- RP1 retinitis pigmentosa. Among 15 included patients, microcavitations were found in at least one eye of all patients with arRP and 7/12 (58%) of patients with adRP. Patients with adRP and microcavitations were older at the time of examination (51 vs. 43 years of age; $P = 0.04$) and their eyes demonstrated worse best-corrected visual acuity (0.09 vs. 0 logMAR; $P = 0.008$), reduced central subfield (256 vs. 293 μ m; $P = 0.01$), average macular thickness (241 vs. 270 μ m; $P = 0.02$), and shorter transfoveal ellipsoid zone widths (1.67 vs. 4.98 mm; $P < 0.0001$). The finding of microcavitations showed a specificity of 0.92 for RP1 -related retinopathy. A novel OCT finding of outer retina microcavitations was commonly observed in patients with RP1 -related retinopathy. Eyes with outer retinal OCT microcavitations had worse visual function and more affected central retinal structure.

Discrepancy Between Fundus Autofluorescence Abnormality and Visual Field Loss in Bietti Crystalline Dystrophy
Sakai D, Maeda T, Maeda A, et al
Retina 2024;44(8):1394-1402
Bietti crystalline dystrophy (BCD), a rare form of retinal dystrophy caused by pathogenic variants in CYP4V2 and characterized by a myriad of yellowish glittering crystalline deposits, followed by progressive RPE, choroid, and subsequent outer retinal degeneration. The aim of this study was to explore the potential benefits of retinal pigment epithelium replacement therapy in patients with Bietti crystalline dystrophy (BCD) by assessing the disease pathology with the distinctive relationship between fundus autofluorescence (FAF) abnormality and visual field defect. Sixteen eyes from 16 patients with BCD and 16 eyes from 16 patients with RHO-associated retinitis pigmentosa were included. In patients with BCD, the FAF abnormality area was not correlated with the overall visual field defect area and median overall visual field defect area (57.5%) was smaller than FAF abnormality area (98.5%). By contrast, the ellipsoid zone width was significantly correlated with the central visual field area ($r = 0.806$, $P < 0.001$). In patients with RHO-associated retinitis pigmentosa, the FAF abnormality area and ellipsoid zone width were significantly correlated with the overall visual field defect area ($r = 0.833$, $P < 0.001$) and central visual field area ($r = 0.887$, $P < 0.001$), respectively. The FAF abnormality shown in patients with BCD involves retinal pigment epithelium degeneration without complete loss of photoreceptors or visual function. These results suggest that patients with BCD are good candidates for retinal pigment epithelium replacement therapy for preservation of residual visual function.

Bi-allelic variants in COQ8B, a gene involved in the biosynthesis of coenzyme Q10, lead to non-syndromic retinitis pigmentosa
Iglesias-Romero AB, Kaminska K, Quinodoz M, et al.
Am J Hum Genet 2024 Aug 28:S0002-9297(24)00291-X There are more than 100 genes associated retinitis pigmentosa the data. This paper presents a new gene associated with autosomal recessive retinitis pigmentosa. They make the case for variants in COQ8B gene to lead to recessive non-syndromic RP, possibly by impairing the biosynthesis of coenzyme Q10, a key component of oxidative phosphorylation in the mitochondria.

Characteristics of Eyes With CRB1-Associated EOSRD/LCA: Age-Related Changes
Ayash J, Woods RL, Akula JD, et al
Am J Ophthalmol 2024;263:168-178
The study aimed to investigate the ocular and retinal features of CRB1-associated early onset severe retinal dystrophy/Leber congenital amaurosis (EOSRD/LCA) and how these features evolve with age. Conducted as a retrospective cohort study, it followed 16 pediatric patients with biallelic CRB1 EOSRD/LCA for up to 18 years. Key findings included a decline in visual acuity, dark-adapted visual sensitivity, and visual field area with age, with initial improvements in visual acuity followed by deterioration after about 2.3 years. Refractive error remained stable as hyperopia throughout childhood and adolescence. OCT analysis showed that while extrafoveal retinal thickness was greater in CRB1 patients than controls, foveal depth and thickness decreased with age, though not strongly correlated with visual acuity declines. Electroretinography revealed severe photoreceptor dysfunction early on. The longitudinal nature of the study and use of various diagnostic tools provided a comprehensive view of disease progression. However, the retrospective design, small sample size, and variable follow-up durations limit generalizability. Clinically, the study highlights the importance of early intervention to preserve visual function and suggests that treatment strategies should focus on younger patients to better manage CRB1-associated retinal diseases.

IQCB1 (NPHP5)-Retinopathy: Clinical and Genetic Characterization and Natural History
Sen S, Fabozzi L, Fujinami K, et al
Am J Ophthalmol 2024;264:205-215
The study investigated the clinical and genetic characteristics of retinopathy linked to IQCB1 variants and explored its natural history in both children and adults. Conducted at a single tertiary care referral center, the retrospective cohort study involved 19 patients with retinopathy associated with likely disease-causing IQCB1 variants. Findings revealed that visual acuity varied, with some patients maintaining good vision while others had severely impaired vision; visual acuity remained stable for many. Notably, 47.4% of patients presented with end-stage renal failure, while the rest had non-syndromic retinopathy with normal renal function. Imaging showed ellipsoid zone disruption with foveal sparing, and electrophysiological tests indicated severe cone-rod dystrophy in adults and extinguished responses in children. The study identified 17 IQCB1 variants, all predicted to cause loss-of-function. Strengths of the study include comprehensive data collection and the identification of novel IQCB1 variants, while limitations involve the small sample size, variability in imaging quality, and lack of direct renal function assessment. The findings underscore the importance of genetic testing and renal

evaluation for IQCB1-related retinopathy and suggest potential for gene therapy due to the preservation of the ellipsoid zone in some cases. Regular monitoring and early intervention are recommended for affected individuals.

Genetic and Clinical Features of ABCA4-Associated Retinopathy in a Japanese Nationwide Cohort
Mizobuchi K, Hayashi T, Tanaka K, et al
Am J Ophthalmol 2024;264:36-43
Stargardt disease (STGD1, MIM: 248200) is caused by biallelic variants of the ATP-binding cassette transporter, alpha 4 subunit (ABCA4) gene. The goal of this manuscript is to clarify the genetic and clinical features of Japanese patients with ABCA4-associated retinopathy.This is a retrospective, multicenter cohort study of 63 patients with ABCA4-associated retinopathy: 19 with missense/missense, 23 with missense/truncation, and 21 with truncation/truncation genotypes. In total, 62 variants were identified, including 29 novel variants. Six patients had a mild phenotype characterized by foveal-sparing or preserved foveal structure, including 4 with missense/missense and 2 with missense/truncation genotypes. The p.Arg212His variant was the most frequent in patients with mild phenotypes (4/12 alleles). Clinical findings showed a disease duration-dependent worsening of the phenotypic stage. Patients with the truncation/truncation genotype exhibited rapid retinal degeneration within a few years and definite fundus autofluorescence imaging patterns, including hyper autofluorescence at the macula and few or no flecks. Results indicate that missense/missense or missense/truncation genotypes, including the p.Arg212His variant, are associated with a relatively mild phenotype. In contrast, the truncation/truncation genotype causes rapid and severe retinal degeneration in Japanese patients with ABCA4-associated retinopathy. These data are vital in predicting patient prognosis, guiding genetic counseling, and stratifying patients for future clinical trials.

Association of Ocular Manifestations of Marfan Syndrome With Cardiovascular Complications
Tran EM, Wai KM, Kossler AL,et al
Am J Ophthalmol 2024;264:85-89
Marfan syndrome (MFS) is one of the most common inherited connective tissue disorders, with an estimated prevalence of 6.5 in 100,000 individuals, caused by mutations in FBN1. Although penetrance of the mutation in MFS is high, its phenotypic expressivity is quite variable and the purpose of this work is to evaluate associations between ocular manifestations of Marfan syndrome and cardiovascular complications. This is a retrospective cohort study. The TriNetX Analytics platform, a federated health research network of aggregated deidentified electronic health record data of more than 119 million patients, was used to identify patients diagnosed with Marfan syndrome. Univariate logistic regression models were used to evaluate the association of ocular manifestations of Marfan syndrome (such as retinal tears/detachment, lens dislocation, and myopia), with cardiovascular comorbidities. Additional sensitivity analyses were performed using propensity matching. Odds ratios and 95% CIs were calculated for incidence of cardiovascular comorbidities (including aortic dissection, valvular disease, and arrhythmias) following diagnosis of Marfan syndrome. A total of 19,105 patients were identified who were diagnosed with Marfan disease without ocular manifestations, and an additional 3887 Marfan patients with ocular comorbidities. Patients who were diagnosed with ocular disease included

883 with ectopic lens, 417 with retinal tear or detachment, 683 with aphakia, 534 with pseudophakia, and 2465 with myopia. Patients with any ocular manifestations of Marfan were significantly more likely to be diagnosed with all cardiovascular comorbidities modeled including aortic aneurysm and dissection (OR 2.035; P < .0001), mitral valve prolapse (OR 2.725; P < .0001), tricuspid valve disorders (OR 2.142; P < .0001), cardiac arrhythmias (OR 1.836; P < .0001), and all cardiovascular outcomes combined (OR 2.194; P < .0001). In a large and diverse cohort of patients with Marfan syndrome, ocular manifestations of the disorder appear strongly associated with cardiovascular comorbidities.

The central retinal thickness and its related genotype in ABCA4-related retinopathy
Wang Y, Li T, Yu S, et al for the Shanghai Inherited Retinal Disease (SHIRD) Study Group
Eye (Lond) 2024 May; Epublished
This is an analysis of a cohort of 66 patients with ABCA4-related retinopathy, looking to evaluate the type of pathogenic variant correlation with the severity of macular atrophy on OCT. They concluded that the average Central retinal thickness was not affected by the mutation type; however, inframe mutations could lead to less Central retinal thickness and possibly accelerate the rate of decrease. This Information can be used as a caveat or as an endpoint in clinical trials.

The Systemic Genotype-Phenotype Characterization of PAX6-Related Eye Disease in 164 Chinese Families
Jiang Y, Yi Z, Zheng Y, et al
Invest Ophthalmol Vis Sci 2024;65(10):46
PAX6 is an important gene that encodes an essential transcription factor important for ocular, olfactory, pancreatic, and CNS development. PAX6 mutations cause a wide variety of phenotypic presentations, including aniridia, nystagmus, foveal hypoplasia, coloboma, cataract, high myopia, and microphthalmia. Complete ophthalmic exams and genetic testing was performed on a cohort of 10530 patients. A total of 119 pathogenic or likely pathogenic PAX6 variants, including 74 truncation, 31 missense, and 14 others, were identified in 228 patients from 164 unrelated families. The most common phenotypes were foveal hypoplasia (97.8%), nystagmus (92.6%), aniridia (76.7%), cataract (36.8%), and iris hypoplasia (22.4%). Mosaicism ranging from 13.9% to 18.8% was identified in 3 unrelated patients' parents with relatively mild phenotypes. Missense variants in the linker region of the paired domain were associated with high myopia, whereas truncation variants in the homeodomain and proline-serine-threonine-rich domain were associated with hyperopia. Similarly, the degree of iris defects, visual acuity, and associated ocular comorbidity varied among the different types and locations of PAX6 variants. Overall, this study adds important information as we move towards precision medicine and the ability to prognosticate based on genetic testing.

Frequency and Genetic Spectrum of Inherited Retinal Dystrophies in a Large Dutch Pediatric Cohort: The RD5000 Consortium
Heutinck PAT, van den Born LI, Vermeer M, et al
Invest Ophthalmol Vis Sci 2024;65(10):40

IRDs are a clinically heterogeneous group of genetic diseases that account for a significant proportion of juvenile blindness. With the advent of gene therapy, these previously untreatable diseases have become potentially treatable. This descriptive study with retrospective analysis studied all children and adolescents registered in the database with a diagnosis with IRD before the age of 20 years. Phenotypes were categorized as nonsyndromic (progressive and stationary IRD) and syndromic IRD. Genetic causes were determined by whole-exome sequencing in a majority of cases. A total of 624 patients were studied with a median age at presentation of 13 years. Retinitis pigmentosa (20%), Leber congenital amaurosis (16%), X-linked retinoschisis (10%), and achromatopsia (10%) were the most frequent phenotypes. The genetic cause was identified in 76% of the genetically examined patients. The most frequent disease-causing genes were RS1 (9%), CEP290 (8%), CNGB3 (6%), and CRB1 (5%). As IRDs increasingly become potentially treatable, knowledge of the most common pathogenic variants will allow targeting of research and interventions to reach as many patients as possible.

Identification of Potential Drug Targets for Myopia Through Mendelian Randomization
Qin Y, Lei C, Lin T, Han X, Wang D
Invest Ophthalmol Vis Sci 2024;65(10):13
Myopia is a growing public health concern that is poorly understood from a genetics standpoint given the complex pathogenesis of myopia. Mendelian randomization analysis utilizes genetic data to deduce causal associations between exposure and outcome variable. Two large cohorts were analyzed with greater than 300,000 patients. The systemic drug target identification revealed 6 possible causal gene targets for myopia – CD34, CD55, Wnt3, LCAT, BTN3A1 and TSSK6. Functional analysis found that dopaminergic neuron differentiation, cell adhesion, Wnt signaling pathway, and plasma lipoprotein-associated pathways may be involved in myopia pathogenesis. Drug prediction and molecular docking corroborated the pharmacological value of these targets with LCAT demonstrating the strongest binding affinity. This large Mendelian study provides additional insights into the pathogenesis of myopia and may aid in identification of future treatments.

High Clinical Exome Sequencing Diagnostic Rates and Novel Phenotypic Expansions for Nonisolated Microphthalmia, Anophthalmia, and Coloboma
Kunisetty B, Martin-Giacalone BA, Zhao X, et al
Invest Ophthalmol Vis Sci 2024;65(3):25
The purpose of this study is to determine the efficacy of clinical whole exome sequencing (cES) in cases of nonisolated microphthalmia, anophthalmia, and coloboma (MAC). Currently only a small subset of these patients have a molecular diagnosis. In this retrospective study of 189 patients with clinical diagnoses of nonisolated MAC referred to Baylor genetics, the efficacy of cES to achieve molecular diagnosis was between 32.3% (definitive and probably diagnosis) to 48.1% (including provisional diagnosis). Most genes affected in this cohort were note among genes currently screened in clinically available ophthalmologic gene panels, and a subset of the genes were not previously associated with MAC. This study demonstrates that cES is an effective method to help establish molecular diagnosis in patients with nonisolated MAC, and should be considered in addition to established gene panels.

In Vivo Assessment of Retinal Phenotypes in Axenfeld-Rieger Syndrome
Untaroiu A, Reis LM, Higgins BP, et al
Invest Ophthalmol Vis Sci 2024;65(4):20
Axenfeld-Rieger syndrome (ARS) is characterized by ocular anomalies including posterior embryotoxon, iridocorneal adhesions, corectopia/iris hypoplasia, and developmental glaucoma. Anterior segment pathology is well known in ARS, but the role of potential posterior segment abnormalities is less well known. This case series aimed to learn posterior segment pathology in ARS patients (3 with FOXC1-ARS and 10 with PITX2-ARS). Results showed average ganglion cell and inner plexiform layer thickness was lower in PITX2-ARS, consistent with the glaucoma history in this group. A novel phenotype of foveal hypoplasia was noted in 40% of individuals with PITX2-ARS (but none with FOXC1-ARS). Analysis of known foveal hypoplasia genes failed to identify an alternative explanation. Foveal cone density was decreased in one individual with foveal hypoplasia and normal in six without foveal hypoplasia. Two individuals (one from each group) demonstrated non-foveal retinal irregularities with regions of photoreceptor anomalies on OCT and adaptive optics scanning light ophthalmoscopy (AOSLO). These findings suggest that PITX2 mutations affect posterior segment development and may contribute to visual deficits in these patients, and that in complete evaluation of these individuals, attention should be directed to the posterior segment in addition to anterior segment studies.

The Systemic Genotype-Phenotype Characterization of PAX6-Related Eye Disease in 164 Chinese Families
Jiang Y, Yi Z, Zheng Y, et al
Invest Ophthalmol Vis Sci 2024;65(10):46
PAX6 plays a vital role in eye development. Variants in this gene can lead to a broad spectrum of phenotypes, with aniridia being the most common ocular malformation due to single gene variants. Other PAX6 phenotypes include nystagmus, foveal hypoplasia, coloboma, cataract, glaucoma, microphthalmia, high myopia, aniridia-related keratopathy (ARK). This study aims to evaluate the genetic and phenotypic characteristics and elucidate the genotype-phenotype correlations of a large Chinese cohort with PAX6-related disorders. A total of 119 pathogenic or likely pathogenic PAX6 variants were identified in 228 patients from 164 unrelated families. Nearly all patients exhibited foveal hypoplasia (97.8%), which was the most common ocular finding. The degree of iris defects, visual acuity, and associated ocular comorbidity varied among the different types and locations of PAX6 variants. Mosaicism ranging from 13.9% to 18.8% was identified in 3 unrelated patients' parents with relatively mild phenotypes. This study confirms findings from other studies that foveal hypoplasia is a very common finding in PAX6 variants, in addition to aniridia. Recognition of mosaicism in atypical cases or parents with very mild phenotypes is important in genetic counseling as their offspring may be at increased risk of more severe phenotype.

Identification of Potential Drug Targets for Myopia Through Mendelian Randomization
Qin Y, Lei C, Lin T, Han X, Wang D
Invest Ophthalmol Vis Sci 2024;65(10):13
Myopia is a common refractive error that has become a significant public health concern globally. This study aims to identify potential drug targets for myopia and explore underlying

mechanisms. Mendelian randomization (MR) is a type of analysis that utilizes genetic data to deduce causal associations between an exposure and an outcome variable. MR was used to assess the effect of 2684 pharmacologically targetable genes in the blood and retina on the risk of myopia from a genome-wide association study (GWAS) for age-at-onset of spectacle wearing-inferred mean spherical equivalent (MSE) in a large European cohort, and further validated in a GWAS for autorefraction-measured MSE. Additional functional studies were carried out to explore the functional roles of these targets. This study found 6 putative genetically causal targets for myopia—CD34, CD55, Wnt3, LCAT, BTN3A1, and TSSK6. Functional analysis identified their associated pathways that may be involved in myopia pathogenesis. Drug prediction and molecular docking corroborated the pharmacological value of these targets with LCAT demonstrating the strongest binding affinity. This study provides interesting preliminary data on potential drug targets for myopia. Candidate genes should be further studied.

Frequency and Genetic Spectrum of Inherited Retinal Dystrophies in a Large Dutch Pediatric Cohort: The RD5000 Consortium
Heutinck PAT, van den Born LI, Vermeer M, et al
Invest Ophthalmol Vis Sci 2024;65(10):40
Inherited retinal dystrophies (IRDs) are a heterogeneous group of monogenic diseases causing retinal degeneration resulting in severe vision loss. With the onset of gene therapies becoming available for some IRDs, it is crucial to identify common phenotypes and causative genes in children, as young patients may benefit the most from such treatments. This study investigated pediatric IRD with the aim of highlighting relevant groups for future therapy. Using Dutch RD5000 database, diagnostic, genetic, and demographic data were collected from medical charts of patients with IRD aged up to 20 years. Subsequent analysis determined frequencies of phenotypes and genetic causes. Phenotypes were categorized as nonsyndromic (progressive and stationary IRD) and syndromic IRD. Results showed that in this population, the most frequent pediatric phenotypes include retinitis pigmentosa, Leber congenital amaurosis, X-linked retinoschisis, and achromatopsia. The genetic cause was identified in 76% of the genetically examined patients. The most frequently disease-causing genes were RS1, CEP290, CNGB3, and CRB1. Diagnostic yield after reanalysis of genetic data increased by 7%. This study provides information on the most common pediatric IRDs and their genetic etiologies, which may be useful to guide the future development of targeted therapies. One limitation of this study is that the data is from a relatively homogenous population of the Dutch registry, and may not reflect findings in other populations.

Gene–Environment Interaction Between CAST Gene and Eye-Rubbing in the Chinese Keratoconus Cohort Study: A Case-Only Study
Yin S, Xu L, Yang K, et al
Invest Ophthalmol Vis Sci 2024;65(10):36
Keratoconus (KC) is a complex disease influenced by the combination of genetic and environmental factors. Eye rubbing has been identified in several studies to have strong associations with KC. CAST has been identified as a susceptibility gene of KC, its protein product is expressed in the corneal epithelium. This study set out to explore potential

gene–environment interaction between the CAST gene and eye-rubbing. 930 patients from the Chinese Keratoconus cohort study were included in this study, excluding individuals with syndrome diseases and concomitant corneal dystrophy. Genotyping of single nucleotide polymorphism (SNP) was conducted. Eye rubbing status of patients were collected from face-to-face interviews with ophthalmologists. The gene–environment interactions between CAST genotype and eye-rubbing were then analyzed. Three SNPs in CAST gene were found to have statistically significant interactions with increased eye rubbing. Notably, the minor alleles of these three SNPs exhibited negative interactions with eye-rubbing. These results propose an interesting hypothesis of a biologic mechanism of KC. Future studies of this gene may help further elucidate the mechanism of disease and provide a therapeutic target.

Ophthalmic features of Lamb-Shaffer syndrome: a case series
Glidai Y, Aung MH, Edmond J, Lawrence L, Vicente GV, Kodsi SR
J AAPOS 2024;28(3):103919
Lamb-Shaffer syndrome (LSS) is a rare neurodevelopmental disorder caused by heterozygous mutations at the SRY-related HMG box (SOX5) gene. LSS is characterized by growth retardation, neurological and speech delay, musculoskeletal abnormalities, heart and genitourinary defects, and characteristic facial features. This case series aims to describe ophthalmic findings in pediatric LSS patients. Six individuals are included in this retrospective chart review. Strabismus was present in 5 patients, with exotropia being most common. All patients had significant refractive errors, mostly commonly significant astigmatism. All patients had optic nerve abnormalities, including pallor, hypoplasia, and anomalous appearance. Other less common ocular findings include ptosis, nasolacrimal duct obstruction, and nystagmus. Based on this study, the authors suggest that all LLS patients undergo a complete eye exam upon diagnosis, ideally with OCT as optic disc disorder is common.

Novel Splicing Variants in the ARR3 Gene Cause the Female-Limited Early-Onset High Myopia
Niu J, Zhu W, Jin X, Teng X, Zhang J
Invest Ophthalmol Vis Sci 2024;65(3):32
Early onset high myopia (eoHM) is a rare condition characterized by severe nearsightedness that manifests in early childhood and has significant implications for vision. Variants in the ARR3 gene have been linked to eoHM with a X-linked female-limited inheritance. This study identified two Chinese families with novel ARR3 splicing variants associated with eoHM. The authors used Minigene constructs to assess the effects of the variants on splicing, which showed that both variants resulted in abnormal splicing and introduced premature termination codons. Based on genetic and experimental evidence, the ARR3–eoHM relationship was classified as “definitive.” The novel splicing variants of ARR3 gene identified by this study should be included in future genetic examination of female eoHM patients.

Association of Novel Loci With Keratoconus Susceptibility in a Chinese Genome-Wide Association Study
Xu L, Zheng X, Yin S, et al
Invest Ophthalmol Vis Sci 2024;65(5):29

Keratoconus (KC) is a complex corneal disorder of progressive thinning and protrusion. In this study, the authors aimed to identify genetic associations with KC and their correlation to phenotypes of corneal thickness and corneal curvature. This is a genome-wide association study conducted on 853 patients with KC and 6248 controls in China. The authors identified four single-nucleotide polymorphisms (SNPs) within four risk loci associated with KC in Chinese patients. This study provides some preliminary targets for futures studies of the genetic basis of KC. One strength of this study is its large study population. Limitation include the limited understanding of the mechanistic roles of these SNPs in KC. Future studies of these SNPs may help further elucidate the pathophysiology.

The LCHADD Mouse Model Recapitulates Early-Stage Chorioretinopathy in LCHADD Patients
Babcock SJ, Curtis AG, Gaston G, et al.
Invest Ophthalmol Vis Sci 2024;65(6):33
Studies have shown that the retinal pigment epithelium (RPE) relies on fatty acid oxidation (FAO) for energy. The only FAO disorder that presents with chorioretinopathy is long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD). In this disorder, young patients with first present with pigment clumping and hypopigmentation at the posterior pole, later develop choroidal atrophy at the posterior pole and report poor night vision. In late stages, loss of photoreceptors, RPE, and choroid in the central fundus lead to blindness. This study characterizes the chorioretinopathy progression in a recently reported LCHADD mouse. The results show that LCHADD RPE/sclera samples had increase in long-chain hydroxyacylcarnitines, altered RPE structure, increased macrophages in the subretinal space, and differentially expressed gene compared to wildtype mice. Visual assessment show that LCHADD mice have progressively decreased visual performance. Behavioral and tissues findings of this LCHADD mouse model recapitulates early-stage chorioretinopathy seen in patients with LCHADD and is a useful model for studying LCHADD chorioretinopathy. Future studies using this mouse model may further elucidate the mechanism of this disease, as well as provide potential therapeutic targets.

Adams-Oliver syndrome associated with refractory glaucoma
Pillai MR, Pabolu C, R R, Chaudhary S, Sr K, Puthuran GV
J AAPOS 2024;28(4):103950
Adams-Oliver syndrome (AOS) is a rare inherited disorder characterized by aplasia cutis congenita, cutis marmorata telangiectatica congenita, and terminal limb defects. Ocular associations have been rarely reported. This case report describes a 6-month-old boy with AOS who presented with bilateral glaucoma, megalocornea, and anterior polar cataract. Topical medication was unsatisfactory in IOP control, and the patient required multiple glaucoma surgeries to achieve IOP control. A third of AOS cases have been linked to mutation in genes in the CDC42/RAC1 or NOTCH signaling pathway. However, in two-thirds of the cases, no genetic cause is identified. The exact mechanism of pathogenesis is unknown, but AOS is thought to be due to vascular disruption during embryogenesis. This case report describes ocular findings in AOS. Eye exam should be considered in infants with AOS to evaluate for vision-threatening disorders.

Alström syndrome mimicking spasmus nutans: report of a novel ALMS1 variant
Rodrigues R, Santos Silva R, Penas S, et al
J AAPOS 2024;28(2):103853
This case report describes a case of an otherwise healthy 6-year-old girl presenting with poor visual acuity, photophobia, and abnormal eye and head movements who was initially diagnosed with spasmus nutans. A remote history of presumed viral cardiomyopathy and further ERG testing raised suspicion for Alström syndrome, which was then confirmed by genetic testing, identifying a novel ALMS1 variant. Alström syndrome is a progressive multisystem ciliopathy disorder with autosomal recessive inheritance. The earliest clinical manifestation in children include nystagmus and photophobia , presenting in the first few months of life. Systemic manifestations become evident in adolescence and adulthood. The diagnosis of spasmus nutans should be one of exclusion. This case demonstrates that thorough history taking and ERG are important in the evaluation of poor vision, nystagmus, and photophobia to establish accurate diagnosis.

Congenital cranial dysinnervation disorder with homozygous KIF26A variant
Gregg AT, Gateman T, Whitman MC
J AAPOS 2024;28(4):103951
Congenital fibrosis of the extraocular muscles (CFEOM) type 1 is associated with heterozygous missense variants in KIF21A, which encodes a kinesin-like motor protein. Individuals with CFEOM1 have severe paralysis of upgaze and ptosis, resulting in a pronounced chin-up head posture. There can also be limitations of horizontal eye movements. Loss of function of KIF26A, an unconventional kinesin motor protein that lacks ATP-dependent motor activity, has been reported to cause a spectrum of congenital brain malformations associated with defects in migration, localization, and growth of excitatory neurons. It has also been associated with megacolon resembling Hirschsprung's disease. This case report describes a young boy with homozygous loss of function of KIF26A, who presented with restricted eye movements, specifically restricted upgaze and downgaze with variable nystagmus and dissociated vertical eye movements. This child was diagnosed with congenital cranial dysinnervation disorder (CCDD), most similar to CFEOM, and is the first report of a congenital cranial dysinnervation disorder caused by a kinesin other than KIF21A. This new finding of a case of CCDD caused by loss of function in an kinesin motor protein that lacks ATP-dependent motor activity suggests that the molecular mechanism of CFEOM may be disruption of microtubule stability.

Duane syndrome in association with 48,XXYY karyotype
Weis A, Bialer MG, Kodsi S
J AAPOS 2011;15(3):295-296
Duane syndrome is an ocular motility disorder consisting of deficient horizontal eye movements, eyelid retraction, palpebral fissure narrowing, and abnormal vertical eye movements. Although most cases are sporadic, it has been reported in several syndromes and chromosome abnormalities. Autosomal-dominant inheritance is seen in up to 10% of cases. This case report describes a young child diagnosed with type 1 Duane syndrome of the right eye, in the setting of having significant developmental delays, which prompted genetic work up and diagnosis of

48,XXYY chromosomal duplication. The 48,XXYY syndrome is a rare syndrome involving duplication of the sex chromosomes. This is the first case of Duane syndrome associated with it.

Duane syndrome in association with congenital disorder of glycosylation type Ig (ALG12-CDG)
Li J, Kolin DA, Nallasamy S, et al
J AAPOS 2024;28(4):103954
Congenital disorders of glycosylation type I (CDG-I) are a group of autosomal recessive genetic multisystem disorders caused by defective glycoprotein biosynthesis. ALG12-CDG (CDG-Ig) is a rare subtype a rare subtype of CDG-I. This is a case report of a 17-year-old female diagnosed with bilateral Duane syndrome, in the setting of other systemic findings including sensorineural hearing loss, primary amenorrhea, and short stature. Genetic testing found compound heterozygous variants in the ALG12 gene. There have been previous reports of ALG12-CDG associated ocular findings including retinal detachment, infantile cataracts, and retinitis pigmentosa. This report provides further information on nonisolated Duane syndrome. Individuals with Duane syndrome who also have dysmorphic features should undergo genetic evaluation.

Duane syndrome associated with Rubinstein-Taybi syndrome type II
Sharma A, Suraneni S, Bitrian E, McKeown CA
J AAPOS Published online September 4, 2024
Rubinstein-Taybi syndrome (RTS) is most commonly caused by pathogenic mutations in CREBBP and EP300 genes. Ocular manifestations of RTS are common and are diverse. This is a case report that describes an 8-month-old infant diagnosed with Duane syndrome of the left eye. Additionally, the child exhibited systemic findings including microcephaly, generalized hypertonia, and torticollis. Genetic work up revealed an autosomal dominant EP300 c.2470 C.Tp.Q824X heterozygous pathogenic variant consistent with a diagnosis of Rubinstein-Taybi syndrome type II. The concurrence of RTS and Duane syndrome is rare but has been previously reported as well. The authors hypothesized that the central nervous system involvement of RTS may affect cranial nerves during a critical period of ocular development during embryogenesis. Further studies of patients with both RTS and Duane syndrome may help elucidate the pathogenesis of both disorders.

Ocular features of NGLY1 deficiency from a prospective longitudinal cohort
Frater CH, Ruzhnikov MRZ, Beres S, et al.
J AAPOS 2024;28(3):103925
NGLY1 deficiency is a rare autosomal recessive disorder characterized by global developmental delay, liver enzyme abnormalities, movement disorder, polyneuropathy, and hypo- or alacrima. This case series of prospective natural history study of 29 individuals with NGLY1 deficiency aims to characterize the full spectrum ocular phenotypes associated with this disorder. The patient received evaluations and follow up over 2 years. Results show at least one ocular sign or symptom in 90% of participants, most commonly decreased tears, refractive error, and chronic infection. Daily eye medication, including artificial tears, ophthalmic ointment, and topical antibiotics were used by 62% of patients. Ophthalmological examination confirmed refractive errors and corneal abnormalities in the majority of patients. A limitation of this study is

that a number of the follow up evaluations were performed virtually, with data reported by caregivers. A strength of this study is the relatively large patient sample representing 10 countries, especially since this is a rare disorder. This study reports hypolacrima and corneal findings to be significant in NGLY1 deficiency, and highlights the importance of eye exams for these patients as well as preventive treatments for the ocular surface to preserve vision.

Retinal detachment, vitreous hemorrhage, and foveal hypoplasia associated with 3q27.1q27.2 microdeletion
Tahbaz M, Ebrahimiadib N, Iyer SSR, et al.
J AAPOS 2024;28(4):103960
Terminal microdeletions on chromosome 3q have been reported to exhibit a heterogenous phenotype including pre- or postnatal growth restriction, developmental delay, intellectual disability, thrombocytopenia, and short stature. Deletions involving the SOX2 gene (3q26.3-q27) are known to cause anophthalmia/microphthalmia. In this case report, the authors describe a 9-year-old boy with 1.4megabase deletion of 3q27.1q27.2 who presented with retinal detachment in one eye, vitreous hemorrhage in the contralateral eye, and foveal hypoplasia in both eyes. This is the first report describing vitreoretinal findings in a patient with terminal deletion of chromosome 3q not involving SOX2. The authors hypothesize that deletions of DVL3, EPHB3, and PARL may have contributed to this patient's ocular pathology. DVL3 and EPHB3 are known regulators of retinal blood vessel growth, while PARL may play a role in promoting retinal ganglion cell death. Given the severity of vision-threatening ocular findings in this patient, the authors suggest that patients with 3q terminal deletions undergo routine ophthalmic exams.

Vitreopapillary Traction in Stickler Type IV COL9A1
Adhan I, Kim JB, Vuppala A
JAMA Ophthalmol 2024;142(5):e235766
Stickler syndrome (SS) is a genetic disorder primarily affecting connective tissue, and typically manifests with ocular, joint, palate, and facial developmental abnormalities. Ocular features include vitreous formation anomalies, high myopia, lamellar quadratic cataract, and retinal perivascular lattice degeneration with high occurrence of retinal detachments. It is genetically heterogenous. This is a case report of patient with genetically confirmed SS type IV caused by a variant of COL9A1 that is rare and recessively inherited. The patient presented with shadows and ghosting of vision bilaterally, and was found to have bilateral vitreopapillary traction associated with pseudoedema, but without other SS ocular manifestations. This is the first report of this specific vitreous abnormality in a patient with SS type IV. This new finding should be considered in the clinical evaluation of SS patients who present with atypical symptoms.

DICER1 Syndrome Discovered Through an Eye Tumor
Fortarezza F, Midena G, Parrozzani R, et al
JAMA Ophthalmol 2024;142(7):682-683
Medulloepithelioma of the ciliary body (MECB) is a rare tumor that could be associated with DICER1 tumor predisposition syndrome. In this case report, a 9-year-old boy presented with unilateral vision impairment and was found to have microphthalmos, a retrolental cyclitic

membrane, and a ciliary body mass and total retinal detachment in the affected eye. Orbital MRI showed a hypervascular lesion with enhancement in the thickened ciliary body consistent with MECB. Enucleation was performed. The real-time polymerase chain reaction conducted on tumor tissue revealed the presence of a mutation of the DICER1 gene associated with a diagnosis of malignant MECB. Subsequently systemic work up revealed multinodular goiter. The concurrent diagnosis of MECB and thyroid disease prompted work up for a genetic syndrome, and a germline heterozygous pathogenic DICER1 mutation was identified. MECB is the most common congenital and early childhood neoplasm of the nonpigmented epithelium of the ciliary body. While most cases are sporadic, it can occur with DICER1 syndrome, an autosomal dominant genetic disorder. In this report, MECB was the initial manifestation of a germline DICER1 mutation, highlighting the importance of systemic work up and genetic consultation in MECB patients.

Simultaneous Pigmented Paravenous Retinochoroidal Atrophy and Retinitis Pigmentosa in the Contralateral Eye
Plaza DG, Jelstrup AB, Navarro R
JAMA Ophthalmol 2024;142(3):e234804
This is a case report of a woman who presented with well-demarcated areas of pigmented retinochoroidal atrophy along the vascular arcades with normal optic disc in the right eye, consistent with pigmented paravenous retinochoroidal atrophy (PPRCA), and in the left eye, diffuse bony spicules, disc pallor, and attenuated arterioles suggestive of retinitis pigmentosa (RP). Over the course of 10 years, her visual acuity in the eye with PPRCA was preserved, while the eye with RP significantly decreased to 20/400, corresponding to the expected evolution of each separated disease. Both PPRCA and RP are conditions that classically present bilaterally and symmetrically. There are few reports where both diseases occur in the same patient. No pathogenic variant was identified in the whole-exome sequencing for this patient, including CRB1. This case reports demonstrates a unique presentation of two different dystrophies in two different eyes of the same patient. Further genetic studies may help elucidate the connection between these two clinical entities.

Glaucoma

Progression to bilaterality in unilateral primary congenital glaucoma
Majumdar A, Panigrahi A, Singh A, et al
J AAPOS 2024;28(4):103967
This study investigated the incidence of increased intraocular pressure (IOP) or glaucoma in the fellow eye of patients with unilateral primary congenital glaucoma (PCG) and aimed to identify risk factors for elevated IOP. Conducted at the All India Institute of Medical Sciences, it included 54 patients with unilateral PCG and analyzed data from medical records at baseline, 5 years, and final follow-up. The study found that 32% of fellow eyes developed ocular hypertension or progressive optic neuropathy, typically after age 5. A larger corneal diameter (>12 mm) in the unaffected fellow eye was a strong predictor of progression to glaucoma. While the study benefits from a long follow-up period and comprehensive data, it is limited by its retrospective nature, small sample size, and potential confounding factors related to normal growth. The findings underscore the need for long-term monitoring and evaluation of fellow eyes in patients with unilateral PCG to detect and manage potential glaucoma.

Incidence of and risk factors for suspected and definitive glaucoma after bilateral congenital cataract surgery: a 5-year follow-up
Wang J, Wu X, Wang Q, et al
Br J Ophthalmol 2024;108(3):476-483
This is a cohort of 351 patients with bilateral congenital cataracts who underwent surgery and had a 5-year follow-up period. Only 57 patients were excluded due to lost to followup. Mean age at surgery was 1.82 years with a mean followup period of 6.26 years. 130 eyes were left aphakic, 219 eyes had primary lensectomy/IOL implantation, and 337 underwent primary lensectomy with secondary IOL implantation. The surgeons' general approach was to leave children under aged 2 years aphakic during the primary surgery. 59 eyes of 35 patients were diagnosed with definitive and suspected glaucoma. By eye counts, the cumulative incidence of definitive and suspected glaucoma was relatively low: 6.12% with definitive glaucoma (42/686 eyes), and 2.48% with suspected glaucoma (17/686). Definitive and suspected glaucoma developed at a mean time of 2.84±1.75 years (range 0.02–7.33 years) after cataract surgery. In the aphakia group, 29 of 130 eyes (22.3%) had definitive and suspected glaucoma. There was no definitive glaucoma or suspected glaucoma in 219 eyes of the primary IOL implantation group. Microcornea, congenital cataract family history, and initial anterior vitrectomy were risk factors, wheras age at surgery was not significant. While it appears that primary IOL implantation may be a protective factor, more research into the contributing factors needs to be done before it can change clinical practice.

Secondary Glaucoma after Cataract Surgery Performed in Infancy in Congenital Rubella Syndrome: A Case Control Study
Panicker GJ, Agarkar S, Khurana M, et al
Ophthalmol Glaucoma 2024 Jul 14:S2589-4196(24)00130-3
This retrospective case control study aimed to compare the rates of secondary glaucoma following infantile cataract surgery in patients with and without congenital rubella syndrome

(CRS). 101 eyes with CRS and 110 age-matched control patients with non-CRS associated infantile cataracts with follow up of at least 1 year were included (mean follow up 5.8±3.7 years for CRS, 6.4± 3.4 years for non-CRS). Surgical intervention was performed within a similar timeframe in both groups, cataract extraction was performed in a similar fashion, and there was no significant difference in pre-operative IOP between the two groups (p=0.86). Post-op glaucoma diagnosis was made based on IATS and CGRN criteria. Eyes with CRS-associated cataract had significantly higher central corneal thickness (p=0.002), lower corneal diameter (p=0.001) and axial length (p=0.0002), with a higher prevalence of microcornea (p=0.0001) and microphthalmos (p=0.0002). While there was a trend toward higher rates of secondary glaucoma in CRS group (32.7%) compared to controls (24.5%), this was not statistically significant (p=0.19). The survival rate of no glaucoma was similar at 5 years post-op, but by 10 years, the cumulative probability of remaining glaucoma free was higher in the control group (0.8) compared to CRS group (0.53) (p=0.034). Univariate analysis showed a significant association between microphthalmos, nuclear cataract, and microcornea with glaucoma development in the CRS group. The authors pointed out that the entire study cohort had not yet reached 10-years post-op, and thus the apparent trend toward later difference in glaucoma rates warrants further study, but at younger ages there was no significant difference between rates of glaucoma development.

A Prospective Study of the Effects of General Anesthesia on Intraocular Pressure in Healthy Children
Oatts JT, Shen S, Zhu H, et al
Ophthalmol Sci 2023;4(3):100455
This prospective study aimed to evaluate the effect of general anesthesia on intraocular pressure to better help understand interpretation of this important ocular vital sign when evaluated in an operative setting. IOP measurements were taken using iCare at seven time points: preop, 1, 3, and 5 minutes post-induction, and 1, 3, and 5 minutes post-airway placement. Anesthetic protocol was also standardized with mask sevoflurane and propofol maintenance for all cases. Of the 85 children, mean age 7.5±2.9 years, the mean pre-op IOP measurement was 20.1±3.7mmHg. Importantly, there was a consistent trough in IOP around 3 minutes post-induction prior to airway placement, before rising again, although IOP did not rise fully to pre-op IOP, even at 5 minutes post-airway. The post-anesthesia measurements that were most predictive of the pre-op measurements were 1 minute after induction and 3 minutes post-airway, although the predictive values were relatively low. The study was also limited by a fairly homogenous population which may limit generalizability. There was also limitation in obtaining pre-op IOP on several patients which limited the sample size of this time-measure.

Continuous Wave Transscleral Cyclophotocoagulation and Endoscopic Cyclophotocoagulation in Childhood Glaucoma: A Meta-Analysis
Elhusseiny AM, Hassan AK, Elsaman AS, et al
J Glaucoma 2024;33(6):456-463
Childhood glaucoma is an important cause of childhood blindness and management is mainly surgical. This meta-analysis aimed to evaluate the effectiveness and safety of single and multiple treatment sessions of trans-scleral cyclophotocoagulation (TS-CPC) and endoscopic

cyclophotocoagulation (ECP) in childhood glaucoma as reported in English ophthalmic literature. IOP and glaucoma medication reduction, success rate (defined as post-op IOP ≤21mmHg with at least 20% IOP reduction and no further need for glaucoma intervention), and adverse effects were evaluated. A total of 17 studies were reviewed (11 TS-CPC, 5 ECP, 1 comparing the two modalities). The mean extent of treatment for TSC was 280 degrees with a mean of 33 shots at 1668mW resulting in mean IOP decrease from 31.2mmHg on a mean of 2.3 glaucoma medications to 20.8mmHg on a mean of 2.2 glaucoma medications. The mean extent of treatment for ECP was 221 degrees with power range 207-542mW, resulting in mean IOP decrease from 32.0mmHg on 1.7 medications to 22.6mmHg on 1.2 mediations. Both TS-CPC and ECP required repeat treatments (45% in TS-CPC and 27% in ECP). ECP was most commonly used in glaucoma following cataract surgery (63%). The authors postulated that the higher rate of retreatment in TS-CPC may be related to higher rate of ciliary body process regeneration as well as anatomic distortion in the setting of buphthalmos in children with glaucoma. Despite this, long term success at 5 years was similar between both treatments (42% TS-CPC, 43% ECP). The retrospective nature of this study limits ability to control for several disease-related factors as well as the extent of treatment/when surgical treatment was initiated. Yet, overall this study is helpful in pointing to at least short-term efficacy in IOP reduction with relatively low complication rates with CPC

Pilot study comparing a new virtual reality-based visual field test to standard perimetry in children
Mesfin Y, Kong A, Backus BT, et al
J AAPOS 2024 Jun;28(3):103933
While the current gold standard for formal visual field testing is standard automated perimetry, typically using Humphrey visual field (HVF) testing, this test can be challenging for children. The purpose of this study was to assess the feasibility and performance of Vivid Vision Perimetry (VVP), a new virtual reality (VR)-based visual field platform, in a pediatric population. Children aged 7-18 years with visual acuity of 20/80 or better who were undergoing HVF testing were recruited to perform VVP. VVP is a VR-based test using suprathreshold stimuli to assess 54 field locations, providing a fraction seen score. Pearson correlation coefficients were calculated to evaluate the correlation between HVF mean sensitivity and VVP mean fraction seen scores. Participants were surveyed about their experience. A total of 37 eyes from 23 participants (average age, 12.9 ± 3.1 years; 48% female) were included. All participants successfully completed VVP testing. Of the 23 HVF tests performed, 9 (39%) were deemed unreliable due to fixation losses, false positives, or false negatives. Similarly, 35% of VVP tests were unreliable based on blind spot detection. Excluding unreliable HVF tests, the correlation between HVF mean sensitivity and VVP mean fraction seen score was 0.48 (P = 0.02; 95% CI, 0.09-0.74). All participants preferred VVP over HVF, with 70% being "very satisfied" with VVP. Limitations of the study included a small sample size, the fact that most participants had normal visual fields, all patients performed HVF first, and only those who could complete both tests were included. While VVP proved to be a feasible VR-based visual field test and was preferred by participants, a significant correlation between HVF and VVP was only observed when unreliable HVF tests were excluded.

Macular and peripapillary vascular parameters in the fellow eyes of unilateral primary congenital glaucoma: a comparative study
Sadek SH, Elhusseiny AM, Saad SA, et al
J AAPOS 2024 Jun;28(3):103921
This study aimed to examine fellow eyes of patients with unilateral primary congenital glaucoma (PCG) using optical coherence tomography angiography (OCTA) and compare them with age- and refractive error-matched healthy controls. It was a prospective, multicenter, case-control study that assessed various OCTA metrics, including foveal avascular zone (FAZ) area, cup:disk ratio, and vessel density (VD) in the optic nerve head (ONH) and macular regions. The study included 48 eyes from 48 children (24 eyes per group). Results showed no significant differences in mean retinal nerve fiber layer thickness, cup:disk ratio, baseline visual acuity, or spherical equivalent between groups. However, the VD of the superficial capillary plexus (SCP) at the fovea was significantly higher in the PCG group (P = 0.04), while VD within the disk was significantly reduced in the PCG group (P = 0.03). No other macular or ONH vascular parameters showed significant differences. Limitations include a small sample size and lack of accounting for systemic factors. The study suggests that OCTA findings in fellow eyes of PCG patients may indicate early glaucomatous changes or risk factors, though further research is needed to establish clinical significance.

Combined trabeculotomy-trabeculectomy for glaucoma after congenital cataract surgery: long-term results
Bayoumi N, Khalil AK, Elsayed EN
Can J Ophthalmol Jun 2024;59(3):194-200
This is a retrospective descriptive chart review of children with glaucoma following cataract surgery (GFCS) in Alexandria, Egypt. The aim of the study was to report the long-term outcomes of children with GFCS. The authors reviewed the charts of 48 children from May 2005 to May 2018. The study included children with at least 5 years of follow-up. After applying the inclusion criteria, 32 eyes were included. The authors defined success as the reversal of optic nerve cupping regardless of IOP value. If the cup-to-disc ratio (CDR) was stable or data was not available, then IOP values were considered to determine if the outcome was a success or failure. Success was classified as true if no IOP-lowering therapy was used, and qualified if medications were used. 60% of eyes received only one procedure, 25% received two surgeries, and 6% received four surgeries. Combined angle and filtering surgery with antimetabolite was the most common procedure (63.8%), and it was also the most common first procedure. The authors reported a statistically significant reduction in CDR at 1, 3, and 6 months postoperatively compared to baseline. There was a statistically significant reduction in IOP that was maintained from the first month up to the end of 8 years of follow-up. After 8 years, there was significant attrition. The statistical plan of this study does not allow for any inferences. The authors compared the CDR to baseline throughout the study, but it would have been more interesting to create a longitudinal analysis.

Factors Associated With Visual Field Testing Reliability in Children With Glaucoma or Suspected Glaucoma
Kumar A, Hekmatjah N, Yu Y, et al

Am J Ophthalmol 2024;264:187-193
The study evaluated the reliability of Humphrey Visual Field (HVF) tests and identified factors influencing this reliability in children diagnosed with glaucoma or suspected of having glaucoma. Conducted at a single-center childhood glaucoma clinic, the retrospective cohort study analyzed HVF tests from 136 patients aged 18 or younger, with a total of 634 tests reviewed. The results indicated that only 51.3% of the HVF tests met all reliability criteria. Factors contributing to higher test-level and patient-level reliability included older age, better baseline visual acuity, and English as the primary language. Fixation losses were identified as the most common reason for unreliable tests. While reliability remained stable over time for most patients, with only 24.4% showing improvement, the study found that the number of prior tests did not significantly impact reliability. Strengths of the study include its large sample size and the use of multivariable models, while limitations involve potential biases due to not considering technician performance and language proficiency, and the limited applicability to younger children. The study highlights that age, visual acuity, and language proficiency affect HVF test reliability in children, suggesting the need for adjustments or additional support for younger or non-native English-speaking children to improve test accuracy.

Impact of social determinants of health on follow-up adherence, testing completion, and outcomes among pediatric glaucoma patients at a tertiary care center
Heckenlaible NJ, Attzs MS, Kraus CL
J AAPOS 2024 Apr;28(2):103856
Childhood glaucoma is responsible for 5% of childhood blindness and requires regular monitoring; however, there is little known about the impact of socioeconomic factors on the care and follow-up of pediatric glaucoma patients. This study aimed to identify patient characteristics associated with follow-up adherence, treatment outcomes, and OCT testing in pediatric glaucoma patients. This was a retrospective chart review done at a major urban tertiary care center. There was no difference in rates of adherence to follow-up appointments or in most recent IOP among the different groups of patients. For visual acuity, patients living within Baltimore City County attained worse outcomes. OCT assessment was less likely to be done in patients who had state insurance and lived closer to the clinic. This study is important because it raises concern that their may be disparities in care based on a patient's geographic location. Limitations of this study include its small patient cohort, single center, and retrospective nature. This study highlights the need to be aware of how patient's SES may impact the care they receive in order to try to rectify this situation.

The Effect of Childhood Obesity on Intraocular Pressure, Corneal Biomechanics, Retinal Nerve Fiber Layer, and Central Macular Thickness
Aydin Eroglu S, Akyuz Unsal AI, Verdi F, et al
J Glaucoma 2024;33(6):417-421
Some studies have previously reported a connection between childhood obesity and increased IOP, and with the increased prevalence of obesity across age groups, greater understanding of the role that this metabolic disorder plays on ocular parameters becomes more important. This study aimed to compare ocular measures including IOP, corneal hysteresis (CH), corneal compensation (CC), corneal resistance (CR), C/d, RNFL, CMT, and association with BMI in

weight normal, overweight, and obese children aged 6-17 years of age in a prospective, cross-sectional, comparative manner. Corneal measurements and IOP were taken using the ORA (Ocular Response Analyzer, Reichert Ophthalmic), and OCT images obtained of the nerve and macula using SD-OCT (Cirrus HD-OCT, Zeiss). Mean IOP, CH, and CR values were significantly higher among obese than normal-weight children. Similarly, overweight children had higher CH and CR values than normal-weight children, but similar IOP and CC values. There was a positive correlation between BMI and IOP (r=0.360, p=0.002), CH (r=0.314, p=0.007), and CR (r=0.386, p=0.001). Yet, there was no significant difference in OCT measurements across groups. The authors postulate that the different in corneal hysteresis and resistance factor in overweight and obese children may be related to changes in corneal composition and structure or possibly obesity-related chronic inflammation that may also effect the deformability of the cornea. Changes in corneal structure may have correlation with lamina cribrosa and long-term glaucoma risk. Unfortunately, this study does not report on central corneal thickness and this may be a confounding factor in interpreting this data, but trends point to a need for better understanding of how obesity may impact the eye and need for screening along with known vascular risk factors.

Visual Field Testing Frequency and Associations in Children With Glaucoma
Hekmatjah N, Kumar A, Yu Y, et al
J Glaucoma 2024;33(7):499-504
While AAO guidelines recommend at least annual visual field (VF) testing for adults with glaucoma, there are no formal recommendations regarding VF testing frequency in children. This study aimed to evaluate current VF testing frequency and clinical and sociodemographic characteristics associated with testing frequency. Patients 6-18 years of age with a diagnosis of glaucoma seen at a single academic center over a 5-year period. Patients were divided into those with vs without any VF testing. Between the groups, those without VF testing were younger (9.8 vs 11.8 years), more likely to have poor vision, glaucoma following cataract extraction, and glaucoma associated with non-acquired systemic disease. Race, ethnicity, insurance status, and distance to provider were not significantly different between those with and without testing ($p \geq 0.32$). Older patients and those with better BCVA were more likely to have VF testing; the odds of having testing increased 28% for every year of age and 27% for every 0.1 improvement in logMAR. The average number of tests per year in this cohort was 1.3; 45.9% of children had 1-2 VF/year, but also 40% had <1 VF/year. Only 44% of the VF in this cohort were considered reliable. Of note, black (-1.2, p=0.002) and multiracial patients (-1.3, p=0.008) had significantly lower VF testing frequency compared to Asian patients. The self-reported nature of race in the study limited some data clarity surrounding sociodemographic data, but the authors suggested a need to further consider these factors and socioeconomic factors as barriers to care in obtaining frequent testing

Accuracy and Reproducibility of Virtual Reality Perimetry in Children
Pruett JK, Linton EF, Donahue SP, et al
J Pediatr Ophthalmol Strabismus 2024;61(4):262-266
Visual field (VF) testing, while important in many eye diseases, is difficult in children due to the need for patient focus and compliance. New “virtual reality” VF has the potential to improve

perimetry testing and compliance in the pediatric population. In this study, the authors assess the accuracy and reproducibility of the 24-2 program of the VisuALL-K (Olleyes, Inc), a portable static automated virtual reality perimeter. A total of 19 healthy children, ages 8-17, performed two 24-2 automated perimetry tests on the device. Mean time to completion for the virtual reality perimeter was 5.1 ± 1.5 min/eye. There was a significant learning effect, with less variability on the second test. Overall, it suggests that this device may a viable alternative to traditional perimetry, though certainly more normative data is needed.

Surgical Outcomes of Early Versus Late Onset Glaucoma Associated With Sturge-Weber Syndrome
Senthilkumar VA, Prakash S, Puthuran GV, et al
J Glaucoma 2024;33(7):516-522
Glaucoma has been reported to occur in 30-70% of patients with Sturge-Weber Syndrome, typically presenting in a bimodal fashion; early onset is typically associated with angle dysgenesis whereas late onset is associated with elevated episcleral venous pressure. This study aimed to compare the long-term surgical outcomes of eyes with early versus late onset SWS-associated glaucoma. This retrospective cohort included 43 eyes of 36 children (26 early-onset, 17 late onset) who underwent surgical intervention (goniotomy, trabeculotomy, trabeculectomy, CTT, GDD, or CPC). Surgery was performed by one of two surgeons and approach was individualized based on patient age, duration and severity of glaucoma. Mean age of presentation for early onset glaucoma was ~1 year compared to ~9 years for late onset. Choroidal hemangiomas were more common in the late onset group (41% vs 16%). IOP was significantly higher (32.8±4.6 vs 26.6±8.2, and CDR was larger (0.78±0.1 vs 0.64±0.15) in the late onset group, whereas the early onset group had higher rates of buphthalmos (92% vs 41%), corneal edema (81% vs 6%), and Haab striae (69% vs 0%). Early onset was more commonly treated with angle surgery whereas late onset more commonly received GDD. By 5 years post-op, the rate of failure was about 50% in both the early and late onset groups, although early failures within the first year post op were more common in the early-onset group 26.9% vs. 5.8%, although not statistically significant p=0.56). The study was limited by a relatively small cohort size and retrospective nature. By reporting on the separate phenotypic presentations of early and late onset glaucoma, this paper highlights the importance of differentiating outcomes in these groups based on the different presentation and treatment considerations needed

Infections

Long-term Ocular Outcomes in Congenital Toxoplasmosis Treated Perinatally
Journé A, Garweg J, Ksiazek E, et al
Pediatrics 2024;153(4):e2023064114
Congenital toxoplasmosis (CT) can be accompanied by serious organ manifestations, particularly retinochoroiditis, and may occur throughout life. Patients with CT diagnosed between 1987 and 2021 were prospectively included and followed for up to 35 years. A total of 646 infected live born children were followed for a median of 12 years (range, 0.5–35); 187 patients (29%) had at least 1 ocular lesion (first at a median age of 5 years; range, 0–26 years) with peaks at 7 and 12 years. Early maternal infection and the presence of nonocular signs at birth were associated with a higher risk of retinochoroiditis, whereas delayed diagnosis of CT (after birth versus before or at birth) was associated with a lower risk (13% decrease for each additional month after birth; P = .01). A period effect for the risk of developing retinochoroiditis in patients born after 2008 was not detected. Despite prenatal screening and prolonged perinatal treatment, retinochoroiditis is not a rare event in French patients with CT and can occur well into adulthood, with peak incidences at 7 and 12 years of age. It rarely causes severe damage but warrants regular follow-up into adulthood. This article reinforces that congenitally infected children with Toxoplasmosis, can present with lesions throughout their life, even when no lesions are found perinatally.

Antibiotic Treatment and Health Care Use in Children and Adolescents With Conjunctivitis
Shapiro DJ, Geanacopoulos AT, Subramanian SV, et al
JAMA Ophthalmol 2024;142(8):779-780
Acute infectious conjunctivitis affects 1 in 8 pediatric patients annually in the US and antibiotics are frequently prescribed. Most cases are mild and self-limited regardless of treatment. The purpose of this study was to evaluate the frequency of topical antibiotic treatment and the association of antibiotic treatment with subsequent health care use among commercially insured children with acute infectious conjunctivitis in the US. Data from the 2021 MarketScan Commercial Claims and Encounters Database was used to identify children ages 1-17 years with a diagnosis of conjunctivitis. There were 44,793 ambulatory encounters included for children with a median age of 5 years (47% female). Topical antibiotics were dispensed within 1 day after 69% of encounters. They were less frequently dispensed after visits to eye clinics (34%), in children aged 6 to 11 years (66%) and children with viral conjunctivitis (28%). Ambulatory care revisits for conjunctivitis within 14 days occurred after 3.2% of index encounters. Hospitalizations for conjunctivitis occurred for 0.03% and ED revisits for 0.12% of children with no difference between those who received and did not receive topical antibiotics. In those who were initially evaluated in eye clinics, ambulatory care revisits occurred for 9.4% and antibiotic treatment was associated with increased odds of ambulatory care revisits (AOR 1.84) which may suggest a higher threshold for treatment and closer follow-up care for presumed bacterial conjunctivitis. Overall, in both those who received antibiotics and those who did not, revisits and new antibiotic prescriptions were rare. Study limitations include the inability to identify scheduled from unscheduled revisits, incomplete clinical data, and inability to confirm the accuracy of the coded diagnosis.

Autism Spectrum Disorder Diagnoses and Congenital Cytomegalovirus
Pesch MH, Leung J, Lanzieri TM, et al
Pediatrics 2024;153(6):e2023064081

The association between congenital cytomegalovirus (cCMV) and autism spectrum disorder (ASD) administrative diagnoses in US children was evaluated using a cohort study using 2014 to 2020 Medicaid claims data using diagnosis codes to identify cCMV (exposure), ASD (outcome), and covariates among children enrolled from birth through ≥4 to <7 years. Among 2 989 659 children, we identified 1044 (3.5 per 10 000) children with cCMV and 74 872 (25.0 per 1000) children with ASD. Of those with cCMV, 49% also had CNS anomaly or injury diagnosis codes. Children with cCMV were more likely to have ASD diagnoses (hazard ratio: 2.5; 95% confidence interval: 2.0–3.2, adjusting for birth year, sex, and region). This association differed by sex and absence of CNS anomaly or injury but not birth outcome. Children with (versus without) cCMV diagnoses in Medicaid claims data, most of whom likely had symptomatic cCMV, were more likely to have ASD diagnoses.

Neuro-Ophthalmology

The Relationship Between Choroidal Abnormalities and Visual Outcomes in Pediatric Patients With NF1-Associated Optic Pathway Gliomas.
Estrela T, Truong S, Garcia A, et al.
J Neuro-Ophthalmol. 2024 Mar; 44(1):p 5-9.
The purpose of this study was to evaluate the relationship between CAs and visual acuity (VA) in children with NF1-OPGs. The study included pediatric patients with NF1-OPGs from three hospitals. The study collected data on patient demographics, visual acuity, optic pathway glioma location, and optical coherence tomography scans. Only patients with good-quality scans and at least 12 months follow-up were included. The study included 41 children with NF1-OPGs, with a mean age of 10.2 years at baseline and 11.8 years at the last follow-up. Choroidal aneurysms (CAs) were identified in 38 eyes (46.3%) at baseline and 39 eyes (47.6%) at the last follow-up. There was no significant association between the presence, number, or area of CAs and visual acuity, retinal nerve fiber layer thickness, or ganglion cell layer inner plexiform layer thickness. These findings suggest that CAs do not have a significant impact on visual function in children with NF1-OPGs. Although prevalent in NF1-OPGs, CAs are not always present and their size and number remain relatively stable over time. The study had limitations due to manual measurements of choroidal aneurysms (CAs) and the limited scope of the optical coherence tomography (OCT) scans. The authors also noted that there is no standardized protocol for identifying CAs, and most are located in the posterior pole, making enhanced depth imaging OCT less helpful for their detection. While this study provides valuable insights, further research is needed to fully understand the impact of CAs on visual function in NF1-OPGs.

Pediatric optic pathway gliomas resource utilization and prevalence in the OptumLabs Data Warehouse.
Stoddard-Bennett T, Yu F, Spiegel S, et al.
J Neuro-Ophthalmol. 2024 Mar;44(1):10-15.
This cross-sectional study utilized deidentified data from the OptumLabs Data Warehouse (OLDW), a commercial insurance claims database. The study included all individuals born in 1999 or later, with claims data from January 2016 to June 2021, to identify those with an optic pathway glioma (OPG) diagnosis using ICD-10-CM codes. Only patients under 18 years of age with at least 6 months of follow-up were included. The extracted data included patient demographics, such as race, region, and insurance type, as well as details of monitoring and treatment modalities like MRI, CT, visual field (VF) testing, and optical coherence tomography (OCT). The study also tracked the use of radiation, surgery, and various chemotherapy agents, with the age at first treatment recorded. Additionally, the association between OPG and strabismus was explored by examining strabismus diagnosis claims, including age, type, and details of strabismus surgery. The estimated prevalence of pediatric optic pathway gliomas (OPGs) is 4.6 per 100,000 children, with 14% receiving chemotherapy and 6% undergoing surgery or radiation. Previous studies, such as those by Dutton et al. and Liu et al., highlight the epidemiology of OPG, showing that most cases are diagnosed before adulthood, with 45% diagnosed in children under 4 years old. While some research suggests a higher prevalence among girls and increased vision loss, this study found no definitive data on sex disparities.

Children with OPG and strabismus were more likely to undergo surgery or radiation, especially within six months of diagnosis. The study found that OPG patients in the Midwest experienced higher rates of strabismus than those in the West. Monitoring typically includes visual acuity assessments, but only 53% of patients received OCT or visual field testing, potentially due to challenges with younger children. MRI is more commonly used than CT to monitor tumor characteristics. Chemotherapy often involved carboplatin and vincristine, with no children receiving MAPK inhibitors, which are under clinical trial evaluation. Over time, surgical interventions have decreased, with more children managed conservatively through observation. Limitations of the study include reliance on insurance claims, potential data inaccuracies, and lack of Medicaid patient data, which could skew findings. Despite these limitations, the study highlights the need for consistent monitoring and early screening for visual impairments and strabismus in OPG patients.

Prevalence, time course, and visual impact of peripapillary hyperreflective ovoid mass-like structures (PHOMS) in pediatric patients with optic nerve pathologies
Jeon-Chapman J, Estrela T, Heidary G, Gise R
J AAPOS 2024;28(4):103966
The presence of peripapillary hyperreflective ovoid mass-like structures (PHOMS) are reported to have a higher prevalence in optic nerve pathology, but this has not been well studied in the pediatric population. The prevalence of PHOMS in pediatric patients with optic nerve pathologies compared to normal control subjects, the natural history of PHOMS, and visual function related to PHOMS were evaluated in this study. This is a retrospective study of a cohort of pediatric patients (<18 years of age) with diagnoses of optic nerve head drusen, optic neuritis, papilledema, papillitis, and neuroretinitis who were examined at the Boston Children's Hospital between October 2011 and April 2022. Normal subjects age 4-18 years were included for a control group. OCT images were examined for presence of PHOMS by two graders and the relationship between PHOMS and diagnosis compared to the normative group as well as associations to visual acuity, RNFL thickness, and visual fields were analyzed. PHOMS were identified in 2.7% of healthy eyes and 54.9% of eyes with optic nerve diagnosis. Compared to the control group, prevalence of PHOMS was statistically significant in patients with papilledema, optic neuritis, and optic nerve head drusen. There was no difference between the groups in RNFL thickness, GCL volume, visual field mean deviation, or visual function. Strengths include large cohort of pediatric patients with a control group and cross-sectional analysis of factors that are clinically relevant. Limitations are due to retrospective nature which leads to variability of evaluation and follow-up as well as selection bias. Tests in young children have known limitations and may result in incomplete testing. PHOMS have an increased prevalence in pediatric patients with papilledema, optic neuritis, and optic nerve head drusen but were not associated with RNFL thickness, GCL volume, or visual function in this study.

Single-line macular optic coherence tomography to confirm optic neuropathies in awake infants and young children
Duff SM, Alvarez-Falcon S, Freedman SF, El-Dairi M
J AAPOS 2024;28(4):103968

This study investigated the use of handheld optical coherence tomography (HH-OCT) to assess ganglion cell layer/inner nuclear layer (GCL/INL) and ganglion cell complex/inner nuclear layer (GCC/INL) ratios in children with optic neuropathies. Children with optic nerve hypoplasia or optic atrophy were prospectively imaged with HH-OCT, focusing on macular scans where the ganglion cell layer is most prominent. The study found that both GCL/INL and GCC/INL ratios were significantly lower in children with optic neuropathies compared to pediatric normative values. However, there was considerable intraobserver and interobserver variability, particularly for the GCC/INL ratio. The study's strengths include its novel application of HH-OCT to evaluate these ratios in a pediatric population, but limitations involve a small sample size, high variability in measurements, and no correlation with visual acuity. Clinically, HH-OCT can be a useful tool for detecting abnormal ratios in young children suspected of non-glaucomatous optic neuropathy, though further research is needed to establish correlations with visual function.

Clinical Course and Visual Outcomes of Papilledema in Pediatric Cerebral Venous Sinus Thrombosis Sun JA, Estrela T, Gise R Am J Ophthalmol 2024;263:126-132 The study aimed to examine the natural history and visual outcomes of papilledema in children with cerebral venous sinus thrombosis (CVST), a condition less studied in the pediatric population compared to adults. This retrospective case series, conducted at a single quaternary care center, reviewed medical records of 35 pediatric CVST patients diagnosed between 2000 and 2023. It assessed the prevalence, progression, and resolution of papilledema, as well as final visual outcomes. The study found that papilledema was present in 89% of patients, with 29% showing progression despite treatment. Most patients received anticoagulation and required additional treatments like acetazolamide or lumbar punctures, with papilledema resolving in an average of 107 days. However, 54% of patients experienced permanent ophthalmic sequelae, and an initial Frisén grade ≥3 was strongly linked to eventual optic atrophy. While the study offers comprehensive data and insights into papilledema's impact in children with CVST, its retrospective nature, single-center scope, and some follow-up limitations may affect the generalizability and completeness of the findings. The results highlight the significant risk of permanent visual impairment and stress the need for diligent ophthalmologic follow-ups to monitor and manage papilledema effectively.

Nausea and Vomiting as Initial Manifestations of Pediatric NMOSD
Cabal Herrera AM, Mandle Q, Varma H, Magaña S
Pediatrics 2024;153(4):e2023062269
Intractable nausea and vomiting are commonly attributed to gastrointestinal (GI) conditions but can sometimes be a symptom of an underlying central nervous system disease. Area postrema syndrome (APS) is a condition characterized by lesions of the dorsal caudal medulla and is considered a core clinical feature of neuromyelitis optica spectrum disorder (NMOSD). APS is present in up to 30% of patients ultimately diagnosed with NMOSD and can be the first presenting symptom of NMOSD in 12% of patients, as our case illustrates. Importantly, APS is highly responsive to immunotherapy. This case presents o a 14-year-old female with a history of migraines persistent nausea, vomiting, and hiccups. Multiple GI diagnoses were considered until she developed additional neurologic symptoms that prompted further workup and revealed the final diagnosis of NMOSD-APS. NMOSD-APS should be considered in the differential diagnosis for patients with intractable nausea and vomiting.

Fetal Growth Restriction Leads to an Enlarged Cup-to-Disc Ratio in Adults Born at Full Term
Fieß A, Gißler S, Mildenberger E, et al
Am J Ophthalmol 2024;262:170-177

The study investigated the impact of fetal growth restriction and excessive fetal growth on optic nerve head morphology in adulthood, focusing on individuals born full term. Conducted retrospectively, it analyzed data from individuals born between 1969 and 2002 who underwent nonmydriatic fundus photography to measure the vertical cup-to-disc ratio (VCDR) and optic disc area. The study categorized participants by birth weight percentile: severe small for gestational age (SGA), moderate SGA, average for gestational age (AGA), moderate large for gestational age (LGA), and severe LGA. It found that severe SGA was associated with a larger VCDR, and placental insufficiency was also linked to a larger VCDR. Additionally, the optic disc area was smaller in those born moderately SGA. While the study benefits from a large sample size and standardized measurement procedures, its limitations include potential selection bias, a lack of generalizability due to the predominance of white participants, and no adjustment for multiple comparisons. Clinically, the findings suggest that severe fetal growth restriction may lead to changes in optic nerve head morphology, potentially increasing the risk of optic disc diseases later in life, which could influence future screening and monitoring practices for individuals with a history of abnormal fetal growth.

Nystagmus

Modernizing the evaluation of infantile nystagmus: the role of handheld optical coherence tomography
Joseph S, Naithani R, Alvarez S, et al
J AAPOS 2024 Jun;28(3):103924
Infantile nystagmus syndrome, an eye movement disorder diagnosed within the first six months of life, can be associated with afferent problems, either in the anterior or posterior segments, or may present as an isolated idiopathic condition. Current clinical guidelines recommend ancillary testing, such as electroretinography (ERG) or magnetic resonance imaging (MRI), based on specific historical and examination findings. The aim of this study was to assess the role of handheld optical coherence tomography (HH-OCT) in the initial diagnostic evaluation of infantile nystagmus. In this cross-sectional case series, the medical records of all children with infantile nystagmus who underwent HH-OCT imaging at Duke Eye Center between August 2016 and July 2021 were retrospectively reviewed. Children with anterior segment disorders, evident retina or optic nerve pathology, bilateral ophthalmoplegia, or Down syndrome were excluded. The study compared the testing recommendations (MRI vs. ERG) made by a pediatric neuro-ophthalmologist based on clinical findings alone against those made using both clinical findings and HH-OCT for each patient. A total of 39 cases were included, with a mean presenting age of 1.3 years. Final diagnoses included retinal or foveal abnormalities (7 cases), optic nerve pathology (13 cases), idiopathic nystagmus (10 cases), and unknown etiology (9 cases). HH-OCT findings identified optic nerve hypoplasia (1 case), optic nerve elevation (3 cases), persistence of the inner retinal layers at the fovea (9 cases), thin ganglion cell layer (8 cases), ellipsoid zone abnormalities (3 cases), and thin choroid (1 case). In 41% of cases (16 children), HH-OCT findings led to changes in initial management, including avoiding MRI in 5 cases and ERG in 10 cases. One of the study's strengths was that all cases were reviewed by a pediatric neuro-ophthalmologist. However, limitations included its retrospective design, small sample size, and the uncertainty regarding the percentage of patients in whom good-quality HH-OCT images were obtained. HH-OCT has the potential to enhance and streamline the evaluation of infantile nystagmus, reducing the number of children who require diagnostically ambiguous and sedation-requiring procedures, thus potentially expediting the time to diagnosis.

ERG Responses in Albinism, Idiopathic Infantile Nystagmus, and Controls
Tu Z, Degg C, Bach M, et al
Invest Ophthalmol Vis Sci 2024;65(4):11
The authors aim was to compare adult full-field ERG (ffERG) responses in albinism, idiopathic infantile nystagmus (IIN), and controls. A secondary aim was to investigate the effect of within-subject changes in nystagmus eye movements on ffERG responses. Dilated Ganzfeld flash ffERG responses were recorded using DTL electrodes under conditions of dark (standard and dim flash) and light adaptation in 68 participants with albinism, 43 with IIN, and 24 controls. fERG responses were recorded near and away from the null regions of 18 participants also measuring the success rate of recordings. Age-adjusted photopic a- and b-wave amplitudes were consistently smaller in IIN compared with controls ($P < 0.0001$) and decreased with age, suggesting underlying retinal abnormalities. In contrast, photopic a-wave amplitudes increased

with age in albinism (P = 0.0035). Nystagmus significantly reduced the success rate of measurable responses. Within-subject changes in nystagmus intensity generated small, borderline significant differences in photopic b-wave peak times and a-and b-wave amplitudes under scotopic conditions with standard flash. Therefore, success at obtaining ffERG responses could be improved by recording responses at the null region. By highlighting differences in ERG responses among these conditions, the study provides insights into the underlying retinal pathophysiology associated with albinism and idiopathic infantile nystagmus.

Measurement of visual function in infantile nystagmus: a systematic review
Almagren B; Nystagmus UK Eye Research Group (NUKE), Dunn MJ
Br J Ophthalmol 2024;108(7):1038-1043
The authors compiled relevant 11 studies reporting data on visual function in infantile nystagmus. Studies were included if a sensory measure was used in people with IN to assess within-participant changes in visual function. Studies were excluded if they used a motor-based measure as they do not measure actual visual function but rather predict it based on nystagmus characteristics. Take home points from the systematic review were: 1) visual acuity measurement in isolation is not appropriate to measure visual function in infantile nystagmus as additional factors such as gaze angle and stress and mental load, and gaze-contingent stimuli play a role in visual performance; 2) no complete measurement technique has yet to be proven, but this analysis provides insights to guide future studies towards the development of appropriate methods for this specific population.

Oculoplastics

The incidence of pediatric dacryocystitis among a population-based cohort of infants with congenital nasolacrimal duct obstruction
Ashby G, Sathiamoorthi S, Mohney BG
J AAPOS 2024 Jun;28(3):103928
To report the incidence, clinical characteristics, and outcomes of acute dacryocystitis among a large, population-based cohort of children born with congenital nasolacrimal duct obstruction (CNLDO) over a 10-year period, this multicenter retrospective, population-based cohort study included all patients diagnosed with acute dacryocystitis in a cohort of patients diagnosed with CNLDO before age 5 years in Olmsted County, Minnesota, USA, from January 1, 1995, through December 31, 2004. Of 1,998 patients with CNLDO, there were 70 cases of acute dacryocystitis among 62 patients (36 female [51%], mean age at diagnosis = 9.0 months), yielding an incidence rate of 243 per 100,000 children (95% CI, 170-316). Patients who developed dacryocystitis were significantly less likely to be born via C-section (OR=0.29, P=0.009). Less than half of the patients with dacryocystitis were treated with oral/intravenous antibiotics (46%), but those who were had a significantly higher odds of requiring probing (OR = 8.50, P = 0.004). Spontaneous CNLDO resolution was significantly less likely to occur in patients diagnosed with acute dacryocystitis compared with those without (OR = 2.46, P = 0.001), and the median age of spontaneous resolution in the dacryocystitis group (6.0 months) was significantly older than in the uncomplicated CNLDO group (P = 0.012). The strengths of the study include its large, multicenter, population-based cohort design, while limitations include its retrospective nature, incomplete and non-standardized documentation, and irregular follow-up. Additionally, because the majority of cases were diagnosed by primary care providers rather than specialists, some cases may have been misdiagnosed, and the limited demographic diversity of Olmsted County compared to the US population limits the generalizability of these findings to other populations. Pediatric acute dacryocystitis is an uncommon complication of CNLDO and is associated with both a lower likelihood of and older age at spontaneous resolution of CNLDO symptoms.

Lacrimal Obstruction in Craniosynostosis: Anatomical and Genetic Risk Factors
Landau-Prat D, Taylor JA, Kalmar CL, et al
Ophthalmic Plast Reconstr Surg 2024 Sep-Oct 01;40(5):507-515
Craniosynostosis, which is characterized by premature fusion of one or more cranial sutures, can be associated with several ophthalmic manifestations, including NLDO. While NLDO has been reported in patients with craniosynostosis, its exact incidence and relationship to specific syndromic/genetic syndromes is unknown. This study aimed to fill in this gap in knowledge. This was a retrospective review. NLDO was found in 6.7% of the patients, which is higher than the prevalence in the general population in a similar age group (avg age 2.4 years). Prevalence of NLDO was higher in patients with associated genetic or syndromic features, particularly in cases of Apert syndrome. Craniofacial surgery were not found to significantly increase the risk for NLDO. For the patients who underwent lacrimal surgery, the first surgery was successful in 67% of the cases, which is lower than the general population. Limitations of the study are its retrospective nature and lack of a control group (compared to normal values in the literature. This study can help guide clinical management of patients with craniosynostosis. Given the high

prevalence of NLDO in this group of pts (as well as other known associations), it would be prudent for all of these patients to have a comprehensive ophthalmic evaluation in early childhood. It can also help with appropriate expectation setting when proceeding with a lacrimal surgery as there is a higher chance of needing multiple surgeries to adequately address tearing.

Differentiation of bacterial orbital cellulitis and diffuse non-specific orbital inflammation on magnetic resonance imaging
Ang T, Tong JY, Patel S, Selva D
Eur J Ophthalmol Published online September 2, 2024
The differentiation between diffuse non-specific orbital inflammation (DNSOI) and bacterial orbital cellulitis (OC) in the acute setting can be quite clinically and radiographically challenging. Despite the challenges, it is critical to make an accurate diagnosis to provide appropriate treatment to reduce morbidity. This retrospective study examined the MRI findings of 32 patients who presented with OC and DNSOI between 2008 and 2023 in a tertiary care center. The mean age of CO patients was 42.5 years and DNSOI was 52 years. An oculoplastic specialist and radiologist reviewed the MRI's of these patients who had similar clinical presentations of periorbital edema, restricted ocular motility, conjunctival injection, and proptosis. The key radiographic differences included different intensities of orbital fat (OC had hyperintense on T2 FS and DNSOI had variable signal intensity on T2 FS), distinct EOM appearance (OC had diffuse involvement of multiple EOM's, T2 hyperintensity, and indistinct EOM margins while DNSOI had single EOM involvement, gross enlargement, and diffuse contrast enhancement), and variations in lacrimal gland involvement (OC had loss of distinct margins without gross enlargement and DNSOI had enlargement and/or contrast enhancement). Additionally, contralateral findings were found predominantly in DNSOI. This study demonstrated several radiological features on MRI which can help with challenging diagnoses. Limitations include the study's retrospective nature, small sample size, lack of quantitative analysis, and the possibly greater disease severity in the subjects. The distinctive radiographic differences between DNSOI and OC can assist ophthalmologists and radiologists make a more definitive diagnosis and direct the patient to critical treatment.

Outcome of silicone sling frontalis suspension in children with simple congenital and complex ptosis
Landau Prat D, Zhao CS, Ramakrishnan M, et al
Can J Ophthalmol Aug 2024;59(4):264-269
This retrospective cohort study compares the surgical outcomes of frontalis suspension (FS) using a silicone sling for simple versus complex ptosis in children at the Children's Hospital of Philadelphia over a 12-year period. The authors analyzed reoperation rates and timing, including both simple congenital ptosis and complex cases. MRD1 measurements, both pre- and post-surgery, were determined from clinical photographs using ImageJ software. The study included 139 simple and 69 complex cases. Complex cases consisted of BPES (35), MGJW (12), oculomotor palsy (8), CFEOM (3), CPEO (3), and eyelid hemangioma (1). A history of prior ptosis repair was more common in the complex group, and the age at intervention was higher in these patients. Bilateral surgery was performed in 36% of cases, more frequently in the complex group. The mean MRD1 improved by an average of 1.3 mm in both groups, and 70% of parents

were satisfied with the outcomes. However, repeat ptosis repair was required in 64 patients (31%), with younger children (under 3 years old) showing higher reoperation rates. This study is limited by its retrospective design and the relatively small number of complex cases, especially when subdivided by specific condition. Grouping conditions with different etiologies under the broad term "complex" poses challenges when comparing them to simple cases. The most significant takeaway from this study is that children older than 3 years had lower reoperation rates compared to those younger than 3, supporting current clinical practice of advising parents that surgical outcomes tend to improve when the child is older.

Congenital epiblepharon in Chinese school-age children: a cross-sectional study
Huang S, Han Y, Zeng X, et al
J AAPOS 2024;28(4):103938
Congenital epiblepharon is characterized by overriding of the lower eyelid margin by pretarsal orbicularis muscle causing misdirection of the eyelashes towards the cornea leading to potential corneal irritation. It occurs frequently in Asian children and may be associated with obesity and refractive errors, particularly astigmatism. Children aged 6-12 years in Beichen District of Tianjin were examined for incidence of epiblepharon, strabismus, visual acuity, and noncycloplegic refraction using Spot photoscreener. BMI was also recorded and overweight and obesity were defined using a grading table issued by the National Health Commission of the People's Republic of China in 2018. From the 28, 225 children screened, the prevalence of epiblepharon was 2% and decreased with age. The prevalence of overweight or obesity was 64% in children with epiblepharon compared with 23-25% in nonepiblepharon children. Children with epiblepharon had higher percentages of moderate to high astigmatism compared to children without epiblipharon. Strengths of the study include large sample size and stratification of age and severity of epiblepharon. Limitations include noncycloplegic refraction with photoscreener and possible underestimation of mild epiblepharon visible only on downgaze. Children with epiblepharon demonstrate higher incidence of obesity and astigmatism, which should be addressed at evaluation.

Orbit

None.

Pediatrics / Infantile Disease / Syndromes

Sensitivity, Specificity, and Cutoff Identifying Optic Atrophy by Macular Ganglion Cell Layer Volume in Syndromic Craniosynostosis
Chang YH, Staffa SJ, Yavuz Saricay L, et al
Ophthalmology 2024;131(3):341-348
This retrospective cross-sectional study evaluated patients with syndromic craniosynostosis over 12 years, focusing on the association between macular ganglion cell layer (GCL) volume and optic atrophy. The study aimed to determine if GCL volume, as measured by optical coherence tomography (OCT), is independently affected by obstructive sleep apnea (OSA), Chiari malformation, or a history of elevated intracranial pressure (ICP) and its relation to optic atrophy. Findings revealed that a GCL volume of less than 1.02 mm^3 is a reliable indicator of optic atrophy, with a sensitivity of 83% and specificity of 77%. OSA was independently linked to lower GCL volume. While factors such as type of craniosynostosis, Chiari malformation, and history of elevated ICP were considered risk factors in univariate analysis, they were not significant in multivariate analysis. The study highlights that reduced GCL volume can predict optic atrophy and that OSA further reduces GCL volume, offering a useful method for assessing vision risk in patients with craniosynostosis, especially given their often limited cognitive abilities and challenges in obtaining visual field measurements.

Ocular features of NGLY1 deficiency from a prospective longitudinal cohort
Frater CH, Ruzhnikov MRZ, Beres S, et al
J AAPOS 2024 Jun;28(3):103925
NGLY1 deficiency is a rare autosomal recessive disorder characterized by global developmental delay, liver enzyme abnormalities, movement disorder, polyneuropathy, and hypo- or alacrima. The authors characterized the full spectrum and evolution of the ocular phenotype in a prospective natural history study of NGLY1 deficiency. The study collected ophthalmological data on 29 individuals with NGLY1 deficiency, and medical records were reviewed to confirm caregiver-reported symptoms. Of the 29 individuals with NGLY1 deficiency, 15 appeared for at least one ophthalmological examination. Caregivers reported at least one ocular sign or symptom in 90% of participants (26/29), with the most common signs being decreased tears (90%) and refractive error (62%). Ophthalmological examination confirmed refractive errors in 93% (14/15), hypolacrima in 83% (10/12), eyelid abnormalities in 73% (11/15), optic disk abnormalities in 73% (11/15), and corneal abnormalities in 67% (10/15). The strengths of the study include the detailed characterization of the ocular phenotype in this rare disorder and the prospective nature of the study. Limitations include the limited number of in-person exams and reliance on caregiver-reported signs and symptoms. Given the nearly universal hypolacrima and additional prominent ocular findings in NGLY1 deficiency, a targeted ocular history and ophthalmologic examination may facilitate prompt diagnosis and early initiation of preventive eye care, thus preserving vision and overall ocular health.

Ophthalmic features of Lamb-Shaffer syndrome: a case series
Glidai Y, Aung MH, Edmond J, et al
J AAPOS 2024 Jun;28(3):103919

Lamb-Shaffer syndrome (LSS) is a rare neurodevelopmental disorder caused by deletions or mutations in the SOX5 gene on chromosome 12p12, with fewer than 100 known cases globally. This case series presents the ophthalmic manifestations in 6 pediatric patients with LSS. Strabismus was observed in 5 of the patients, with exotropia being the most common type. All subjects had significant refractive errors, with 5 exhibiting astigmatism of at least 2 diopters. Optic nerve abnormalities were found in all patients, including pallor (4), hypoplasia (2), and anomalous appearance (1), with retinal nerve fiber layer thinning noted in one case. Other ophthalmic issues included ptosis (1), nasolacrimal duct obstruction (1), and nystagmus (2). This study is the first to detail the ophthalmic features of LSS in the literature. It suggests that a comprehensive eye examination, including OCT of the optic nerves, should be conducted for all patients diagnosed with LSS to assess for optic nerve abnormalities.

Screening for Autism Spectrum Disorder in Children and Adolescents With Leber's Congenital Amaurosis
Sallum JMF, Pellissari MC, Carreiro LR, et al
Am J Ophthalmol 2024;265:257-274
The study aimed to explore the prevalence of Autism Spectrum Disorder (ASD) in children with Leber Congenital Amaurosis (LCA) and to determine if specific genetic causes of LCA are associated with ASD. Conducted at the Institute of Ocular Genetics and the Department of Ophthalmology at Federal University of São Paulo, Brazil, the cross-sectional study involved 46 participants aged 2 to 16 years with genetically confirmed LCA. The participants were divided into two groups based on genetic subtypes: ciliopathies and other gene mutations. ASD was assessed using the Autism Behavior Checklist (ABC). The study found that 6 out of 46 participants had ASD scores, with a significant correlation between worse visual acuity and ASD, and between male gender and ASD. No significant correlation was found between ASD and the genetic subtype of LCA or age. The study highlights the importance of visual acuity in ASD risk, suggesting that severe visual impairment may influence ASD outcomes. However, the study’s small sample size, lack of a control group, and cross-sectional design limit its findings. The results emphasize the need for improved visual rehabilitation and tailored developmental interventions for children with LCA to potentially enhance ASD outcomes. Further research with larger samples and longitudinal designs is recommended to confirm these findings and develop better assessment tools for ASD in visually impaired individuals.

The prevalence of autism among children with albinism
Gunz S, Rozen-Knisbacher I, Blumenfeld A, Hendler K, Yahalom C
European Journal of Ophthalmology 2024;34(3):666-671
Since the association between autism spectrum disorders (ASD) and visual impairment has been suggested in the literature, the aim of this study was to investigate the prevalence of autism among children with albinism compared to the prevalence of ASD in children with visual impairment secondary to other causes. The study was designed as a retrospective review of children with albinism from January 2015 to December 2020. The control group consisted of children with early onset visual impairment of similar visual range and age, secondary to diagnosis other than albinism. Patients with associated autism were identified in both groups. A total of 708 children aged 1-18 years with visual impairment were included in the study. 401

children had a diagnosis of albinism, of whom 14 were also diagnosed with ASD. In the control group, composed of 307 patients, only 3 patients had ASD (p: 0·03). In this particular study, the prevalence of ASD in patients with albinism was 1 in 28, while in children with visual impairment from other causes was 1 in 102. The high incidence of ASD in the albinism group in this study cannot be explained by visual impairment alone, as visual acuity was similar or even slightly worse in the control group. The authors assert that these findings require more investigation and wish to raise awareness of the extent to which ASD may be an associated diagnosis in children with albinism to emphasize that earlier diagnoses of ASD may lead to better patient outcomes.

Ocular hemodynamics in epileptic children treated with antiepileptic drugs
Gultutan P, Nalcacioglu P, Icoz M, et al
European Journal of Ophthalmology 2024;34(3):843-851
The aim of this study was to investigate whether epilepsy patients receiving anti-epileptic drugs (AEDs) experienced changes in ocular hemodynamics compared to age- and gender-matched healthy subjects. As far as the authors are aware, this is the first study to evaluate the ocular hemodynamics using OCT-A in epileptic children treated with AEDs. This observational, cross-sectional study included 124 patients divided into 4 groups: Group-1: patients receiving carbamazepine (n = 30), group-2: patients receiving levetiracetam (n = 31), group-3: patients receiving valproic acid (n = 32), and group 4: healthy controls (n = 31). A fully automated microstructural analysis of the vessel density (VD) of the retinal superficial capillary plexus (SCP), deep capillary plexus (DCP), and the choriocapillaris (CC) layers and radial peripapillary capillary, and total retinal thickness (Trt), p-RNFL thickness were analyzed by OCT-A. The mean age, gender distribution and the duration of epilepsy were similar in all groups. Evaluation of the p-RNFL thickness and perifoveal Trt between the groups showed a statistically significant difference in all quadrants. The p-RNFL thickness was lower in patients receiving carbamazepine and valproic acid. The lowest values of the luminal area and choroidal vascular index (CVI) were found in patients receiving valproic acid; comparison with matched healthy controls showed statistically significant differences. The study was limited by its relatively small sample size, and its findings would more clinically applicable if the authors also compared changes on OCT-A parameters with visual function in patients.

Evaluation of Retinal Nerve Fiber Layer, Ganglion Cell Thickness, and Macular Thickness in Children With Comorbid Specific Learning Disorder and Attention-Deficit Hyperactivity Disorder
Tonkaz GY, Özyurt G, Çakir A, et al
J Pediatr Ophthalmol Strabismus 2024;61(2):128-136
Recent literature has demonstrated at least some connection between numerous neuropsychiatric conditions – schizophrenia, bipolar disorder, and the like - and RNFL, GCL, and/or macular thickness on OCT. Given this, the authors hypothesize that there may be differences in the OCT findings of children with attention-deficit hyperactivity disorder (ADHD) and specific learning disorder (SLD). To test this hypothesis, the authors performed OCT testing on 40 children with ADHD and SLD, 40 with ADHD alone, and 40 without either diagnosis. While the RNFL was thinnest in all 4 quadrants in children with both ADHD and SLD, none of the values reached significance. This suggests that OCT measurements alone may not serve as an adequate biomarker for ADHD or SLD, though it is certainly an area that merits more study.

The EFEMEREYE Study: prenatal medication exposure and ocular anomaly occurrence in EFEMERIS health database
Dubucs C, N'Go V, Caillet A, et al
J AAPOS 2024 Jun;28(3):103931
This study aimed to describe ocular anomalies (OAs) in children and fetuses within a French population, estimate their prevalence, and explore any links between prenatal medication exposure and OA occurrence. Utilizing the EFEMERIS cohort database, which includes pregnancy outcomes from Haute-Garonne, the study assessed OA descriptions from fetuses at pregnancy termination or children at birth and conducted eye exams at various ages. Out of 140,065 individuals, 2.13% had OAs, with 0.04% being congenital ocular malformations (COMs) such as cataract, glaucoma, ano/microphthalmia, and coloboma. Analysis of 2,968 cases and 136,619 controls revealed that maternal exposure to magnesium during and up to 1 month before pregnancy was associated with a higher risk of OA in children, but not COMs. The study's strengths include its large database, while limitations involve its reliance on available database information and a small number of COM cases. The findings suggest a modest association between magnesium exposure and OA risk, though the impact on clinical practice is limited.

Successful Treatment Response of a Juxtapapillary Retinal Capillary Hemangioblastoma Due to von Hippel-Lindau Syndrome with Belzutifan in a Pediatric Patient
Mustafi D, Huang J, Ting MA, et al
Retina 2024;44(5):e31-e33
Retinal capillary hemangioblastomas associated with VHL may be asymptomatic or cause severe visual impairment. Juxtapapillary retinal capillary hemangioblastomas pose a particular challenge as they are more prone to cause visual impairment and also less amenable to local treatment owning to their central location. Belzutifan is approved for systemic treatment of VHL. This paper presents successful anatomic treatment of a juxtapapillary retinal capillary hemangioblastoma in a pediatric patient on belzutifan. Her vision remained 20/400 but the lesion demonstrated anatomic regression.

Practice management / Health care systems / Education

Evaluating ChatGPT's efficacy and readability to common pediatric ophthalmology and strabismus-related questions
Ahmed HS, Thrishulamurthy CJ
Eur J Ophthalmol Published online August 7, 2024
Artificial intelligence has increased in popularity and utilization among the general publics to learn more about medical problems. ChatGPT 3.5 have been recognized as capable of providing free and personalized medical information, but its accuracy and readability has not been tested by pediatric ophthalmologists. 817 patient centered questions were developed by pediatric ophthalmologists and submitted into ChatGPT 3.5. The answers analyzed by pediatric ophthalmologists for accuracy, evaluated by the Flesch-Kincaide Grade level, and checked for character count. Two pediatric ophthalmologists rated the accuracy of the answers on a 1–4-point scale. If there was disagreement, a third pediatric ophthalmologist also evaluated, and the scores were averaged. A total of 638 (78.09%) of questions were scored to be perfectly correct, 156 (19.09%) were scored correct but incomplete, and only 23 (2.81%) were scored as partially incorrect. None of the responses were scored as completely incorrect. The readability score of the responses was higher than the desired 8th grade level. The study is the first to evaluate the accuracy of large language models of patient education materials for pediatric ophthalmology. The limitations of the study include unpredictable nature of ChatGPT responses and its ever-evolving accuracy. Also, the questions were not generated by patients or their families but rather derived from pediatric ophthalmologists' assumption of what parents/patients would like to know. The study was also limited to the English language so its applicability to non-English responses. ChatGPT shows promise as a reliable information source for pediatric ophthalmology and strabismus but human oversight is crucial to evaluate its accuracy, safety, and readability.

Using Large Language Models to Generate Educational Materials on Childhood Glaucoma
Dihan Q, Chauhan MZ, Eleiwa TK, et al
Am J Ophthalmol 2024;265:28-38
The study evaluated the quality, readability, and accuracy of patient education materials (PEMs) on childhood glaucoma generated by large language models (LLMs) such as ChatGPT-3.5, ChatGPT-4, and Google Bard. It assessed the models' ability to produce content that is both understandable and accurate by using three prompts: one requesting easily understandable content, one specifying a 6th-grade reading level, and one asking for rewrites of existing materials to meet the same readability level. Results showed that all LLMs produced high-quality PEMs with minimal misinformation, and content generated for the 6th-grade level was notably more readable. ChatGPT-4 produced the most readable content and improved existing online materials closest to the desired readability level. While the materials were accurate and of high quality, none achieved high actionability scores, indicating a lack of practical steps for patients. The study suggests that LLMs can enhance the readability and quality of health information but highlights the need for integrating actionable content to improve practical utility. The findings underscore the potential of LLMs to support the creation of

accessible and accurate health information but also indicate areas for further development, particularly in making content actionable.

Lack of racial and ethnic diversity in pediatric ophthalmology clinical trials from 2000 to 2022
Kuo A, Yazji I, Abbass N, Chong DD, et al
J AAPOS 2024 Apr;28(2):103870
Randomized control trials (RCTs) are important in both informing clinical care decisions and policy decisions. Lack of diversity in RTCs is problematic for several reasons, including less generalizable results. This study aims to look at this issue specifically in pediatric ophthalmology as there is a lack of knowledge regarding the prevalence of reporting racial/ethnic data and whether each race/ethnicity is under- or over-represented in peds ophtho RCTs. An extensive literature search was done to identify peds ophtho RCTs from 2000-2022. Once the trials were identified, reviewers collected data on racial/ethnic breakdown. Just over half of the articles reported race or ethnicity. This increased in trials published after 2010. In the studies that reported race, the majority of pts were White (88.6%) followed by Black (9.7%) and Asian (1.6%). In those reporting ethnicity, the majority of pts were non-Hispanic (87.5%). The major strengths of this study is the extensive literature search to find a good representation of RCTs over the years. Limitations include the observational design and discrepancies in how this data was labelled/defined between studies. This information is important for all pediatric ophthalmologists to be aware of as RCTs have a major impact on how we treat patients. It is imperative that we know that the results from these studies might not apply to all of our patients. It is also important that we are aware of this problem and work to identify ways to try to remedy it.

Utilization of apple vision pro in ophthalmic surgery: A pilot study
Orione M, Rubegni G, Tartaro R, et al
Eur J Ophthalmol Published online August 14, 2024
Apple Vision Pro is a new augmented reality tool that merges the physical and digital realm that can enhance visual perception, environmental awareness, and hand tracking capabilities. The study aims to assess to the potential of Vision Pro to enhance the surgical experience in oculoplastic surgery. 10 surgeons performing 10 ectropion and entropion repair surgeries utilized the Apple Vision Pro instead of their typical microscope. The headset was worn during the entire procedure displaying the preoperative image of the patient in augmented reality on the right side of the patient's head while the left side presented a step-by-step list of surgical actions. Other displayed items included a stopwatch and a graph showing the relationship between the injection time and the level of efficacy of anesthetic. Following the procedure, the surgeon took 2 surveys to assess the Vision Pro's wearability, practicality, freedom of movement, safety, visual comfort, clarity of information, collaboration with surgical team, integration into workflow and learning. A second survey assessed 10 items in a validated System Usability Scale. From the questionnaires, the surgeons gave the Apple Vision Pro high ratings in practicality, freedom of movement, integration in workflow, and learning. The lowest ratings were in visual comfort and clarity of information. The surgeons rated the device highly on the SUS scale overall. This pilot study had limited surgeons and limited number of procedures with only one use of the device per surgeon. This study only provides first

impressions of the device. By piloting the device, the study tests the utilization of a potentially useful tool in expanding information available to a surgeon during a surgery as well as an valuable educational tool.

Characteristics of pediatric ocular trauma in a tertiary hospital in Israel 2011–2020 – How can public prevention policy be improved?
Israeli A, Wald M, Safuri S, et al
European Journal of Ophthalmology 2024;34(3):852-858
This was a retrospective study that evaluated a total of 1676 children with ocular injuries who presented to the emergency department (ED) at an academic medical center in Israel between 2011 and 2020. The median age of presentation was 6 (range 1–17). Males accounted for 70.6% of the cases. Median BCVA at presentation was 0.96 (logMAR). Males and non-adolescent males specifically were the most prominent groups (70.6% and 44.7%, respectively). The authors found that the ratio of ocular trauma cases to total pediatric emergency department (ED) visits was stable during the 2011-2020 time period ($p = 0.714$) regardless of gender ($p = 0.832$ and $p = 0.545$ for boys and girls, respectively). The leading causes of trauma were partial thickness eyelid laceration, periorbital hematoma, and extraocular muscle contusion, all of which were stable over the study period ($p = 0.678$, $p = 0.203$ and $p = 0.398$, respectively). Falls and accidental injury while playing were the most common mechanisms of ocular trauma (25.8% and 18.4%, respectively), but differed between age groups. From these findings, the authors conclude that pediatric ocular injuries to pediatric ED visits ratio remained stable during the 2011-2020 period in this study population, regardless of gender. The study is limited by its retrospective design and single center model, which may not be generalizable to all populations.

Factors associated with pediatric ophthalmology follow-up adherence before and during the COVID-19 pandemic
Hekmatjah N, Turner CH, Mesfin Y, et al
J AAPOS 2024;28(4):103963
The COVID-19 pandemic led to disruption of routine healthcare in children. This study aims to evaluate the effect of COVID-19 on follow-up of patients in a pediatric ophthalmology practice and possible factors leading to adherence or non-adherence to follow-up recommendations. Retrospective, single-center study, that included new pediatric ophthalmology patients seen in January, April, August, and December of 2019 and 2021. Adherent patients presented for follow-up within 0-30 days after recommended time and nonadherent patients presented for follow-up greater than 30 days after recommended time. Factors evaluated were age at first visit, sex, self-reported race and ethnicity, primary language, primary insurance type, provider type (ophthalmologist or optometrist), distance to provider, and recommended follow-up. Less adherence to recommended follow-up was similar prior to and after the COVID-19 pandemic. Poor adherence was associated with public insurance, declining to self-report race, optometry visit, or recommended follow-up greater than or equal to 3 months. Patients who traveled greater than or equal to 177 miles were more likely to be adherent. This study identified factors associated with nonadherence to follow-up recommendation. Limitations include retrospective study in a single-center that may not be generalizable. Lack of follow-up is a complex issue and

other factors, such as diagnosis, health literacy, education level, cost of care, and extended clinic wait times, were not included. Less adherence to recommended follow-up (55.3% in this study) has been an issue prior to and after the COVID-19 pandemic, and there are multiple factors identified that contribute and could be addressed to improve follow-up.

Race, Ethnicity, and Sex in Pediatric Eye Disease Investigator Group Clinical Studies
Dihan QA, Alzein AF, Ibrahim OM, et al
JAMA Ophthalmol Published online September 5, 2024
Race, ethnicity, and sex disparities contribute to non-equitable vision care. This retrospective, cross-sectional study evaluated representation of different racial and ethnic groups in Pediatric Eye Disease Investigator Group (PEDIG) clinical trials and prospective cohort studies between 1997 and 2022 compared with 2010 US Census data. 41 PEDIG studies (29 RCTs and 12 prospective observational cohort studies) with 11,658 total participants were included. White participants were overrepresented in PEDIG studies compared to the 2010 US Census pediatric population ($p<0.001$). Asian participants ($p=0.009$), Black participants ($p<0.001$), and Hispanic participants ($p<0.001$) were underrepresented. Female participants were proportionately represented ($p=0.21$). From 1997 to 2019, Asian participants ($p=0.01$), Black participants ($p=0.04$), and White participants ($p=0.002$) had decreasing proportional enrollment and Hispanic participants had increasing proportional enrollment ($p<0.002$). PEDIG studies that had proportional representation enrolled fewer than 200 participants. Patient-derived factors such as medical mistrust may contribute to overall underrepresentation. Interventions by PEDIG such as Spanish-language informed consent forms and online interpreters for Spanish-speaking families may have contributed to increased Hispanic patient participation. Study limitations include use of 2010 US census data for comparison which may have underestimated the level of representation needed to achieve adequate generalizability for findings in minority groups relative to the prevalence of certain pathologies within these populations. This study shows that racial and ethnic disparities exist in PEDIG studies which may impact the generalizability of these studies to underrepresented groups. PEDIG formed the equity, diversity, and inclusion committee in 2022 which may help to improve biases.

Gauging Public Interest in Pediatric Ophthalmology Conditions Using Google Trends
Aldhahwani B, Shaheen A, Tibi C, Capo H, Cavuoto KM
J Pediatr Ophthalmol Strabismus 2024;61(4):e39-e42
Many patients now receive a substantial portion of their health information from the internet; as such, it behooves us to understand what is being searched for and how it is being consumed. To this end, the authors use Google Trends data to ascertain information-seeking behavior regarding pediatric ophthalmology and strabismus topics.Of common topics in the field, “Strabismus,” lazy eye,” and “vision therapy” had the highest search volumes. While many terms had stationary levels of interest, “lazy eye,” “myopia,” “near-sightedness,” “crossed eyes,” and “squint” demonstrated an increasing search volume with time, indicating an increasing level of public awareness and interest. There was also significantly more interest in “lazy eye” compared to “amblyopia” and in “near-sightedness” compared to “myopia.” These trends are interesting to note and suggest that capturing public attention will require an avoidance of jargon. Pediatric

ophthalmologists should be aware of what their patients are searching and work to present medically accurate information to them.

Access to Pediatric Eye Care by Practitioner Type, Geographic Distribution, and US Population Demographics
Siegler NE, Walsh HL, Cavuoto KM
JAMA Ophthalmol 2024;142(5):454-461
Vision disorders such as amblyopia can be prevented if detected and addressed early in childhood, yet problems with access to care may limit the ability for children to receive necessary care. The shortage of pediatric ophthalmologists, especially in lower-income and rural communities, is well documented, but there is limited evidence on the distribution of pediatric optometrists. The purpose of this study was to evaluate the geographic distribution of pediatric optometrists and pediatric ophthalmologists and correlate the locations with population demographics from the 2020 US census. 586 pediatric optometrists (51.5% female) and 1060 pediatric ophthalmologists (44.3% female) were identified using 4 online public databases in April 2023 (American Optometric Association, American Academy of Optometry, American Academy of Ophthalmology, and AAPOS). Among US counties, 6.5% had at least 1 pediatric optometrist and 9.7% had at least 1 pediatric ophthalmologist with substantial geographic overlap (P<0.001). Of the counties without pediatric ophthalmologists, 96.4% also lacked pediatric optometrists. Counties with pediatric ophthalmologists had higher mean household incomes compared to counties with pediatric optometrists (P=0.003) and higher mean population with bachelor's degrees (P<0.001). Counties without pediatric optometrists or pediatric ophthalmologists had lower median household incomes, smaller populations with bachelor's degrees, lower home internet access, and a great population younger than 19 years than counties with both practitioners. This study is limited due to the dynamic nature of databases used to collect practitioner information and US census data that may omit certain demographics such as undocumented immigrants.

The Epidemic of Congenital Syphilis in the Indigenous and Rural Populations of South Dakota
Nicolet N, Bhagia A, Torve M, et al
Pediatrics 2024;154(1):e2023063823
From 2020 to 2023, South Dakota witnessed a substantial increase in cases of congenital syphilis (CS), with the highest rates identified in rural and Native American (NA) communities. This article discuss 3 severe cases of CS in premature infants born to NA . This article talks about the need for outreach and care for this condition especially in marginalized communities. It reminds us of the increasing prevalence of congenital syphilis.

The Economic and Workforce Issues in Pediatric Ophthalmology and Their Effect on Eye Care.
Lavrich J, Mungan N, Wang FM, Nelson LB.
J Pediatr Ophthalmol Strabismus 2024;61(3):157-159.
This article is a discussion among the authors about the viability of pediatric ophthalmology as a profession and what we can do to sustain it. We should also use our leverage, given the scarcity of pediatric ophthalmologists. A residency program can't run without a pediatric ophthalmologist. Neonatal intensive care units, which are a huge revenue-generating part of most children's

hospitals, also can't stay open without pediatric ophthalmologists. Practice efficiently and effectively, and charge for everything you do. Charge for refractions when they are not related to the medical examination. Charge for phone conversations. No one thinks about this in medical school, but unfortunately it is necessary to practice effectively to be successful in maintaining your business.

Prematurity

Longitudinal Changes in Choroidal Thickness in Children with a History of Prematurity: An 18-Month Prospective Cohort Study
Lee YS, Liu L, Wang NK, et al
Retina 2024;44(6):1063-1072
As a highly vascular structure, the choroid is involved in many physiologic functions of the eye, particularly during development. Studies have shown that choroidal thickness is lower in preterm children compared to full-term infants, but limited information exists on changes in choroidal thickness in premature infants under a variety of conditions. This is a prospective longitudinal observational study conducted in China. Participants were part of an ongoing cohort – full-term, pre-term without ROP, ROP with regression, ROP treated with bevacizumab, and ROP treated with laser. Children aged 3-12 were eligible for inclusion. Exclusion criteria included hyperopia greater than 2 diopters, visual acuity worse than 20/25, use of mydriatic agents, or stage 4 or 5 ROP. A total of 416 eyes of 208 patients were included. Choroidal thickness was measured with OCT 4 times at 6-month intervals. Of all the groups, the laser-treated children had the thinnest choroid compared with full-term children. Preterm children exhibited greater attenuation in choroidal thickness over time than did full-term children, whereas no difference was observed between injection of bevacizumab and laser treatments. In all groups, the changes in axial length were negatively associated with the changes in choroidal thickness. Overall, this study provides interesting information on changes in choroidal thickness in infants and interestingly showed no different between anti-VEGF and laser treated eyes.

Foveal Avascular Zone in Adults Born Preterm with and Without Retinopathy of Prematurity:
Fieß A, Zange M, Gißler S, et al
Retina 2024;44(8):1431-1440
Prematurity is very common, with around 10% of infants born prematurely globally. Little is known regarding effects of prematurity on the foveal avascular zone, particularly the long-term effects. This is a retrospective cohort study conducted in Germany including individuals born preterm or at term between 1969 to 2002, ages 18-52 at the time of the study. In total, 380 right eyes were examined and subdivided into groups based on gestational age and ROP status. FA was measured with OCTA in all participants. The FAZ area decreased as gestational age decreased. In the multivariable analyses, smaller FAZ was independently associated with gestational age, increased foveal retinal thickness, and foveal hypoplasia. No association was seen between visual acuity and FAZ. Overall, this study suggests that there are lasting effects on prematurity on retinal anatomy, although given the older age of participants and many confounders, it is challenging to draw definite conclusions.

Refractive Error

Long-term effect of orthokeratology on choroidal thickness and choroidal contour in myopic children
Xu S, Wang M, Lin S, et al
Br J Ophthalmol 2024;108(8):1067-1074
Subjects from the Atropine Combined Orthokeratology (ACO) study, a previously conducted 2-year RCT, who completed the OCT scanning in the control and the ortho-k group, were included in this analysis to investigate the long-term effect of ortho-k on the choroid. Patients were 8-12 years old, had spherical equivalent refraction (SER) of −1.00 to −6.00 D in both eyes, astigmatism of no more than 1.50 D and anisometropia of no more than 1.50 D; a best-corrected visual acuity of no worse than 20/25 in both eyes; and no other ocular pathology. 64/80 patients (80%) successfully completed all the followup visits. The control group demonstrated more choroidal thinning and more prolate contour over the study period compared to the ortho-k group. The 2-year change in choroidal thickness was significantly associated with the 2-yearAL change in the control group, but this trend was not significant in the ortho-k group. The effect was seen to diminish in the long-term, however. The question remains regarding treatment duration, long-term effects vs rebound, and best patient populations for this myopia control intervention, but this study does contribute to knowledge on what role choroidal thickness and contour plays in myopia progression.

Light exposure therapy for myopia control: a systematic review and Bayesian network meta-analysis
Zaabaar E, Zhang XJ, Zhang Y, et al
Br J Ophthalmol 2024;108(8):1053-1059
The authors included 12 relevant studies published as of February 2023 in this systematic review of studies comparing red, violet, or full-spectrum light with controls. To compare and rank the different light wavelengths, the Bayesian network meta analysis (NMA) was conducted for all the included clinical studies (12 studies) and found that only red light significantly slowed axial elongation and SE refraction progression compared with controls. These data remained the only statistically significant findings when the analysis was done separately for only randomized controlled trials (8 studies) as well. While this systematic review suggests red-light therapy may have an effect on myopia, not much is known on this emerging topic of light therapy for myopia control and more studies are certainly warranted.

A pilot study of axial length changes associated with myopia control spectacles in subjects reading under mesopic conditions
Szeps A, Dankert S, Saracco G, et al
J AAPOS 2024 Apr;28(2):103857
Myopia control is an area of significant concern. One modality for trying to halt myopia progression is using plus lens defocus. Prior studies looking at people watching movies or reading on computers in dark rooms showed that plus lens defocus led to shortening of the axial length in emmetropes but did not lead to any difference in myopes. This paper aimed to see if a pair of novel defocus glasses that led to shortening of the axial length in myopes in photopic

conditions would also lead to shortening of the AL in myopes in mesopic conditions. Patients read on a computer in a dark room, first in their normal monofocal correction then in the defocus glasses. The axial length increased by a significant amount after reading in the monofocal glasses and by an insignificant amount int eh defocus glasses. Most importantly, the defocus glasses did NOT lead to any shortening of the eye like they did in photopic conditions. Limitations of this study include that they only used one type of defocus lens and did not compare myopes to emmetropes. This study is important in that it highlights the possible role of lighting conditions on the progression of myopia, even in the setting of treatment. These results should make us consider recommending that patients do not spend time reading or doing other visual activities in mesopic conditions.

A Novel Time-Aware Deep Learning Model Predicting Myopia in Children and Adolescents
Varošanec AM, Marković L, Sonicki Z
Ophthalmol Sci 2024;4(6):100563
Increasing prevalence of myopia has made both myopia control as well as understanding of how to best predict likelihood of progression important areas of research. This study aimed to leverage time-aware long short-term memory machine learning to create a deep learning model for myopia prediction. The cohort included 10,170 children aged 4-18 years with follow up of 0.25-7 years, resulting in 156, 230 encounters, diagnosed with primary myopia or compound myopic astigmatism with a minimum of two visits, excluding patients with ocular comorbidities including mixed astigmatism, strabismus, corneal disease, ROP, and amblyopia. Utilizing this deep learning model, this study demonstrated a quantitative prediction of spherical equivalent as far as 7 years in the future with mean absolute error (MAE) of 0.10±0.15D on the testing set; greater sequence length provided higher degree of accuracy. MAE of <0.75D for spherical equivalent is considered clinically acceptable based on previous standards in literature. Predictive models such as this may be helpful in assist in early and accurate prediction of myopia and aid in appropriate initiation of myopia control treatment when indicated. Of note, this model only utilized CRx and vision variables and not structural measures such as corneal curvature or axial length in its predictions. The authors also acknowledge other external factors that may contribute to myopia progression (time outside, near work, screen time, etc) which separately impact this type of predictive model. Nonetheless, development of models such as this may be beneficial in the future as we progress toward higher rates of myopia with time.

Choroidal Changes During and After Discontinuing Long-Term 0.01% Atropine Treatment for Myopia Control
Lee SS, Lingham G, Clark A, et al
Invest Ophthalmol Vis Sci 2024;65(10):21
Low-dose atropine has emerged as a treatment for myopia control, with recent studies showing choroidal thickening with low-dose atropine which were sustained during the study period. There is also a documented “rebound” effect with cessation of low-dose atropine. This study analysis was conducted as part of a double-blind randomized control trial that compared 0.01% atropine to placebo. SD-OCT was used to obtain images which were analyzed for choroidal thickness. A total of 148 children were included in the analysis. During the treatment phase, the subfoveal choroid in both treatment and control groups thickened by 12–14 μm. During the washout

phase, the subfoveal choroids in the placebo group continued to thicken by 6.6 μm, but those in the atropine group did not change. Participants with good axial eye growth control had greater choroidal thickening than the fast-progressors during the treatment phase regardless of the treatment group ($P < 0.001$), but choroidal thickening in the atropine group's fast-progressors was not sustained after stopping eye drops. Overall, 0.01% atropine did not cause a difference in choroidal thickness, but abrupt cessation of long term atropine may disrupt normal choroidal thickening in children. Overall, this study challenges the positive data on low-dose atropine and suggests caution with sudden cessation of atropine for myopia control.

Age-matched analysis of axial length growth in myopic children wearing defocus incorporated multiple segments spectacle lenses
Graff B, Lam CSY, Vlasak N, Kaymak H
Br J Ophthalmol 2024;108(8):1060-1066
This group developed a system of classifying the actual annual axial length (AL) growth rate of myopic children again the average physiological AL growth rate of an age matched control, called the age-matched myopia control (AMMC) system. They reassessed first-year data from the first publication on DIMS spectacle lenses by Lam et al using this AMMC system to investigate whether AL growth is sufficiently inhibited by DIMS lenses to achieve the treatment goal of physiological AL growth. They found that eyes with DIMS spectacle lenses are 65% within the range of physiological AL growth rate, compared to 16% of eyes with SV spectacle lenses. Median AL growth rate of eyes with DIMS spectacle lenses is also within the range of physiological growth. Notably, they also found that 28% of eyes with DIMS lenses showed excessive AL growth rate, and 16% for single vision lenses eyes (without any treatment) achieved treatment goal physiologic AL growth rate. This indicates that additional factors are at play in terms of myopia progression.

Correlation of Refractive Error with Anisometropia Development in Early Childhood
Kinori M, Nitzan I, Szyper NS, et al
Am J Ophthalmol 2024;264:145-153
The study examined the relationship between various types and severities of refractive errors (myopia, hyperopia, and astigmatism) and the development of anisometropia in preschool children. In this retrospective cohort study, isometropic children aged 1 to 6 years were followed for an average of 5.1 years after an initial examination between 2012 and 2022. Logistic regression models, adjusted for sociodemographic factors, revealed that 7.7% of the 33,496 children developed anisometropia. The risk of developing anisometropia increased with the severity of initial refractive errors: severe myopia had an odds ratio (OR) of 13.90, severe hyperopia had an OR of 4.19, and high astigmatism had an OR of 12.10. The study's strengths include its large sample size, long follow-up, and comprehensive analysis. However, limitations include variability in examination procedures, potential selection bias, and differences in cycloplegic agents used. The study underscores the importance of regular refractive monitoring in preschool children with significant refractive errors to detect and address anisometropia early, helping to prevent visual complications and amblyopia.

Daily Low-Level Red Light for Spherical Equivalent Error and Axial Length in Children With Myopia: A Randomized Clinical Trial
Cao K, Tian L, Ma DL, et al
JAMA Ophthalmol 2024;142(6):560-567
Low-level red light (LLRL) has been shown to help slow myopia progression without major safety concerns. However, it is unclear if LLRL has similar effects on children without myopia. The purpose of this single-masked, single-center, randomized clinical trial was to evaluate the effects of daily use of 650-nm LLRL over 1 year in children with myopia, emmetropia, and low hyperopia. 336 children ages 6 to 12 years with cycloplegic spherical equivalent error (SER) between -6 D and 3 D were randomly assigned to the LLRL group or control group. Children who previously received other myopia interventions, anisometropia of 1.5 D or greater, strabismus, amblyopia, refractive media opacity, or astigmatism greater than 2.5 D were excluded. Children in the LLRL group were given a head-worn device with a 650-nm single-wavelength light source and advised to use it 3 minutes twice daily 4 or more hours apart. Of the 336 participants, 224 had low to moderate myopia and 112 had emmetropia or low hyperopia. The mean age of all participants was 9.0 years and mean SER was -1.3 D (-1.3 D for the control group and -1.4 D for the treatment group). Mean AL was 23.8 mm in the control group and 23.9 mm in the treatment group at baseline. Intervention compliance in the LLRL group ranged from 63% to 100% (median 86%). Mean change in AL was -0.06 mm in the LLRL group and 0.13 mm in the control group at 6 months (difference 0.19 mm, P<0.001) and -0.11 mm in the LLRL group and 0.26 mm in the control group at 12 months (difference 0.37 mm, P<0.001). Mean change in SER were 0.15 D and -0.26 D for the LLRL group and control group respectively at 6 months (difference -0.41 D, P<0.001) and 0.24 D and -0.65 D (difference -0.89, P<0.001) at 12 months. By fundus exam and OCT there was no evidence of damage to the retina. Limitations of this study include lack of masking participants, single center trial in 1 area, and follow-up duration of 1 year only. In conclusion, 1 year of daily irradiation using 650-nm LLRL compared with no LLRL group slowed progression of SER without any structural adverse effects to the retina.

Effective Decrease in Myopia Progression With Two Mechanisms of Management
Erdinest N, Atar-Vardi M, Lavy I, et al
J Pediatr Ophthalmol Strabismus 2024;61(3):204-210
The purpose of this study was to investidate the effectiveness of 0.01% atropine treatment to inhibit myopia progression and the possible additive potency with peripheral defocus contact lenses over 3 years and the rebound effect 1 year after cessation of treatment. This prospective study included 127 children aged 8 to 5 years, divided into three treatment groups: 0.01% atropine and single-vision spectacles (At+SV, n = 36), 0.01% atropine and peripheral defocus contact lens (At+PDCL, n = 30), and 0.01% atropine and dual-focus contact lens (At+DF, n = 25). A control group was prescribed single-vision spectacles (n = 36). Cycloplegic spherical equivalence refraction was measured every 6 months during 3 years of treatment and 1 year after cessation. Myopia progression decreased over 3 years of treatment, more during the second and third years than the first year, to a statistically significant degree in the atropine groups (P < .01): in the first, second, and third years respectively, -0.42 ± 0.34, -0.19 ± 0.18, -0.22 ± 0.19 diopters (D) in the At+SV group, -0.26 ± 0.21, -0.14 ± 0.37, and -0.15 ± 0.31 D in

the At+PDCL group, and -0.22 ± 0.15, -0.15 ± 0.22, and -0.11 ± 0.14 D in the At+DF group. Myopia progressed 1 year after cessation of treatment: -0.29 ± 0.28 D in the At+SV group, -0.13 ± 0.28 D in the At+PDCL group, and -0.09 ± 0.18 D in the At+DF group. After 3 years, there was no statistically significant difference in myopia progression between the At+SV and At+PDCL or At+DF groups. A limitation of this study is the absence of a separate peripheral defocus contact lens monotherapy arm. Nonetheless, peripheral defocus has, and is, being extensively researched, as discussed. The most effective addition in the soft contact lens's periphery and the desired visual field area needed to create effective myopic peripheral defocus is still being researched.

Association of Tessellation Density with Progression of Axial Length and Refraction in Children: An Artificial Intelligence-Assisted 4-Year Study
Wei R, Li J, Yang W, et al
Retina 2024;44(3):527-536
Myopia is a growing global health concern due to its increasing prevalence and significant burden on individuals and society. High myopia in particular is associated with a variety of vision-threatening conditions and identifying early markers of early-age rapid eye growth may be helpful for patient care. Fundus tessellation, defined as the visibility of the of large choroidal vessels at the posterior pole outside of the parapapillary zone, may be associated with axial length prolongation. This is a school-based cohort study based in China, with 1997 children in grades 1 and 2 enrolled in the study. Children received a full ophthalmic exam including slit lamp exam, cycloplegic auto-refraction, biometry, and fundus photography at enrollment and at 4-year follow-up. A subset of images were manually labelled by experts to assist in creation of several deep-learning-based segmentation models. The clinician chose the best mask and made corrections as needed. The tessellation density was defined as the ratio of the sum of the tessellated area to preprocessed region of interest. The overall prevalence of tessellation in this study was 29%. Higher tessellation density was associated with longer baseline axial length, more myopic baseline refraction, rapid axial length elongation, and myopic progression. Overall, tessellation density may be a marker for increased risk of rapid myopic progression, although this software and analysis are not available for clinical use and requires complex image analysis.

The Onset and Progression of Myopia Slows in Chinese 15-Year-Old Adolescents Following Vocational Rather Than Academic School Pathways
Hu Y, Liao L, Morgan IG, Jin L, He M, Ding X
Invest Ophthalmol Vis Sci 2024;65(10):42
Myopia is quickly becoming a public health concern due to its high prevalence and potential for vision-threatening complications. Decreased outdoor time and intensive education have been causally associated with myopia. A population twin-registry in China was analyzed. First born twins age 7 to 15 were enrolled. Those with strabismus, amblyopia, or nystagmus were excluded. Refraction and biometric parameters were measured annually at each summer holiday. 583 children were divided into two groups, those attending vocational high school and those attending academic high schools. The study found that non-myopic children who discontinued formal education to pursue vocational pathways had significantly lower rates of

incident myopia than those who pursued formal education. In children with myopia, those in vocational pathways had slower myopic shifts and a lower proportion of high myopia. Altogether, this suggests that children who do not receive a formal education will develop less myopia, although there are limitations with the methodology. Parents of the children who pursued vocational pathways ha significantly less myopia than parents of children pursuing a formal education, which is a significant confounder. Overall, this is an interesting study associating formal education with increasing myopia.

Five-year results of atropine 0.01% efficacy in the myopia control in a European population
Moriche-Carretero M, Revilla-Amores R, Gutiérrez-Blanco A, et al
Br J Ophthalmol
According to the authors, this was an experimental, analytical, prospective, randomized and longitudinal study which aimed to evaluate the long-term outcomes of 0.01% atropine for myopia control in Spanish children over 5 years. It is unclear how many patients were initially recruited and eventually excluded due to failure to comply with the treatment regimen or followup protocol, but 361 eyes were included in the analysis 51% atropine vs 49% controls) with a mean age of 6.7 years. The SE increased −0.63±0.42D in children after 5 years of treatment with 0.01% atropine, while in the control group, the increase was −0.92±0.56D, resulting in a statistically but maybe not clinically significant efficacy over the SE of 31.5% ($p<0.001$). Findings were similar for AL elongation: 0.26mm increase in the atropine group vs 0.49mm in the control group for an overall efficacy of 47% which was statistically significant but again maybe not clinically significant.

Assessment of the Responses of the Artificial Intelligence-based Chatbot ChatGPT-4 to Frequently Asked Questions About Amblyopia and Childhood Myopia
Nikdel M, Ghadimi H, Tavakoli M, Suh DW
J Pediatr Ophthalmol Strabismus 2024;61(2):86-89
Artificial intelligence (AI) has become increasingly prominent in the medical field over the last few years, both as a resource for physicians and a resource for patients. Ensuring the accuracy of these AI tools is paramount, then, for patient care and safety. In order to ascertain the accuracy of currently available AI models in pediatric ophthalmology, the authors prepared 55 commonly asked questions about childhood myopia and amblyopia and proposed them to ChatGPT-4. Each question was asked twice to ensure reproducibility. The responses were then independently graded by two pediatric ophthalmologists as acceptable, incomplete, or unacceptable. Overall, performance of the AI model was good; a full 84.6% of the answers were deemed “acceptable” by the graders, with the remainder being incomplete or unacceptable. However, one must point out that even a 15% rate of poor answers might produce some level of harm to patients. AI is certainly a useful tool, but likely needs further improvement prior to being used in any official capacity.

Pediatric refractive surgery: current opinion in ophthalmology
Kim AJ, Shahraki K, Suh DW
Curr Opin Ophthalmol Jul 1 2024;35(4):292-297

This review article discusses the use of refractive surgery in children. The procedure is increasingly being used to achieve emmetropia or reduce anisometropia in children, particularly to address the challenge of glasses compliance during the amblyogenic period. However, refractive surgery in children poses unique challenges, especially given the ongoing changes in eye development throughout childhood, which make refractive predictions difficult. Additionally, the need for general anesthesia during the procedure adds complexity.Surface treatments such as LASEK and PRK have been noted to offer advantages in pediatric patients by avoiding flap-related complications, but these techniques are limited by prolonged healing times and the risk of haze formation. The authors highlight that regression remains a significant issue in this population, and patient selection should focus on children with high anisometropic amblyopia who have failed conventional treatments. The authors conclude that refractive surgery is well tolerated and effective in in children that are at risk of amblyopia and who have failed penalizing therapy.

Two-Year Myopia Management Efficacy of Extended Depth of Focus Soft Contact Lenses (MYLO) in Caucasian Children
Díaz-Gómez S, Burgos-Martínez M, Sankaridurg P, et al
Am J Ophthalmol 2024;260:122-131
The study aimed to assess the impact of extended depth of focus (EDOF) soft contact lenses (MYLO) on myopia progression in Caucasian children aged 6-13, comparing these lenses to traditional distance single-vision spectacles. This prospective non-randomized clinical trial included 90 children, with 45 wearing MYLO contact lenses and 45 using single-vision spectacles. Over two years, cycloplegic refraction and axial length (AL) were measured every six months. Visual acuity, contrast sensitivity, and subjective comfort were also evaluated. Results showed that the contact lens group had a mean change in spherical equivalent (SE) of –0.62 ± 0.30 diopters (D) and an AL increase of 0.37 ± 0.04 mm, with 53% experiencing SE progression ≤ –0.50 D and 100% showing AL increase ≤0.50 mm. In contrast, the spectacles group had a mean SE change of –1.13 ± 0.20 D and an AL increase of 0.66 ± 0.03 mm, with all participants showing an AL increase >0.50 mm and a cumulative absolute reduction in AL (CARE) of 0.29 ± 0.06 mm. Although there was a slight reduction in high-contrast visual acuity (HCVA) with contact lenses compared to spectacles, the difference was statistically significant but minimal, and subjective responses to the contact lenses were overwhelmingly positive. Strengths of the study include the significant reduction in myopia progression with MYLO lenses, high compliance, and a comprehensive evaluation approach. Limitations include the non-randomized design, lack of blinding, and data collected from a single center. The study suggests that MYLO EDOF contact lenses are more effective in controlling myopia progression than single-vision spectacles and highlights the importance of patient comfort and compliance, recommending further research across diverse populations.

Association Between Physical Indicators and Myopia in American Adolescents: National Health and Nutrition Examination Survey 1999-2008
Chen N, Sheng Y, Wang G, Liu J
Am J Ophthalmol 2024;260:132-139

This study explores the relationship between physical indicators and myopia among American adolescents using data from the National Health and Nutrition Examination Survey (NHANES). In this retrospective case-control study, which included 9,008 adolescents aged 12-19 years, researchers analyzed demographic data, physical indicators (height, weight, BMI), and vision data using weighted methods, regression models, cumulative odds logistic regression, and restricted cubic spline analysis. The results revealed that myopia was significantly associated with age and race, with older adolescents and those of Mexican American, other Hispanic, or other races having a higher likelihood of myopia. Among physical indicators, weight in the fourth percentile was linked to increased odds of myopia (OR 1.38), and a higher BMI, particularly around BMI 30, was associated with increased myopia risk (OR 1.26). Taller adolescents also had a higher degree of myopia (OR 1.02). A nonlinear relationship was found between BMI and myopia, with the highest risk at a BMI around 30. The study concludes that weight and BMI are related to the occurrence of myopia, while height and race are associated with the degree of myopia. These findings underscore the significance of physical indicators in understanding myopia risk and suggest a need for further research on these associations. Clinicians should be aware of the impact of both race and physical factors on progressive refractive error.

Corneal Biomechanical Characteristics in Myopes and Emmetropes Measured by Corvis ST: A Meta-Analysis
Liu MX, Zhu KY, Li DL, et al
Am J Ophthalmol 2024;264:154-161
The study aimed to examine corneal biomechanics differences between individuals with varying degrees of myopia and those with emmetropia using the Corvis ST device. This systematic review and meta-analysis analyzed data from 11 studies, involving 1947 myopes and 621 emmetropes for the general comparison, and 443 high myopes versus 449 non-high myopes for more specific insights. The results showed that myopes had a longer time at the first applanation (A1t) and a shorter length at the second applanation (A2L) compared to emmetropes. High myopes exhibited significantly greater A1t, velocity at the second applanation (A2v), deformation amplitude at the highest concavity (HC-DA), and peak distance at the highest concavity (HC-PD), but had decreased time at the second applanation (A2t) and radius of the highest concavity (HC-R) compared to non-high myopes. The study's strengths include its comprehensive analysis and large sample size, though limitations include high heterogeneity among studies, a lack of diversity due to all studies being from Asia, and the use of only cross-sectional data. Clinically, the findings suggest that corneal biomechanical assessments could be useful for monitoring and managing myopia, especially in adolescents, and highlight the need for further research to understand the progression of biomechanical changes in myopia.

Axial length elongation profiles from 3 to 6 years in an Asian paediatric population: the Growing Up in Singapore Towards Healthy Outcomes birth cohort study (GUSTO)
Chen DZ, Wong C, Lam JSH, et al
Br J Ophthalmol 2024;108(7):1018-1023
This is a longitudinal cohort study of 194 subjects/273 eyes recruited from the GUSTO cohort. Visual acuity, cycloplegic autorefraction, and AL measurements (IOL master) were taken at age

3 and 6 years. They found that AL elongates at an average length of 0.80mm from 3 to 6 years, with myopes demonstrating the greatest elongation. The 95th percentile limit of axial length elongation was 1.59mm in myopic eyes, which was significantly greater than emmetropic eyes (1.34mm) and hyperopic eyes (1.00mm). This may help in identifying myopia development in Asian preschool children and further supports the growing push to include AL elongation as data points for myopia control studies.

Prevalence of myopia among children and adolescents aged 6-16 during COVID-19 pandemic: a large-scale cross-sectional study in Tianjin, China
Li T, Wei R, Du B, et al
Br J Ophthalmol 2024;108(6):879-883
This was a cross-sectional study using data from the Tianjin Child and Adolescent Research of Eye March -June 2021. A total of 909 835 children and adolescents aged 6–16 years (mean age 11 years) from 1348 primary and secondary schools were recruited (95% participation rate). . The overall prevalence of myopia was 54.71% and was higher among girls. Students living in the 6 central districts (with the best educational resources and therefore greatest study burden per the authors) had the highest prevalence of moderate and high myopia. The progression of myopia started to increase dramatically at 8 years and then slowed at 14 years. One large limitation is the use of non-cycloplegic refraction which may overestimate the true prevalence of myopia in these children. It would also be more powerful to compare these prevalence data to pre-COVID years in order to comment more accurately on the COVID-19 pandemic's association with myopia prevalence as the article aimed to do.

Prevalence and associated factors of myopia in children and adolescents in Russia: the Ural Children Eye Study
Bikbov MM, Kazakbaeva GM, Fakhretdinova AA, et al
Br J Ophthalmol 2024;108(4):593-598
This is a school-based case-control study including 4933 children age 6-18 years old to explore the prevalence of myopia and its associated factors in in a population of ethnically mixed urban school children. The prevalence of any myopia (≤−0.50 D) was 46%, while the prevalence of high myopia was only 1.4%. Axial length increased by 0.12mm per year or age and myopic refractive error by −0.18 D. Larger myopic refractive error was associated with the typical factors: older age, female sex, higher prevalence of parental myopia, more time in school, reading or playing on cell phone, and less time outdoors.

Normative value of hyperopia reserve and myopic shift in Chinese children and adolescents aged 3-16 years
Wang J, Qi Z, Feng Y, et al
Br J Ophthalmol 2024;108(7):1024-1029
The aim of this study was to generate normative values of hyperopia reserve and refractive progression among Chinese children age 3-16 years by conducting a 1 year follow up study of 3118 children using cluster sampling from selected schools. They suggest this can help identify and monitor myopia in Chinese children and lead to earlier intervention on at-risk children. At baseline, 19% of included children were myopic. The 50th percentile of spherical equivalent

estimated by the lambda-mu sigma method (LMS) decreased from 1.04D at 3 years to –2.04D at 16 years in boys, and from 1.29D to –2.81D in girls. The normative value of hyperopia reserve was 2.64D at 3 years and −0.35D at 16 years, with the maximum progression of 0.35 D at the age of 6 years. It's still unclear what the optimum age, SE, or hyperopia reserve would be to initiate intervention.

Low-dose atropine 0.01% for the treatment of childhood myopia: a pan-India multicentric retrospective study
Saxena R, Gupta V, Dhiman R, et al
Br J Ophthalmol
This retrospective study was conducted on 732 children age 6-14 years across 20 centers in India to monitor the progression of myopia over 2 years after initiating treatment with 0.01% atropine eye drops. At baseline, the mean refractive error was −3.55D, which increased to −3.82D after 1 year of atropine treatment and further to −4.06D after 2 years of atropine treatment, resulting in a statistically significant reduction in myopia progression rate to −0.27D in the first year (relative reduction 64% from baseline) and −0.24 in year 2 (relative reduction 11.11% from the first year). This was compared to the mean myopia progression rate 1 year before treatment of -0.75D. Unsurprisingly, younger age and higher baseline myopia was associated with greter myopia progression and poor treatment response. This study demonstrates that 0.01% atropine works similarly in this pan-Indian population to slow to some degree but not stop myopia progression over a 2 year period.

Pseudomyopia as an independent risk factor for myopia onset: a prospective cohort study among school-aged children
Sun W, Yu M, Wu J, et al
Br J Ophthalmol 2024;108(6):873-878
Pseudomyopia refers to SE ≤−0.50D before cycloplegia and >−0.50D after cycloplegia, which 24% of Chinese children were found to have. This population based cohort study aimed to investigate whether pseudomyopia is an independent risk factor for myopia using a cohort of 2328 children aged 4-17 years with exams at baseline and 6 month followup. 21% of pseudomyopic eyes developed myopia at the 6-month followup compared to 4% of non-myopic and non-pseudomyopic eyes. . After adjusting for multiple myopia risk factors, including baseline cycloplegic SE, near work and outdoor time, pseudomyopia was found to be an independent risk factor for myopia onset (relative risk=2.52). Pseudomyopic children with higher cycloplegic myopic SE, smaller difference between cycloplegic and non-cycloplegic SE, and higher binocular amplitude of accommodation also had high risk of myopia development.

Myopic maculopathy among Chinese children with high myopia and its association with choroidal and retinal changes: the SCALE-HM study
Deng J, Xu X, Pan CW, et al
Br J Ophthalmol 2024;108(5):720-728
This cross-sectional study included 579 children aged 4-18 years with high myopia (mean SE –8.44D) and sought to investigate prevalence of myopic maculopathy and associated choroidal and retinal changes. Fundus grading was performed by 2 independent graders based on

photographs and OCT images. The proportions of tessellated fundus and diffuse chorioretinal atrophy were 43.52% and 8.64%, respectively. Tessellated fundus was associated with thinner macular choroidal thickness and retinal thickness, longer axial length, older age, and female gender. Only a thinner macular choroidal thickness was independently associated with diffuse chorioretinal atrophy. Nasal macular choroidal thickness was most closely associated with severity of myopic maculopathy and could potentially be used clinically for evaluating maculopathy severity.

Sympathetic nervous system activity is associated with choroidal thickness and axial length in school-aged children
Lin S, Zhu B, Wang T, et al
Br J Ophthalmol 2024;108(3):405-410
The authors sought to investigate whether the stress response caused by education could be a contributing factor in myopia progression. They followed 273 students in grades 2 and 3 (mean age 7.5 years) for 1 year and collected morning urine samples to measure epinephrine, norepinephrine, and dopamine levels to determine SNS activity in addition to visual acuity, refraction, axial length and choroidal thickness. Every 1 μg/L increase in epinephrine was associated with 1.60 μm decrease in average ChT. Every 1 μg/L increase in norepinephrine is associated with 0.53 μm decrease in ChT in inner-superior region. Every 1 μg/L increase in norepinephrine was associated with 0.002mm quicker AL elongation. These numbers are statistically significant, but it's not clear what true association this may have or whether it's clinically significant. While multiple studies have correlated education with myopia, the mechanism for this is unclear and presumably multifactorial.

Myopia trends among children and adolescents: a nationwide study in South Korea
Kim H, Shahraki K, Suh DW
J AAPOS 2024;28(4):103969
There is evidence that the prevalence of myopia is increasing among Asian school-age children, more so after the COVID-19 pandemic, among adolescents, and among females. This study aims to evaluate myopic trends and differences between trends in school-age girls and boys over a 10 year period using Korea National Health and Nutrition Examination Surveys (KNHANES). The KNHANES data from years 2011 and 2021 was analyzed for children age 10-18 years, separated into three age groups (10-12 years, 13-15 years, and 16-18 years) and stratified for myopia and nonmyopia. Demographic data collected included age, sex, household income, height, weight, body mass index and onset of menarche. Comparing 2011 data to 2021 data, there was no statistically significant increase in the prevalence of myopia among boys; however, there was a statistically significant increase in the prevalence of myopia among girls. A later onset of menarche was associated with a lower prevalence of myopia. Strengths of the study include a large, nationwide population sample and long study period. Limitations include cross-sectional analysis, non-cycloplegic refraction, lack of assessment of onset of puberty in boys to correlate with onset of puberty in girls and myopic progression. Other risk factors for myopia progression, such as near-work activity, genetic factors and outdoor activities were not assessed in this study. In this study, the prevalence rate of myopia in Korean girls increased significantly from 2011 to 2021 compared to Korean boys with early onset of menarche in girls

being associated with increased myopia prevalence. Further study is needed to identify other contributing factors.

Choroidal Vascularity and Axial Length Elongation in Highly Myopic Children: A 2-Year Longitudinal Investigation
Xuan M, Wang D, Xiao O, et al
Invest Ophthalmol Vis Sci 2024;65(10):7
The highly vascular choroid is crucial for retinal and visual function, and many studies have found associations between high myopia and a significantly thinner choroid. This prospective, longitudinal, observational study recruited patients 8 to 18 years of age with bilateral high myopia (<-6D) without pathologic myopia. 163 participants (74%) completed 2 years of follow-up. All participants underwent baseline and follow-up evaluations with axial length, autorefraction, fundus photography and swept-source OCT. An inverse relationship was observed between axial length elongation and increases in baseline age, baseline subfoveal choroidal thickness, and choroidal vascular index, as well as a decrease in baseline axial length. The study suggests a possible association between a thinner choroid and axial length elongation over 2 years in children with high myopia. Although changes in choroidal vascular index did not reach statistical significance, a lower choroidal vascular index may be associated with axial length elongation. A larger sample is needed to confirm their findings, as many did not rise to statistical significance.

Refractive Surgery

None.

Retina

Electroretinogram as a Screening Tool to Assess Vigabatrin-Induced Retinal Toxicity in Children With Infantile Spasms
Nagarajan S, Prabu R, Parachuri N, et al
J Pediatr Ophthalmol Strabismus 2024;61(4):273-278
Vigabatrin is well-known to cause retinal toxicity leading to peripheral vision loss; however, monitoring this in young children is difficult, as they often cannot comply with visual field testing. One potential solution for this is electroretinogram (ERG) testing, which can provide an objective measure of retinal function in these children. Here, the authors subjected children with infantile spasms receiving treatment with vigabatrin to a 30-Hz flicker potential ERG using the RETeval system (LKC Technologies). This was done at baseline before starting vigabatrin, at 6 months after starting, and at 1 year after starting. Overall, 11 children with a mean age at initiation of 7.14 months were tested. The mean decrease in ERG amplitude was 3.21 and 5.72 μV at 6 and 12 months of follow-up, with 8/11 children (72.7%) showing signs of vigabatrin-induced retinal toxicity. While limited by its small size, this study does suggest that a 30 Hz flicker ERG can function as a screening tool, and that rates of retinal toxicity may be quite high. It is worth further investigating the pros and cons of routine ERG testing for infants on vigabatrin.

Longitudinal Characteristics of Choroidal Neovascular Membrane in Pediatric Patients
Hoyek S, Lu Y, Mukai S, Patel NA
Am J Ophthalmol 2024;261:76-84
This retrospective clinical cohort study evaluated the clinical and imaging characteristics, including Optical Coherence Tomography Angiography (OCTA) findings, and treatment outcomes for choroidal neovascular membranes (CNVMs) in children. It involved 30 eyes from 25 children examined at two centers between 2005 and 2022. The study found that idiopathic (48%) and inflammatory (20%) causes were common, with most CNVMs being unilateral (80%), active (83.3%), and juxtafoveal (46.7%). Symptoms at presentation were diverse, with reduced vision being the most common. Treatment was administered to 83.3% of eyes, primarily with intravitreal anti-VEGF injections (92%), often requiring an average of 2.3 injections per eye for retreatment. Other treatments included photodynamic therapy and surgery. The average follow-up duration was 56.46 months, showing significant visual acuity improvement (3 lines or 15 ETDRS letters) and OCTA revealing reduced CNVM vessel density and retinal pigment epithelium detachment height. Strengths of the study include its extensive follow-up period and the use of advanced imaging techniques, while limitations involve its retrospective nature, variability in imaging and follow-up, and a limited number of patients with specific etiologies. The findings suggest that anti-VEGF injections are effective and relatively safe for treating pediatric CNVM, with OCTA being a valuable tool for monitoring treatment response. Early diagnosis and tailored treatment approaches are crucial for managing pediatric CNVM effectively.

Four-Year Progression of Myopic Maculopathy in Children and Adolescents With High Myopia
Jiang F, Wang D, Xiao O, Guo X, Yin Q, Luo L, He M, Li Z
JAMA Ophthalmol 2024 Mar 1;142(3):180-186
Myopic maculopathy is one of the major causes of blindness or visual impairment. It is defined as degeneration of chorioretinal tissues in the setting of excessive elongation of the axial length

(AL) in myopic eyes. The purpose of this observation study was to investigate the progression of myopic maculopathy in children and adolescents with high myopia and explore factors associated with progression. 548 eyes of 274 Chinese children aged 7 to 17 years (50.4% female, mean age 13.60 years) with high myopia (-6.0 D or less, mean SE -9.12 at baseline, mean AL at baseline 27.08 mm) were included. Participants receiving treatment to prevent myopia progression, refractive or intraocular surgery, and those with other ocular or severe systemic diseases were excluded. Examinations and fundus photography were done at baseline and at 4-year follow-up visits. Myopic maculopathy was divided into 5 categories: absence of myopic-related fundus lesions (C0), tessellated fundus (C1), diffuse chorioretinal atrophy (C2), patchy chorioretinal atrophy (C3), and macular atrophy (C4). Three plus lesions, lacquer cracks (LCs), fuch spot, and choroidal neovascularization, were also evaluated. At baseline, 74.5% were C0, 11.3% C1, 14.1% C2, and 0.2% C3. At 4 years follow-up, AL increased to mean 27.74 mm and SE progressed to mean -10.99 D. Prevalence of myopic maculopathy changed to 71.2% C0, 12.2% C1, 16.1% C2, and 0.6% C3. Progression of myopic maculopathy was found in 12.2%. with 88 lesion changes (new signs of tessellated fundus in 16, diffuse atrophy in 12, patchy atrophy in 2, lacquer cracks in 9, and enlargement of diffuse atrophy in 49). Worst BCVA (P=0.04), longer AL (P<0.001), faster AL elongation (P<0.001), and more severe myopia maculopathy were associated with myopic maculopathy progression over 4 years. Enlargement of diffuse atrophy was the most frequent progressive change, comparable to other studies. Strengths included the large longitudinal design and standardized methods to assess progression. Limitations included the short follow-up time, unmasked graders, different fundus photography lighting, and lack of red-free imaging. This study may help identify those at higher risk for myopic maculopathy progression.

Early-Onset of Familial Exudative Vitreoretinopathy: Clinical Characteristics, Management, and Outcomes
Kitic N, Chapron T, Metge-Galatoire F, et al
Retina 2024;44(4):669-679
FEVR is a genetic disease featuring abnormal vascular development. It exhibits marked phenotypic variation, even amongst families, with some presenting early in life with severe manifestations and others presenting much later. This retrospective case series reviewed all patients diagnosed with FEVR before the age of 3. All patients underwent genetic evaluation as well as a complete ophthalmic exam including FA and fundus photographs. 54 patients were included, with a mean age at diagnosis of 10.9 months. Poor visual behavior (33%) and strabismus (26%) were the most common presenting symptoms. Half of included patients had severe disease (stage 4-5). Genetic testing was positive in 41%. Surgery was performed in 44% and was successful in 70%. Most eyes (76%) had vision of hand motion or better. Overall, this is an interesting study on the manifestations of FEVR in young children, showing that earlier age at presentation is associated with severe stage and a greater need for surgery.

Fluorescein Angiography Parameters in Premature Neonates
da Cruz NFS, Hoyek S, Sengillo JD, et al
Ophthalmol Sci 2024;4(6):100561

Fluorescein angiography is an important testing modality used in the diagnosis and characterization of retinal disorders. In the neonatal population, FA can be particularly helpful in identifying subtle neovascular changes in peripheral retinal disease including ROP, Coats, and FEVR. Unfortunately, there is little standardized data regarding FA phase timing in the neonatal population and the ideal fluorescein dosing. This retrospective case series reviewed images from 72 eyes of babies with ROP. Images were obtained at 50.5±40.8 weeks. While the overall times for each FA phase were noted to be shorter than those in adults, particularly due to the smaller size and anatomy of babies compared to adult patients, there was significant variability in FA phase time. The 7.7mg/kg dosing described in previous literature was used in this study without complications and with good imaging quality. The study was limited by retrospective nature and lack of video imaging (as opposed to still images), but the average timing of retinal phase (8-16 seconds), peak phase (21-29 seconds), and recirculation (1.3-3.1 minutes) serve as a helpful benchmark for further study.

Contemporary Patterns and Underlying Causes of Vitrectomy in Pediatric and Adolescent Patients: A Nationwide, Population-Based Analysis
Lee JY, Kim K, Bae K Am
J Ophthalmol 2024;261:28-35
This study investigated the incidence, causes, and trends of vitreoretinal diseases requiring pars plana vitrectomy (PPV) among pediatric and adolescent populations in South Korea, using data from the Korean National Health Claims database spanning 2009 to 2020. The study found a cumulative incidence of 21.42 PPV procedures per 100,000 individuals under 20 years, with a higher incidence in males (29.30) compared to females (13.10). Notably, the incidence among males aged 5-19 decreased by about 55% from 2011 to 2020. The primary etiologies for PPV were retinal detachment (67.1%) and lens disorders (37.2%), with retinopathy of prematurity (ROP) being the leading cause in infants (72%). Comorbid conditions included myopia (30.3%) and atopic dermatitis (31.8%), with congenital systemic diseases and cerebral palsy being common in infants. Trends showed a decline in PPV incidence among adolescent males while remaining stable for females, along with an increased use of ultrawide-field fundus photography. Strengths of the study include its large, comprehensive sample and use of a reliable national database, while limitations involve reliance on claims data without detailed clinical records and a lack of ethnicity-specific data. The findings suggest the need for targeted patient education, preventive measures focusing on trauma reduction, and adoption of advanced diagnostic tools to improve early detection and treatment.

Unusual anterior and posterior segment features of coats disease
Girolamo MM, Hadjistilianou T, Lembo A, et al
European Journal of Ophthalmology 2024;34(2):419-424
This study was designed as a retrospective review of 45 eyes in 45 patients affected by Coats disease and was conducted at the Retinoblastoma Referral Center and Ophthalmology Unit of the University of Siena in Italy, analyzing data from 2000 to 2022. The authors identified 4 unusual clinical associations among the study population: retinal macrocysts, anterior chamber cholesterolosis, fovea-sparing Coats disease and secondary vasoproliferative tumor. Unusual anterior and posterior segment features of Coats disease such as retinal macrocyst and anterior

chamber cholesterolosis have been more frequently reported in younger children while fovea-sparing and vasoproliferative tumors have been more commonly described in older patients. The authors suggest that age at diagnosis is a significant prognostic indicator, as patients presenting with Coats disease younger than 3 years old often manifest a more aggressive disease phenotype.

Vitreoretinopathy in Asymptomatic Children With CTNNB1 Syndrome
Bedoukian EC, Forbes G, Scoles D
JAMA Ophthalmol Published online August 15, 2024
B-catenin is encoded by CTNNB1 and is critical for embryonic development. CTNNB1 syndrome is due to de novo missense, nonsense, frameshift, and splice variations and deletions in CTNNBI and can cause microcephaly, developmental delay, and ophthalmic manifestations including familial exudative vitreoretinopathy (FEVR). A prior study reported that 22.8% of those with CTNNB1 variants had FEVR, however most of these cases were stage 4 or 5 FEVR, and there have been no reports on the prevalence of FEVR in children with CTNNB1 syndrome without advanced FEVR. This study included 11 children with variants in CTNNB1 and previously documented normal retinal examinations who underwent an exam under anesthesia with fluorescein angiography. Those with a known history of retinopathy or retinal detachment were excluded. Mean age at diagnosis of CTNNB1 syndrome was 2 years and mean age at examination was 6 years. 9 children had a previous diagnosis of strabismus and 6 had undergone strabismus surgery. FEVR was present in 9 eyes of 5 patients, and 6 of these eyes required treatment including 1 eye with retinal detachment requiring scleral buckling. There were no clear high-risk loci in CTNNB1 in association with high severity of FEVR. This study showed that almost all patients with CTNNB1 syndrome required ophthalmic care and some who had previously documented normal retinal office exams required treatment for FEVR after undergoing an exam under anesthesia with FA. These findings may support considering ultra-widefield fluorescein angiography in those with CTNNB1 syndrome. This study is limited in its small sample size.

Quantitative analysis of choriocapillaris flow deficits and choroidal thickness in children with Marfan syndrome
Ng K, Xu P, Jin G, et al
Br J Ophthalmol 2024;108(2):274-279
This was a cross-sectional study of 51 children with Marfan syndrome and 50 healthy controls with mean age 8 years to evaluate the characteristics and associated factors of choroidal thickness (CT) and choriocapillaris flow deficit percentage (CCFD%) in children with Marfan. The authors looked at the CT of the subfoveal area and increasing diameters away from the fovea as well as the CCFD% if circular regions of various diameters using Zeiss OCT/OCTA imaging. Patients also had doppler echos to evaluate aortic sinus diameter and ejection fraction and a Z score was calculated for analysis. CT thinning and an increased CCFD% were measured in patients with Marfans compared with the healthy controls. An increased choriocapillaris flow deficit percentage (CC FD%) was significantly associated with worse best-corrected visual acuity and cardiac function in MFS children. The authors suggest that

CCFD% could be a predictor of future visual impairment or even early cardiovascular events in these patients.

Anatomic Outcomes of Lens-Sparing Vitrectomy for Stage 3 or 4 Familial Exudative Vitreoretinopathy
Liu H, Peng J, Zhang W, et al
Retina 2024;44(9):1538-1545
FEVR is a hereditary vitreoretinal disease with considerable variation in presentation. In serious cases, proliferative tissue can result in a tractional retinal detachment which requires surgical intervention. This is a retrospective observational study of patient with FEVR who underwent lens-sparing vitrectomy. 133 eyes of 119 patients were included, with an average age of 13 months. One hundred twenty-nine eyes (97.0%) achieved traction relief through one lens-sparing vitrectomy operation. The extent of retinal detachment improved in 98 eyes (73.7%), remained stable in 32 eyes (24.1%), and progressed in three eyes (2.3%). At long-term follow-up, 39 (29.3%) and 60 (45.1%) eyes had completely or partially reattached retina, respectively. This study suggests that lens-sparing vitrectomy is a viable treatment for FEVR, although the lack of comparison to other surgical techniques and variable prior treatment of patients limits the generalizability.

Retinoblastoma

Aqueous VEGF-A Levels as a Liquid Biopsy Biomarker of Retinoblastoma Vitreous Seed Response to Therapy
Daniels AB, Sishtla KL, Bogan CM, et al
Invest Ophthalmol Vis Sci Jun 3 2024;65(6):18
Retinoblastoma (RB) is an oxygen-sensitive tumor; however, RB vitreous seeds (VSs) exist in the hypoxic vitreous. The authors hypothesize that VSs experience a strong hypoxia response, leading to the elaboration of proangiogenic cytokines, and that these cytokines could be measured in the aqueous humor (AH). The authors aimed to use these cytokines as predictive biomarkers of VS burden and response to intravitreal chemotherapy.A rabbit xenograft model was used, where RB VSs were injected into the vitreous of immune-suppressed rabbits and allowed to grow for 2 weeks. After 2 weeks, the right eyes were treated with a series of weekly injections of intravitreal chemotherapy (melphalan, topotecan, or belinostat), while the left eyes were treated with saline injections. AH levels of seven angiogenic proteins were measured, and VEGF-A was the only cytokine that showed a clear pattern. After the injection of RB cells, VEGF-A levels rose in all eyes as the VS grew and formed seeds. The levels of VEGF-A decreased in all eyes with each serial injection of chemotherapy. In saline-treated eyes, AH VEGF-A continued to rise—by the end of the experiment, VEGF-A was sixfold higher than baseline, while in treated eyes, it was one-fifth the baseline level, resulting in a 30-fold difference between chemotherapy-treated and saline control eyes. Chemotherapy-treated eyes averaged a reduction of 92.4%. To confirm that VEGF-A was arising from VS and not the retina, the authors performed RNAscope in situ hybridization. Additionally, VEGF-A levels were collected from the AH of patients undergoing intravitreal chemotherapy for RB vitreous seeds, and VEGF-A levels dropped during periods of clinical regression and ceased to decrease during inter-injection periods. The authors conclude that VEGF-A could serve as a biomarker of disease burden and treatment response, potentially aiding in minimizing chemotherapy treatments, which are toxic to the retina.The authors acknowledge the limitations of the study, including that the data are currently only experimental in animal models and the sample size in humans was very small.

Retinoblastoma Outcomes in the Americas: A Prospective Analysis of 491 Children With Retinoblastoma From 23 American Countries
Berry JL, Pike S, Rajagopalan A, et al for Global Retinoblastoma Study Group
Am J Ophthalmol 2024;260:91-101
This study, a subanalysis of a larger prospective cohort study, focuses on retinoblastoma outcomes in American countries, addressing disparities between high-income countries (HICs) and low-income countries (LICs). The analysis, spanning 57 centers across 23 countries and including 491 treatment-naïve retinoblastoma patients diagnosed in 2017, used Kaplan-Meier and Cox proportional hazard models to assess survival and globe salvage rates. Patient distribution was as follows: LIC (8 patients, 1.6%), lower-middle income (LMIC) (58 patients, 11.8%), upper-middle income (UMIC) (235 patients, 47.9%), and HIC (190 patients, 38.7%). Survival rates varied significantly: LIC patients had a 3-year survival rate of 60.0% (95% CI 12.6-88.2), while HIC patients had a 3-year survival rate of 99.2% (95% CI 94.6%-99.9%).

Factors influencing survival included age >4 years (hazard ratio [HR]= 0.45, P= .048), advanced tumor stages (e.g., cT3 vs cT1, HR= 4.65 × 10^9, P < .001), and a higher hazard of death for females compared to males (HR= 1.98, P= .04). Globe salvage rates were 13.3% (95% CI 5.1%-25.6%) in LMICs and 46.2% (95% CI 38.8%-53.3%) in HICs. At 3 years, salvage rates were 70.1% (95% CI 54.5%-81.2%) for cT1 eyes and 8.9% (95% CI 5.5%-13.3%) for cT3 eyes. Advanced tumor stage was associated with a higher risk of enucleation (subhazard ratio= 4.98, P < .001). The study highlights significant disparities in outcomes based on economic status and tumor stage, with LIC patients showing a threefold higher risk of death and a threefold lower likelihood of globe salvage compared to HIC patients. These trends reflect those in global studies, emphasizing the need for improved cancer care and resources in lower-income settings to address these disparities.

Aqueous Humor Liquid Biopsy as a Companion Diagnostic for Retinoblastoma: Implications for Diagnosis, Prognosis, and Therapeutic Options: Five Years of Progress
Berry JL, Pike S, Shah R, et al
Am J Ophthalmol 2024;263:188-205
The study explored the use of aqueous humor (AH) as a molecular diagnostic and prognostic tool for retinoblastoma (RB) over a five-year period, addressing challenges related to tumor biopsy and the lack of molecular biomarkers for intraocular prognosis. This prospective, observational study involved AH liquid biopsies at diagnosis and during therapy, analyzing tumor-derived cell-free DNA for RB1 gene mutations and somatic copy number alterations (SCNAs). Among 26 eyes from 21 patients, ocular salvage was successful in 73.1% of cases. Pathogenic RB1 variants and focal deletions were identified, and SCNAs, including 6p gain and focal MycN gain, were associated with poorer therapeutic outcomes. Higher tumor fraction (TFx) was linked to disease progression. The study is notable for its prospective validation of AH as a liquid biopsy tool, offering real-time molecular insights into RB. However, its small sample size and technical challenges in measuring TFx limit its current applicability. The findings suggest that AH liquid biopsy could enhance prognostic capabilities and guide personalized treatment for RB, though further validation is needed.

Retinoblastoma in Asia: Clinical Presentation and Treatment Outcomes in 2112 Patients from 33 Countries
Kaliki S, Vempuluru VS, Mohamed A, et al
Ophthalmology 2024;131(4):468-477
This study's aim is to investigate the clinical presentation, availability of resources for treatment, and outcomes of retinoblastoma in different regions in Asia. 2112 patients from 96 retinoblastoma treatment centers from 33 Asian countries participated. Regions were divide as follows: Central Asia (Azerbaijan, Kazakhstan, Kyrgyzstan, Uzbekistan), East Asia (China, Japan, Mongolia, Russia, South Korea, and Taiwan), South Asia (Bangladesh, India, Iran, Nepal, Pakistan, and Sri Lanka), Southeast Asia (Indonesia, Laos, Malaysia, Philippines, Singapore, Thailand, Timor-Leste, and Vietnam), and West Asia (Iraq, Israel, Jordan, Kuwait, Lebanon, Saudi Arabia, Turkey, UAE, and Yemen). Please refer to table 1 in the paper for demographic data. The mean age of presentation was 27 months, slightly higher than the global average of 23 months. The mean lag-time between onset of symptoms to presentation was 5

months and was greatest for Central Asia (15 months), which was significantly different from other regions. The mean distance from patient's home to a center was highest for Western Asia (742km) and Central Asia (725km). Leukocoria was the most common presenting symptom in all regions. Advanced disease (stage T3 or T4) was more common in Central, Southeast, and South Asia. In terms of resources, genetic testing was available for 36% of patients, imaging for 100%, pathology for 99%. Enucleation was available if needed for all patients, intravenous chemotherapy for 99%, laser for 90%, cryotherapy for 83%, intra-arterial chemotherapy for 51%, intravitreal chemotherapy for 77%, plaque radiotherapy for 25%, and external beam radiotherapy for 76% - this varied significantly between regions. Intravenous chemotherapy was the primary treatment for most patients, followed by enucleation in most regions. For bilateral disease, intravenous chemo was the most common treatment in all regions. For outcomes, overall globe salvage was achieved in 41% of patients with the highest rate in East Asia (48%) and lowest in Southeast Asia (27%). Metastasis was seen in 8% of patients after a mean follow-up of 26 months and was highest in Southeast Asia. Death resulted in 8% of patients and was also highest in Southeast Asia. The strength of this investigation its large cohort, but the weakness is that it only included data on patients from the centers that participated. This study also only includes data on patients between 2017-2021, so the environment may have changed since that time due to efforts for increasing screening/access at participating centers. The study shows that significant heterogeneity is present in the availability of resources and outcomes through Asia and that approaches to improve detection and access to resources through collaboration could play a significant role in improving outcomes.

Consensus Guidelines for Ocular Surveillance of von Hippel-Lindau Disease
Daniels AB, Chang EY, Chew EY, et al
Ophthalmology 2024;131(5):622-633
This paper was written as recommendations for screening and early treatment of retinal hemangioblastomas in patient with VHL as part of the effort by the International VHL Surveillance Guidelines Consortium to develop a comprehensive evidence-based set of guidelines for patients with VHL disease to help promote universal and standardized care. The ophthalmology task force performed a retrospective study with de-identified subject details and a comprehensive literature review within the committee. The papers were reviewed and based on the type and strength of evidence the group made recommendations. 1) individuals with known of suspected VHL should undergo periodic ocular screening. This was recommended as the detection and treatment of small asymptomatic lesions may lead to better visual outcomes. 2) patients at risk for VHL or those with single or multifocal RHs should undergo genetic testing for the VHL gene. This could lead to earlier surveillance and detection of life threatening manifestations of the disease and may lead to increased life expectancy. 3) ocular screening should begin within 12 months of birth and continue throughout life. 4) screening should occur every 6-12 months until 30 and then yearly thereafter. 5) ocular screening should be performed before a planned pregnancy and every 6-12 months during pregnancy. 6)Ultra-widefield fundus photos and IVFA may be useful to monitor RHs and detect small RHs but should be used as adjuncts to detailed dilated fundus exam. 7)Patients should be managed in a setting with subspecialists experienced with VHL or RHs. 8) Extramacular or extrapappilary RHs should be treated promptly especially in places with poor follow-up or in patients with whom poor reporting

of symptoms is concerned. This paper is significant as it sets out a clear set of guidelines for the surveillance and possible management of RHs in VHLdisease. Overall the early detection and treatment of the RHs seems to indicate an improvement in vision preservation and thus the recommendations could provide a framework to better improve outcomes.

Association of Neighborhood Opportunity With Severity of Retinoblastoma at Presentation
Altamirano-Lamarque F, Lim C, Shah AS, et al
Am J Ophthalmol 2024;261:1-6
This study aimed to examine how neighborhood opportunity levels, as measured by the Community Opportunity Index (COI), impact the severity of retinoblastoma at diagnosis. Using a cross-sectional design, the researchers analyzed data from 125 children under 18 treated for retinoblastoma at a tertiary care center between January 2000 and May 2023. They utilized residential census tracts to calculate COI scores and assessed the association between these scores and disease severity using mixed effects regression models, adjusting for individual-level socioeconomic factors. The findings revealed that children from neighborhoods with lower COI scores, particularly in the education domain, were more likely to present with advanced retinoblastoma. Specifically, a 20-point decrease in overall COI score increased the odds of advanced disease by 62%, with educational factors contributing an even higher risk. This suggests that socioeconomic factors at the neighborhood level significantly affect diagnostic timing and disease severity. The study highlights the need for improved access to preventative and specialty care in low-resource areas to address these disparities. Limitations include the potential lack of generalizability to other regions of the US and potential selection bias due to exclusions. The study calls for policy changes to enhance early diagnosis and care in underserved communities and further research into how neighborhood characteristics and healthcare access influence diagnostic delays.

The Pediatric and Young Adult Choroidal and Ciliary Body Melanoma Genetic Study, A Survey by the European Ophthalmic Oncology Group
van Poppelen NM, Cassoux N, Turunen JA, et al
Invest Ophthalmol Vis Sci 2024;65(4):12
This paper, Conducted by the European Ophthalmic Oncology Group, investigates the genetic factors associated with choroidal and ciliary body melanoma in patients under 25 years old. They focus on quantifying BAP1 germline variants in this age group. Patients under the age of 25 and with confirmed choroidal or ciliary body melanoma were included in this retrospective, multicenter observational study. Nuclear BAP1 immunopositivity was used to evaluate the presence of functional BAP1 in the tumor. Next-generation sequencing was used to determine pathogenic variants of BAP1, EIF1AX, SF3B1, GNAQ and GNA11 and chromosome 3 status in the tumor or in DNA extracted from blood or saliva. Survival was analyzed using Kaplan-Meier estimates. The authors did not find a stronger-than-average BAP1 germline predisposition for choroidal and ciliary body melanoma among children and young adults compared to adults. Males had a more favorable survival and disomy 3, and the absence of a BAP1 mutation in the tumor tissue predicted the most favorable metastasis-free survival. A BAP1 germline pathogenic variant was identified in one patient (1%), and a somatic variant based mainly on immunohistochemistry in 13 (42%). This paper offers significant insights into the genetic factors

associated with choroidal and ciliary body melanoma in younger patients, with potential implications for personalized medicine and clinical practice. However, limitations related to sample size, generalizability, and long-term data should be considered.

A Review of Pediatric Ophthalmic Tumors
Yeager LB, Kassotis A, Frank T, et al
Pediatr Rev 2024;45(3):119-131
Tumors of the eye, orbit, and ocular adnexa can arise in the pediatric population. These entities can be both vision- and life-threatening and may be associated with systemic disease. Given their relative rarity, pediatricians must be aware of these conditions and understand what findings warrant immediate referral to an ophthalmologist for initiation of further testing. We aimed to review these conditions and highlight clinical features to promote awareness and expedite diagnosis. Tumors are subdivided into the following categories for review: anterior tumors of the eyelid and ocular surface, orbital tumors, and intraocular tumors. This is an informational review article

Risk factors for cataract in retinoblastoma management
Jia S, Wen X, Yu J, et al
Br J Ophthalmol 2024;108(4):571-577
This is a retrospective cohort study of patients with retinoblastoma receiving eye-preserving therapies 2017-2021 looking at cataract as the main outcome. The mean followup period was 27.6 months, and 16.8% (31/184) of eyes had a cataract. Cataract eyes were more likely to have endophytic disease and greater IOP. Multivariable analysis showed that higher IOP, higher melphalan dose per IAC cycle and increasing number of intravitreous chemotherapy cycles were independent risk factors for cataract. There was no significant difference in the drug dose per injection between the two groups. These data can help fine-tune treatment regimens to optimize RB treatment and minimize vision-related side effects.

Retinal Reactive Astrocytic Tumor and Astrocytic hamartomas in patient with Neurofibromatosis type 1: Case Report and Literature review
Hadjistilianou T, Carnicci A, D'Alessandro C, et al
Eur J Ophthalmol Published online August 14, 2024
Neurofibromatosis type I (NF1) is the most common phakomatosis and may be associated with several ocular findings including Lisch nodules, plexiform neurofibromas, optic pathway gliomas, retinal astrocytic hamartomas, and choroidal nodules. It is important to provide examples in the literature of uncommon manifestations such as retinal reactive astrocytic tumor (RRAT) to help physicians diagnose and manage them. This study is a case report of a 15-year-old with NF1 who has two retinal astrocytic hamartomas (RAH) and one RRAT. The report provides clinical information as well as photographs, OCT, pictures of fluorescein angiography and ICG-angiography to document RAH's and RRAT with its fine telangiectasias, feeder vessel, intraretinal and subretinal exudation, and epiretinal membrane. The patient received cryotherapy which resulted in gradual reduction in peri-tumoral exudation and stabilization of the lesion. The case report provides clear information about a case of RRAT but is limited by discussion of only one patient. It supports the idea that retinal vascular abnormalities are

associated with NF1 but this association continues to be debated. This severe but asymptomatic ophthalmologic finding in a patient with NF1 supports the periodic examination of these patients for tumor detection and treatment.

Differences in Childhood Growth Parameters Between Patients With Somatic and Heritable Retinoblastoma
Hicks RM, Ji X, Zou Y, et al
Invest Ophthalmol Vis Sci 2024;65(4):39
The aim for this study was to compare childhood growth parameters between somatic and heritable Rb cohorts at birth and at time of diagnosis with Rb. Somatic (n = 39) and heritable (n = 214) Rb cohorts were analyzed from 11 centers in 10 countries who presented with treatment naïve Rb from January to December 2019. Variables of interest included age, sex, and size characteristics at birth and at time of presentation, as well as germline mutation status. Children with Rb seem to have normal birth and childhood growth patterns. There is no definitive evidence that somatic or heritable Rb has a biological or environmental impact on childhood growth parameters.

Retinopathy of Prematurity

Initiation of retinopathy of prematurity screening examinations in extremely premature infants
Souverein EA, Siegel BA, Siegel LM, et al
J AAPOS 2024;28(4):103956
This study aimed to assess whether extremely premature infants (born at gestational age [GA] 22-24 weeks) should undergo earlier screening for retinopathy of prematurity (ROP) compared to infants born at GA 24-30 weeks, for whom current American Academy of Pediatrics (AAP) guidelines are well-established. Using data from 2,061 infants born over a ten-year period, it was found that infants born before 24 weeks GA were more likely to develop plus disease or require treatment compared to those born at 24-30 weeks. Although these extremely premature infants developed ROP earlier in terms of post-menstrual age, they were older in chronological age when they developed the disease. Strengths of the study include its large dataset from multiple sites, while limitations include regional variation and evolving standards for evaluating ROP over time. The study suggests that clinicians should consider starting ROP screening earlier for infants born before 24 weeks GA, especially those with lower birth weights, due to their higher risk of requiring treatment before 31 weeks PMA.

The Incidence and Timing of Treatment-Requiring Retinopathy of Prematurity in Nanopremature and Micropremature Infants in the United States: A National Multicenter Retrospective Cohort Study
Scarboro SD, Harper CA 3rd, Karsaliya G, et al
Ophthalmol Retina 2024;8(3):279-287
With advances in neonatology, premature babies with younger gestational ages and lower birth weight are surviving. This unique population of extremely premature infants was not well included in landmark ROP trials evaluating prevalence and treatment of ROP. This is a multicenter retrospective cohort study from five sites across the United States focused on ROP in micropremature (<800g BW and/or <26 weeks GA) and nanopremature (<600g BW and/or <24 weeks GA). Primary data collected were number of patients treated for ROP, type of initial treatment pursued, and post-menstrual age at development of treatment-requiring ROP. A total of 7293 patients were screened for ROP across all sites, and 8.52% required treatment with an average PMA of 37.2 weeks. Infants defined as nanopremature had a 63% chance of requiring treatment at an average postmenstrual age (PMA) of 36.6 weeks, whereas those defined as micropremature had a 30% chance of requiring treatment at an average PMA of 36.3 weeks. Those with the highest risk are nanopremature infants by both weight and gestational age, being 26.2 times more likely to require treatment than the entire group of infants screened, Interestingly, the average postmenstrual age at treatment did not differ between groups. Overall, this is an important study highlighting the increased risk of ROP in micropremature and nanopremature infants and assists in screening and counseling for these extremely premature infants.

Exposure to persistent hemodynamically significant patent ductus arteriosus is associated with retinopathy of prematurity
Ford A, Beauchene M, Stanford AH, et al

J AAPOS 2024 Jun;28(3):103923
Hemodynamically significant patent ductus arteriosus (hsPDA) shunt may predispose infants to retinopathy of prematurity (ROP) due to its higher preductal cardiac output and blood oxygen content, which may augment ocular oxygen delivery. Summary of design: A retrospective cohort study included preterm infants born at <27 weeks' gestation who underwent universal and standardized PDA screening. The primary composite outcome was death at <32 weeks or moderate-to-severe ROP (≥stage 2 or requiring treatment) in either eye. Infants with hsPDA were compared to those without hsPDA. Summary of results: The study included 86 infants (54 with hsPDA and 32 controls). hsPDA patients were younger and lighter at birth and had a higher burden of hyperglycemia and respiratory illness. Compared to those without hsPDA, hsPDA patients were more likely to develop the composite primary outcome of death or moderate-to-severe ROP (P<0.001), more likely to die (P<0.001), had more ROP of any stage (P = 0.002), and had more severe ROP when present (P = 0.027), with a non-significantly higher incidence of ROP intervention. Strengths and limitations: The strength of the study lies in its strict definition of hsPDA and PDA exposure. Limitations include its single-center retrospective cohort design, which limits generalizability, and the small number of infants who developed treatment-indicated ROP. Impact on clinical practice: This study highlights the association between hsPDA and ROP among infants <27 weeks and suggests that shunt modulation may be a potential strategy to reduce ROP incidence, though it was not associated with treatment-indicated ROP, indicating a potential modifiable risk factor.

Extending Peripheral Retinal Vascularization in Retinopathy of Prematurity Through Regulation of VEGF Signaling
Sauer L, Chandler M, Hartnett ME
Am J Ophthalmol 2024;260:190-199
The study aimed to evaluate whether intravitreal anti-VEGF treatment with bevacizumab promotes vascularization in the peripheral avascular retina of infants with type 1 retinopathy of prematurity (ROP) compared to a control group with less severe ROP. Conducted from January 2019 to December 2022, this retrospective, nonrandomized study compared 11 preterm infants with type 1 ROP treated with bilateral bevacizumab (0.25 mg) to 11 matched infants with less severe ROP. Fundus imaging was performed within 2 weeks of treatment and 1-3 weeks later, with temporal retinal vascular extent as the primary outcome. The treatment group showed a trend toward shorter temporal vascular extent at baseline, though not statistically significant (P=0.084), and no significant difference at follow-up (P=0.945). However, the treatment group exhibited significantly greater vascular extension compared to controls (872±521 pixels vs. 253±151 pixels, P=0.003), suggesting catch-up growth. Strengths of the study include the well-defined control group, rigorous imaging analysis, and consistency in imaging parameters. Limitations involve the small sample size, retrospective design, lack of fluorescein angiography, and exclusion of some infants due to poor-quality images. The study supports the hypothesis that anti-VEGF treatment enhances peripheral retinal vascularization in type 1 ROP, indicating that this therapy not only inhibits pathological angiogenesis but also promotes developmental vascular growth. Further research with larger samples and additional imaging techniques is needed to validate these findings and refine ROP treatment protocols.

Multinational External Validation of Autonomous Retinopathy of Prematurity Screening
Coyner AS, Murickan T, Oh MA, et al
JAMA Ophthalmol 2024;142(4):327-335
Retinopathy of prematurity (ROP) is preventable but remains a leading cause of childhood blindness, particularly in regions where there are not enough ophthalmologists to screen and treat ROP. The purpose of this study was to evaluate if autonomous artificial intelligence (AI) based ROP screening can detect more-than-mild ROP (mtmROP- eyes with type 2 ROP or type 1 ROP or any eye with pre-plus disease) and type 1 ROP. An AI algorithm was developed using 2,530 examinations from 843 infants in the imaging and informatics in ROP study (i-ROP). This technology was used to assess 2 external datasets- 6,245 exams from 1,545 infants in the Stanford University Network for Diagnosis of ROP (SUNDROP) cohort in the US and 5,635 exams from 2,699 infants in the Aravind Eye Care Systems (AECS) cohort in India. The mean birth weight was 423 g lower (P<0.001) and the mean gestational age was 4.2 weeks lower (P<0.001) in SUNDROP compared with AECS. Infants who developed mtmROP had lower birth weight and GA compared with infants with no or mild ROP. The prevalence of mtmROP and type 1 ROP were 5.9% and 1.2% in the SUNDROP dataset and 6.2% and 2.5% in the AECS dataset. mtmROP detection had high sensitivity (SUNDROP: mtmROP 83.5% and type 1 ROP 82.2% and AECS: mtmROP 80.8% and type 1 ROP 87.8%). All infants who developed type 1 ROP had a positive screen prior to diagnosis. This study shows that AI could aid ROP prevention efforts globally though there are implementation challenges.

Early Single-Examination Optical Coherence Tomography Biomarkers for Treatment-Requiring Retinopathy of Prematurity
Chen X, Mangalesh S, He J, et al
Invest Ophthalmol Vis Sci 2024;65(4):21
The authors intend to highlight using OCT in a single examination to detect early OCT biomarkers that predict treatment-requiring ROP, potentially reducing the need for repeat evaluations and facilitating earlier intervention. They intend to identify biomarkers by reviewing an 11-year research database of OCT data largely acquired on preterm infants at 32 ± 1 weeks postmenstrual age (PMA). Total retina, inner retinal layer (IRL), and outer retinal layer (ORL) thicknesses at the fovea and the parafovea, inner nuclear layer (INL) and choroidal thickness, parafovea/fovea (P/F) ratio, and presence of macular edema was recorded for 277 eyes. Of these infants, 7 eyes had TR-ROP. Lower P/F ratio (P < 0.0001), thicker foveal IRL (P = 0.0001), and thinner choroid (P = 0.03) were associated with TR-ROP in univariable analysis, but lost significance of association when adjusted for gestational age and race. Absence of macular edema was associated with TR-ROP when adjusted for gestational age and race (P = 0.01). In 185 eyes without macular edema, P/F ratio was associated with TR-ROP in both univariable analysis (P < 0.0001) and multivariable analysis (P = 0.02) with adjustment for gestational age and race. The authors conclude the presence of macular edema at 32 ± 1 weeks PMA in infants with lower gestational age may be protective against TR-ROP. In infants without macular edema, P/F ratio may be an early OCT biomarker for development of TR-ROP. This paper's strengths include its innovative use of OCT for early ROP detection and its potential to limit examinations. However, limitations such as issues with generalization, the need

for follow-up assessments, practical challenges, and lack of long-term outcome data should be considered.

Implementation of optical coherence tomography in retinopathy of prematurity screening
Hanif AM, Jian Y, Young BK, et al
Curr Opin Ophthalmol May 1 2024;35(3):252-259
This literature review explores the use of optical coherence tomography (OCT) in screening for retinopathy of prematurity (ROP). Traditional ROP exams often suffer from interobserver variability due to their subjective nature, and they can be stressful for newborns. OCT offers several advantages over these exams, primarily through the use of infrared light, which avoids the stress of bright visible light. Additionally, some handheld OCT devices can capture images without direct contact or the use of a speculum, further reducing stress and minimizing infant instability, such as episodes of bradycardia and apnea. Importantly, OCT is also faster than traditional indirect ophthalmoscopy. One of the key benefits of OCT is its ability to reduce the subjectivity of clinical examinations by providing quantifiable measurements for disease classification and identifying novel biomarkers. Recent advancements, such as handheld ultra-widefield OCT, have demonstrated the ability to capture high-contrast vascular images across up to 140 degrees of the retina, enabling longitudinal tracking and more objective assessments of disease progression. Moreover, en face imaging may be leveraged to generate AI-based predictors for more precise diagnosis. OCT angiography (OCTA) complements these advancements by measuring vascularization, detecting neovascularization, and identifying areas of non-perfusion. When combined with OCT B-scan, OCTA could improve ROP staging accuracy. The observation of avascular regions and additional biomarkers, such as vitreous opacities, choroidal thinning, and cystoid macular edema (CME), has been linked to disease severity, further enhancing the precision of diagnosis. The widespread adoption of OCT for ROP screening will depend on several factors, including its technological feasibility, clinical utility, and support from the industry.

Five-Year Visual Outcome of Treatment for Retinopathy of Prematurity in Infants Weighing <500 g at Birth: A Multicenter Cohort Study from J-CREST
Tomioka M, Murakami T, Okamoto F, et al
Retina 2024;44(4):652-658
Management of extremely premature infants weighing less than 500g at birth is challenging. Several studies have shown an increased risk for ROP in these infants as well as a higher frequency of treatment. This retrospective study evaluated visual outcomes in infants weighing less than 500g at birth with at least 5 years of follow-up. A total of 24 eyes of 13 patients were included. Snellen visual acuity was greater than or equal to 20/40 in 73% and 20/20 or better in 27%. Median spherical equivalent was -2.37D, with 25% having high myopia of greater than -6D. Eyes treated with anti-VEGF showed less myopia than laser-treated eyes, with no difference in BCVA or astigmatism. Overall, this study shows relatively good visual outcomes following ROP treatment in extremely premature infants. It suggests that anti-VEGF therapy may be superior to laser in terms of ROP, but the small sample size supports that further studies are needed.

Fluorescein Angiography Evaluation of Children Previously Treated with Anti-Vascular Endothelial Growth Factor Monotherapy for Retinopathy of Prematurity
Poslu Karademir F, Vural A, Özbaş M, et al
Retina 2024;44(5):901-908
In recent years, anti-VEGF has increasingly been used to in the treatment of ROP. It has particular advantages over conventional laser in cases with vitreous hemorrhage, poor dilation, or very posterior ROP. A theoretical advantage of anti-VEGF is that it allows peripheral retinal vascularization to continue, although it is unknown when vascularization is complete. Fluorescein angiography images from 486 eyes of 250 patients with type 1 ROP or A-ROP treated with a single dose of anti-VEGF were analyzed in this study. In all cases, FA was performed at age 1 or older. 17% of eyes had vascular termination in Zone II 83% in Zone III. Abnormal vascular findings were noted, including circumferential vessels (41.2%), finger-like projection anomaly (36.2%), hyperfluorescence (16.9%), fine branching and blunt termination (15%), and arteriovenous shunt (9.9%). This study illustrates that retinal abnormalities are frequently seen following anti-VEGF treatment in ROP. 17% of eyes required prophylactic laser photocoagulation for peripheral avascular retina. Fluorescein angiography was able to detect neovascularization that was not present on clinical examination and may aid in treatment of these infants, particularly with timing of laser.

Circulating VEGF-A Levels in Relation to Retinopathy of Prematurity and Treatment Effects: A Systematic Review and Meta-Analysis
Sjöbom U, Hellqvist T, Humayun J, et al
Ophthalmol Sci 2024;4(6):100548
While VEGF is known to play an important role in the ROP development and both anti-VEGF and laser treatment are aimed at decreasing activity of VEGF, the relationship of systemic VEGF with ROP development remains unclear. This study aimed to provide a systematic review, summarizing the reported levels of VEGF in blood samples associated with ROP and secondarily evaluate whether ROP treatment affects circulating VEGF levels. A total of 54 publications were reviewed, 26 of these investigating VEGF-A before and after ROP treatment (7 for laser, 20 for anti-VEGF, 3 for both). While VEGF-A levels decreased at week-1 and month-1 post-treatment for both modalities, anti-VEGF had a more pronounced decrease compared to laser ($P<0.01$ and $P=0.02$) which lasted several weeks longer than that of laser. There was no significant difference in the degree of systemic VEGF reduction when comparing anti-VEGF drugs (bevacizumab, ranibizumab, conbercept, and aflibercept) at the first week of treatment, but by 1 month there was a difference; Bevacizumab> Aflibercept> Ranibizumab/conbercept. There were 31 publications reporting VEGF levels in ROP cases compared to control groups; no discernable trend was noted, thus was not felt to have utility in predicting ROP development. Of note, there remains significant variability in the protocols used to evaluate blood-VEGF levels and this leads to limitations in comparison of outcomes in these studies. Future studies on the timeline of VEGF suppression after ROP treatment would be helpful to continue to address gaps in knowledge regarding systemic effects of ROP treatment.

Outcome of Eyes Treated for Retinopathy of Prematurity in Posterior Zone I: An Eastern India Study

Padhi TR, Bhunia S, Shah M, et al
Retina 2024;44(6):1073-1082
The eyes with ROP in zone 1 often progress rapidly and have a poor visual outcome. ROP in posterior Zone 1, between the optic disc and foveal center, is particularly challenging due to a nonperfused macula, rapid progression, and often critically ill infants. This study is a retrospective review of data from a tertiary hospital in India from 2012-2022. All babies with treated for ROP in posterior Zone 1 with 6 months of follow-up were included, for a total of 109 eyes. Eyes were sub-grouped into favorable or non-favorable anatomic features, with unfavorable anatomic features including ROP stage 4A, 4B, or 5 or falciform retinal fold in the macula. Anti-VEGF was the initial treatment modality in 101 eyes (93%), either alone (27 eyes) or combined with laser or vitreous surgery (73 eyes). Laser was the initial treatment modality in 8 eyes, either alone (3 eyes) or in combination with surgery (5 eyes). At the final follow-up, 89.9% (out of 109) of eyes did well anatomically. Good outcome was significantly linked to no detachment at presentation. Overall, this study shows the importance of timely screening and treatment of ROP prior to development of retinal detachment, which was associated with an unfavorable anatomic outcome.

Enhancing the Retinopathy Of Prematurity Risk Profile Through Placental Evaluation of Maternal and Fetal Vascular Malperfusion
El Emrani S, Jansen EJS, Goeman JJ, et al
Invest Ophthalmol Vis Sci 2024;65(11):9
The placenta plays an important role in providing nutrients to the fetus, and placental dysfunction is strongly associated with fetal growth restriction and fetal death. Maternal fetal malperfusion involves changes in the maternal decidual vasculature or villous parenchyma that affect the maternal circulation to the fetus. Fetal vasculature malperfusion involves pathological conditions such as umbilical cord lesions or other abnormalities that result in hypoxia for the fetus. This retrospective cohort study analyzed infants born between 1991-1995 and 2001-2005. Histological examination form tissue samples of the placenta were evaluated for 591 neonates with a gestational age < 32 weeks or birth weight < 1500g. Maternal vascular malperfusion was associated with higher GA, lower BW, and increased SGA rates, except placental abruption, which was associated with lower SGA rates. Fetal vascular malperfusion was associated with lower BW, increased SGA rates and lower duration of mechanical ventilation. Subgroup analysis of placentas without inflammation showed increased rates of distal villous hypoplasia (44% vs. 31%) and hydrops parenchyma (7% vs. 0%) in neonates with ROP. Multivariate regression analyses revealed three placenta factors to be independently associated with ROP: distal villous hypoplasia, severe acute histological chorioamnionitis and funisitis. Overall this study supports that intrauterine environment may effects on the risk of ROP, which could be helpful in better identifying infants most at risk for ROP.

Validation of the East London Retinopathy of Prematurity algorithm to detect treatment-warranted retinopathy of prematurity: a cohort study
Moorthy S, Adams GGW, Smith G, et al
Br J Ophthalmol 2024;108(3):471-475

The EL-ROP algorithm is specifically designed for premature infants in the UK and includes ethnicity as a factor associated with the development of severe ROP along with BW and GA and early weight gain. This study retrospectively applied the EL-ROP algorithm to data collected on 568 infants eligible for ROP screening in 2 tertiary NICUs in England in order to validate the algorithm in this population. The EL-ROP recommendation to screen or not was compared with the development of treatment-warranted ROP for each infant. 58(10%) developed treatment warranted-ROP and in every case this was predicted by the EL-ROP algorithm. Its sensitivity was 100% (95% CI 94-100%) specificity: 44% (95% CI 39-48%) positive predictive value: 17% (95%CI 16-18%), negative predictive value: 100%. The authors seek to further validate this in additional cohorts before its clinical usefulness can be assessed.

Genetic Variants of the Beta-Adrenergic Receptor Pathways as Both Risk and Protective Factors for Retinopathy of Prematurity
Paradis H, Werdyani S, Zhai G, et al
Am J Ophthalmol 2024;263:179-187
The study investigated the association between genetic variations in β-adrenergic receptor (ADRβ) signaling pathways and the risk of developing retinopathy of prematurity (ROP). Given the concerns about the safety of ADRβ antagonists being tested for ROP treatment, this research aimed to explore how genetic polymorphisms in these pathways might influence ROP risk. Utilizing an observational case-control design, the study included two cohorts: a discovery cohort with 30 premature infants with ROP, 34 premature infants without ROP, and 20 full-term controls, and a validation cohort with 14 additional premature infants and 1 repeat participant. Targeted sequencing of 20 ADRβ pathway genes revealed 543 bi-allelic variants, with ten single-nucleotide variants (SNVs) in five genes (PRKAR1A, RAPGEF3, ADCY4, ADCY7, ADCY9) significantly associated with ROP. The most significant SNV was in PRKAR1A. Validation with PCR and restriction enzyme analysis confirmed the association of RAPGEF3 SNVs with ROP. The study's small sample size limited statistical power and generalizability, and findings were not linked to gestational age. Nonetheless, the identification of specific SNVs related to ROP may offer new genetic markers for predicting and preventing severe ROP, potentially informing the development of targeted therapies and improving early diagnosis. Further multicenter studies with larger cohorts are needed to validate these findings and assess their clinical relevance.

Corneal Endothelial Morphology and Ocular Biometric Indexes in Premature Children With and Without Retinopathy of Prematurity
Chen HC, Yang SF, Lee CY, et al
Invest Ophthalmol Vis Sci 2024;65(5):37
The purpose of this study was to analyze human corneal endothelial cells (HCECs) morphology and ocular biometrics in premature (PM) children with or with-out retinopathy of prematurity (ROP). Retrospective data on 173 PM patients without ROP and 139 patients with ROP was collected. The main outcomes were endothelial cell density (ECD), coefficient of variation (CV), hexagonal cell ratio (HEX), central corneal thickness (CCT), axial length, anterior chamber depth, keratometry, corneal diameter, pupil diameter, and refraction status. Change with age was also noted. The ROP group had higher spherical power, myopic spherical equivalent (SE),

and steeper steep keratometry (K; P < 0.05). The ROP group had higher CV (P =0.0144), lower HEX (P = 0.0012) and thicker CCT (P = 0.0035). In the HCECs parameters, the ROP group had slower ECD decrement (P < 0.0001), faster CV decrement (P =0.0060), and faster HEX increment (P = 0.0001). A difference in corneal morphology changes between the ROP and PM no-ROP groups were prominent in patients with lower gestational age (GA) in the subgroup analysis. ECD and HCECs morphology improved with age, especially in patients with low GA. Corneal endothelial morphology and ocular biometric indexes differ between premature children with and without retinopathy of prematurity, suggesting that ROP can influence corneal and ocular development.

Image Analysis-Based Machine Learning for the Diagnosis of Retinopathy of Prematurity: A Meta-analysis and Systematic Review
Chu Y, Hu S, Li Z, et al
Ophthalmol Retina 2024;8(7):678-687
The incidence of ROP has been increasing worldwide due to the high number premature infants. Diagnosis of ROP requires careful screening, and there are challenges in access to care, particularly in low- and middle-income countries. Machine learning has shown promise in other medical disciplines, and this study sought to evaluate the performance of machine learning algorithms for diagnosis and classification of ROP in a structured systematic review and meta-analysis. Two researchers independently reviewed the literature to find studies evaluating image-based machine learning algorithms for diagnosis and classification of ROP. The primary endpoints were sensitivity, specificity, and positive and negative likelihood ratios. The secondary endpoint was assessing the similarity between machine learning and human experts. All studies were evaluated for risk of bias, indirectness, inconsistency, imprecision, and publication bias. A total of 22 studies were included. The overall sensitivity was 93%, and specificity was 95%. The area under the receiver operating characteristic curve (AUC) was 0.98. For the classification of clinical subtypes of ROP, the sensitivity and specificity were both 93%, and the AUC was 0.97. The classification results were highly similar to those of clinical experts. Overall, this is a well-conducted meta-analysis of machine learning algorithms for ROP diagnosis and classification. It emphasizes the potential role of machine learning algorithms in the future, although further studies are needed, as this analysis merely pooled studies and did not report the characteristics of any specific algorithm.

Treated Cases of Retinopathy of Prematurity in Germany: 10-Year Data from the Retina.net
Pfeil JM, Barth T, Lagrèze WA, et al
Retina 2024;8(6):579-589
While ROP remains a significant concern, it is overall a rare disease, especially in countries with adequate access to medical care and ROP screening and treatment. In 2012, a German ROP registry was established to collect clinical data for infants treated for ROP. This is a presentation of 10-year data from the database, for infants born between 2011 and 2020. Due to the registry not covering all treating centers, around 15% of all infants treated for ROP in Germany were included in this observational study. A total of 353 infants requiring ROP treatment were included in the analysis. The most prevalent ROP severity stage at treatment was stage 3+ in zone II (76.6% of all treated eyes). Treatment patterns changed considerably from

predominantly laser treatments in 2011 (75% of all treated eyes) to predominantly ranibizumab treatments in 2020 (60.9% of all treated eyes). The overall re-treatment rate was 15.6%. Re-treatment rates differed between initial treatment modalities (14.1% after laser coagulation, 12% after bevacizumab and 24.5% after ranibizumab). Gestational age, weight at birth, and weight at treatment remained stable over the study period. Postmenstrual and postnatal age a treatment increased moderately over the same time period. Overall, this study provides important longitudinal trends in ROP treatment. Given it was performed at a limited number of centers in Germany, the generalizability to other settings may be limited.

Development of a joint set of database parameters for the EU-ROP and Fight Childhood Blindness! ROP Registries
Catt C, Pfeil JM, Barthelmes D, et al
Br J Ophthalmol 2024;108(7):1030-1037
An international Core Working Group of clinicians and ROP experts was formed following communication about mutual interest in developing ROP registries with the goal to develop a data set that focused on real-world parameters and outcomes that were patient-centered, minimal and feasible to collect in routine clinical practice. They used the EU-ROP registry (formerly German retina.net), which includes multinational data entry from countries across geographical Europe and the Fight Childhood Blindness! ROP Registry to develop the list of data variables for the registry which are nicely outlined in the tables in the article. Key variables include: patient demographics, systemic comorbidities, ROP status, treatment details, ophthalmic and systemic complications of treatment, ophthalmic and neurodevelopmental outcomes at initial treatment, any episodes of retreatment and follow-up examinations in the short and long-term.

Outcomes of Modified Limbal Lensectomy-Vitrectomy in Stages 4B and 5 Retinopathy of Prematurity with Extended Retrolental Fibroplasia
Chehaibou I, Abdelmassih Y, Metge F, et al
Ophthalmol Retina 2024;8(6):590-599
Surgical treatment of advanced ROP remains a challenge, especially in low and middle-income countries, where there is limited access to screening and treatment. Despite technological advancements, surgical techniques and outcomes have had little advancement. The study authors report a modified limbal lensectomy-vitrectomy technique for use in advanced cases with retrolental fibroplasia that would preclude a pars plana vitrectomy. 128 eyes of 81 patients were included, all with stage 4B or 5 ROP. The surgical technique involved 25-gauge instrumentation inserted through limbal paracentesis. Iris hooks were used to widen the pupil followed by removal of the lens with vitrectomy probe. Retrolental fibroplasia was dissected along with preretinal fibrosis. No tamponade was used. Of the total, 57.8% of eyes had anatomic success, with the macula attached. 12.5% had partial success, with RD continuing to involve parts of the macula. 18% of eyes had a total RD and were considered an anatomic failure. 11.7% of eyes were lost, due to opacified cornea, secluded pupil, or phthisis. In terms of functional outcome, 17.4% of eyes could fix and follow an object, 15.2% fix and follow light, 31.5% had light perception, and 35.9% had no light perception. Overall, this study describes an interesting limbal technique for repair of these complex RD's which resulted in an over 50%

attachment rate. The study is unable to directly compare to other methods, however, which limits interpretation of this method compared to open sky vitrectomy and other techniques.

Strabismus

Effects of orbital decompression on duction, cyclotorsion and diplopia
Jellema HM, Althaus M, Merckel-Timmer E, et al
Br J Ophthalmol 2024;108(8):1075-1080
This is a retrospective review of 281 eyes/orbits of 156 patients with Graves' orbitopathy who underwent orbital decompression 2016-2020. The mean age of patients was 48 years and the majority (88%) were female. Some patients received previous therapies like steroids or radiation. Statistically significant changes in proptosis were noted after both bony decompression and fat decompression only. A significant change in ductions was noted only with patients who underwent bony decompression. The horizontal deviation for near and distance changed significantly towards esodeviation whereas the vertical deviation did not. Cyclodeviation in primary and downgaze showed a significant change towards incyclotorsion. Diplopia improved in 22% (18 patients), whereas new-onset constant diplopia developed in 11% (12 patients). Elevation has an excellent predictive value of causing new-onset constant diplopia when measured preoperatively as <19°. These factors are important when counseling patients on post op expectations and to consider when addressing their strabismus concerns.

Combining Fresnel and block prisms to measure large angles of strabismic deviation
Yaida M, Fujii S, Sun W, Mito Y, et al
J AAPOS 2024;28(4):103961
Large strabismus angles are difficult to measure due to unavailability of ophthalmic prisms greater than 50 prism diopters. This study evaluates a novel method of stacking Frensel and block prisms to accurately measure large strabismus angles. In this study, a green laser pointer, positioned 2 cm away from a Fresnel and block prism and perpendicular to the flat face, is used as a light source to measure the deviation of the prisms 100 cm away on a tangent screen. The Fresnel prism was affixed to the posterior (flat) surface of the block prism. The maximum combined effect was observed around 156 prism diopters (using Fresnel/block combination of 30/50). In 11% (8 of 71), a laser spot could not be identified on the screen. The additivity error and combined effect of the two prisms were plotted. The additivity error was always positive and increased exponentially with increased prism. This study plots the combined effects of Fresnel and block prisms to present a novel and practical method to measure large angle strabismus. The authors include a useful table of Fresnel prism and block combinations and the combined effect prism angle with either the block or Fresnel prism fixed. Chromatic dispersion and diffusion can occur with high-power Fresnel prisms leading to reduced visibility of the fixation target. This study provides a method to measure large angle strabismus while accounting for the additive effect of combining prisms.

Prematurity May Affect the Postoperative Sensory Results in Children With Strabismus
Niyaz L, Kocak N, Subası M, Yucel OE
J Pediatr Ophthalmol Strabismus 2024;61(4):267-272
Significant prematurity has effects on many systems, including the eyes. Here, the authors hypothesize that prematurity may affect surgical outcomes in strabismus. They set out to test this hypothesis by retrospectively reviewing all children undergoing strabismus surgery at a

single institution over an 8 year period. This included 70 patients in the premature group (defined as born prior to 37 weeks gestation) and 242 patients in the control (non-premature) group. They then collected both motor (alignment) and sensory (stereopsis) outcomes for these patients. The amount of preoperative deviation and postoperative deviations was similar between the premature and non-premature groups. There were also similar rates of overcorrection and undercorrection between the groups. However, the premature group showed significantly less improvement in stereopsis post-surgery than the control group (560 to 300 arc/sec postoperatively in the premature group and 1,156 to 685 arc/sec in the control group). Thus, despite similar improvements in motor outcomes, children born premature showed less improvement in stereopsis. This suggests that prematurity may serve, as the authors state, as a "barrier for normal development of sensory function." This is important for pre-operative counseling of any premature patient undergoing strabismus surgery.

Comparison of simultaneous prism and cover test (SPCT) and prism and alternate cover test (PACT) measurements with final power of Press-On prism power dispensed
Christoff A
J AAPOS 2024 Jun;28(3):103918
The purpose of this study was to investigate the association between the strabismic angle obtained by simultaneous prism and cover test (SPCT) and prism alternate cover test (PACT) with the final power of Press-On prism used in adults with symptomatic strabismus. A retrospective chart review was conducted on consecutive patients seen by a single orthoptist at an urban tertiary care hospital over a 36-month period. All subjects were prescribed Press-On prism for diplopia after being evaluated with SPCT and PACT measurements during distance fixation. The prism power dispensed was chosen by the patient using a trial Press-On prism set. Out of 244 charts reviewed, 32 adult patients had both prism dispensed and SPCT and PACT measurements. The mean SPCT measurement was 7Δ (median, 6Δ; range, 3Δ-14Δ), and the mean PACT measurement was 13Δ (median, 11Δ; range, 8Δ-20Δ). The mean prism power dispensed was 7Δ (median, 6Δ; range, 1Δ-15Δ), which was not significantly different from the mean SPCT ($P = 0.35$) but significantly different from the mean PACT ($P < 0.001$), with a difference of 6Δ. Limitations of the study include its retrospective nature, small sample size, and potential examiner bias, as the author favors addressing symptomatic strabismus with smaller amounts of prism. The study's findings suggest that the power of Press-On prisms used was more closely aligned with the strabismic angle obtained by SPCT rather than PACT. The overall success rate of Press-On prisms was high when the prism power dispensed closely matched the SPCT measurement, indicating that starting with a weaker prism, based on the SPCT, is a reasonable approach, with adjustments made if symptoms persist.

The effect of teprotumumab infusion on ocular alignment in patients with symptomatic thyroid eye disease
Zhang C, Ersan S, Yousef Y, et al
J AAPOS 2024;28(4):103959
Teprotumumab, a humanized antibody targeting the IGF-1 receptor, has been used to treat active thyroid eye disease (TED) and has shown benefits in reducing symptoms like proptosis and diplopia. This study retrospectively analyzed the effects of teprotumumab on ocular

alignment in patients with moderate-to-severe active TED by reviewing electronic records of patients treated with teprotumumab infusions at a single institution. The study included 19 patients, with 58% presenting TED-associated strabismus. Among those with strabismus, 73% experienced improvement and 46% had resolution of diplopia following the treatment. Factors such as age, sex, initial strabismus severity, Hertel measurements, smoking history, and prior treatments were not predictive of the therapy's response. Limitations of the study include variability due to previous treatments, small sample size, and retrospective biases. The findings suggest that teprotumumab may reduce strabismus in over 70% of patients and resolve diplopia in 46% of cases, highlighting its potential clinical benefits for managing active TED.

Evaluating distance stereoacuity in children 4-17 years of age with a novel digital application
Barnett-Itzhaki G, Barnett-Itzhaki Z, Ela-Dalman N, et al
J AAPOS 2024 Jun;28(3):103904 The study aimed to evaluate the feasibility of the STab, a digital iPad application for measuring distance stereoacuity in children, compared to standard tests like the Distance Randot Stereotest (DRS) and M&S random dots (M&S). Researchers tested 87 children aged 4-17 using these methods and found strong correlations between the STab and both M&S (0.81) and DRS (0.85), indicating that STab performs similarly to established tests. The limits of agreement between M&S and DRS, M&S and STab, and DRS and STab were 0.45, 0.47, and 0.38, respectively, suggesting that these methods can be used interchangeably. However, the study's limitation includes its recruitment from a hospital-based pediatric ophthalmology clinic, where only 7% of participants had a normal ocular exam, which may not be representative of the general population. Clinically, the STab's comparable performance to standard tests supports its use as a reliable tool for assessing distance stereopsis in children, potentially aiding in the management of conditions like intermittent exotropia by providing an objective measure of stereoacuity.

Refractive Error Change and Overminus Lens Therapy for Childhood Intermittent Exotropia
Writing Committee for the Pediatric Eye Disease Investigator Group; Pediatric Eye Disease Investigator Group, Chen AM, et al
JAMA Ophthalmol 2024;142(5):417-428
Intermittent exotropia is the most common type of divergent strabismus in childhood and overminus glasses is a nonsurgical treatment option for this condition. In a PEDIG study previously comparing overminus glasses (n=189) to nonoverminus glasses (n=169) in children aged 3 to 10 years with IXT, children with overminus glasses (-2.50 D for 12 months, -1.25 D for 3 months, and nonoverminus for 3 months) had improved distance IXT control after 12 months but treatment effect did not remain after weaning and discontinuation. During this study, it was noted that overminus treatment was associated with increased myopic shift over 12 months, especially in children with myopia at baseline. The purpose of this study was to evaluate refractive error 2 years after weaning and discontinuing overminus spectacle treatment to see if the myopic shift persisted. Of the 386 children in the initial trial, 223 (57.8%) agreed to 18 months of additional follow-up. The 36-month follow-up visit was completed by 112 in the overminus group and 93 in the nonoverminus group. The overminus group showed a greater mean myopic shift from baseline than the nonoverminus group at both 24 months (-0.61 vs -0.14 D, $P<0.001$) and 36 months (-0.74 vs -0.44 D, $P= 0.003$). However., between 12 and 36

months there was no difference in mean myopic shift between the overminus and nonoverminus groups (-0.34 D in overminus and -0.36 D in nonoverminus group, P=0.99). Thus, the group difference of 0.37 D in myopic shift at 1 year persisted but did not increase during the 2 years after weaning and discontinuing overminus glasses (i.e. stopping overminus treatment did not exacerbate or lessen the myopic shift). The relative risks for developing more than 1.00 D myopic shift over 3 years between the overminus and nonoverminus groups were 2.6 for those with baseline SER of -0.50 to -6.00 D, 2.5 for those with baseline SER -0.375 to 0.375 D, and 0.7 for those with baseline SER 0.50 to 1.00 D. This study was limited in that only 53% of the original participants completed the 36-month visit which may lead to selection bias. Additionally, those performing cycloplegic retinoscopy were not masked to the participant's treatment which may lead to bias, though the subset with autorefraction showed similar results. This study suggests that the risk of myopic shift should be discussed when considering overminus lens treatment for children with IXT, especially for those with pre-existing myopia.

Evaluation of 3D tablet-based stereoacuity test ASTEROID in children with normal and abnormal visual acuity
Wong BM, Fung SSM, Velez FG, et al
J AAPOS 2024 Jun;28(3):103930
The study evaluated the utility of the Accurate STEReotest (ASTEROID), a digital, 3D, glasses-free test for assessing stereopsis in children, comparing it with the Titmus test. In this single-center, observational comparison involving 112 children aged 5-13 years, both ASTEROID and Titmus tests were administered. Stereoacuity was categorized into fine, moderate, coarse, or very coarse to nil. The agreement between ASTEROID and Titmus was moderate overall ($\kappa = 0.52$), with fair to substantial agreement in various subgroups. Specifically, ASTEROID showed poorer scores compared to Titmus in 94% of cases where there was a discrepancy. The study's limitations include a small sample size, a single institution setting, and lack of testing for color vision and accuracy differences between tests. Despite these limitations, ASTEROID demonstrates good agreement with the Titmus test and may be a useful alternative for assessing stereoacuity in clinical settings, potentially being more sensitive in detecting stereovision deficits.

Correlation of Strabismus Surgical Outcomes Graded by Goal-Determined Metric With Patient Satisfaction Survey
Elhusseiny AM, Agrawal S, Staffa SJ, et al
Am J Ophthalmol 2024;260:140-146
The study aimed to evaluate the outcomes of strabismus surgery by comparing a "goal-determined metric" with patient satisfaction, seeking to understand how well patient perceptions align with objective measures. Data from 275 patients treated by two surgeons for esotropia or exotropia between 2018 and 2021 were analyzed. Inclusion required completion of a postoperative examination and satisfaction survey within 2-6 months of surgery. Among the 228 patients who met the criteria, 87% had outcomes rated as "excellent" by the goal-determined metric, while 78% reported being "very satisfied" with the results. Agreement between patient and surgeon grading was 75%-79% for reconstructive surgeries and esotropia with diplopia, but lower at 64% for exotropia with diplopia. Factors such as preoperative risk,

concurrent surgeries, and sex did not significantly impact outcomes or satisfaction. Notably, 62% of previously esotropic and 72% of exotropic patients reported increased self-confidence post-surgery. Strengths of the study include its comparison of objective metrics with patient satisfaction and its substantial sample size. However, limitations include the reliance on a non-validated, in-house satisfaction survey, lack of preoperative surveys, and a limited sample size affecting the detection of specific risk factors. The study supports the use of goal-determined metrics for assessing strabismus surgery outcomes, highlighting their close correlation with patient satisfaction and emphasizing the importance of considering patient-perceived improvements for a more patient-centered evaluation of surgical success.

Comparison of anterior segment optical coherence tomography and ultrasound biomicroscopy in localizing horizontal rectus muscle insertions
Duan R, Yang J
European Journal of Ophthalmology 2024;34(3):656-665
The authors aimed to evaluate the reliability of measuring the distance from the limbus to extraocular muscle insertion using anterior segment optical coherence tomography (AS-OCT) and panoramic ultrasound biomicroscopy (UBM) before and after strabismus surgery. Patients with strabismus underwent evaluation with AS-OCT and UBM preoperatively, 2 weeks, an 1,3 and 6 months post-operatively, specifically looking at the distance between limbus to muscle insertion. These measurements were also manually obtained using calipers in the operating room at the start and end of the surgical procedure. Preoperative AS-OCT and UBM values were compared to intraoperative caliper measurements as the gold standard. Postoperative AS-OCT and UBM values were compared to the new postoperative limbus-insertion distance. The limit of agreement deemed clinically acceptable was defined as 1 mm. A total of 85 horizontal muscles of 40 patients, including 48 lateral rectus muscles and 37 medial rectus muscles, were analyzed. The rectus muscles were successfully detected by preoperative AS-OCT (95%) and UBM (100%). At 2 weeks and 1, 3, and 6 months postoperatively, the new rectus muscle attachment site detection rate by AS-OCT was 6%, 32%, 80%, and 89%, respectively, and that by UBM was 24%, 60%, 85%, and 93%, respectively. The accuracy of UBM measurements of preoperative muscles was 81%, and this decreased to 59% at 6 months postoperatively ($P = 0.001$). The findings in this study suggest that AS-OCT and UBM performed well in terms of imaging horizontal rectus muscles prior to surgery, but showed decreased accuracy and reproducibility in measuring the positions of rectus muscles postoperatively. The study is limited by its small sample size and single center design.

Mental Health Conditions Associated With Strabismus in a Diverse Cohort of US Adults
Jin K, Aboobakar IF, Whitman MC, Oke I
JAMA Ophthalmol 2024;142(5):472-475
Strabismus affects 2 to 3% of individual in the US and may negatively affect psychosocial well-being and predispose individuals to mental health conditions. This cross-sectional study used data from the National Institutes of Health's All of Us Research programs to investigate the association between strabismus and mental health. 3,646 adults with a code for strabismus (median age 67, 55% female) and 3,646 1:1 propensity score-matched controls (age, gender, race and ethnicity, income, educational level, and health insurance) were included. Compared

with controls without strabismus, those with strabismus had a higher prevalence of anxiety (32% vs 14%, P<0.001), depression (33% vs 14%, P<0.001), substance use and addiction (3% vs 1%, P<0.001), bipolar disorder (7% vs 3%, P<0.001), and schizophrenia spectrum disorder (3% vs 1%, P<0.001). Among those with strabismus, higher odds of mental health conditions were associated with younger age, female gender, Black or African American race and ethnicity, low income, and high school education or less. Overall, in this study, adults with strabismus were about 2 to 3 times more likely to have mental health conditions compared to adults without strabismus. Limitations of this study include the use of diagnostic codes susceptible to coding errors, potential barriers to receiving a diagnosis of a mental health condition, and potential confounding factors.

0.01% Atropine Eye Drops in Children With Myopia and Intermittent Exotropia: The AMIXT Randomized Clinical Trial
Wang Z, Li T, Zuo X, et al
JAMA Ophthalmol 2024;142(8):722-730
Myopia and exotropia frequently occur together. Previously studies of low dose atropine for myopia control have excluded children with strabismus. The purpose of this double-masked, single-center, randomized clinical trial was to evaluate the efficacy and safety of 0.01% atropine eye drops on myopia, exotropia, and binocular vision in individuals with myopia and IXT. 300 children (mean age 9.1 years, 49.3% female) with basic-type IXT and myopia of -0.50 to -6.00 D were included and randomly assigned 2:1 to receive 0.01% atropine drops (n=200) or placebo drops (n=100) nightly for 12 months. At 1-year, mean change from baseline cycloplegic spherical equivalent was -0.51 D in the atropine group and -0.75 D in the placebo group (P<0.001), and the mean increase in AL was 0.31 mm in the atropine group and 0.42 mm in the placebo group (P<0.001). There were no differences for change in BCVA or near vision at 1 year in both groups. The mean accommodative amplitude (AA) change was -3.06 D in the atropine group and 0.12 in the placebo group (P<0.001) at 1 year. The decrease in AA started at 2 months and remained stable. Mean change in distant magnitude of exodeviation was -1.04 PD in the atropine group vs -0.02 D in the placebo group (P=0.09), -0.05 vs 0 in distant exotropia control (P=0.69), and -0.12 PD vs -0.05 PD in near exotropia control (P=0.53) at 1 year. Near exodeviation magnitude fluctuated over time with mean change from baseline to 1 year of -1.24 PD (decrease in magnitude) vs 0.74 PD (increase in magnitude) in the atropine and control groups respectively (P=0.03). At 1 year, 0.01% atropine eye drops did not show an effect on binocular vision. In conclusion, compared to the control group, the 0.01% atropine group had slower myopia progression and did not have aggravated exotropia conditions or worsening binocular vision. The use of 0.01% atropine appeared safe with mild decrease in AA and stable BCVA and near vision. This study was limited in its single-center design and lack of long-term follow-up.

A Comparative Analysis of Surgical Outcomes for Infantile Esotropia With and Without Prior Botulinum Toxin A Injection
Yigit DD, Kockar A, Gurez C, et al
J Pediatr Ophthalmol Strabismus 2024;61(4):245-251

The purpose of this study was to compare the surgical outcomes in patients who had a failed botulinum toxin A injection before surgery versus those who had surgery as primary treatment (primary surgery) for infantile esotropia. The files of patients who had strabismus surgery in the Strabismus Unit of Beyoglu Eye Training and Research Hospital between January 2012 and March 2022 were reviewed. This study included 104 eyes of 52 patients with infantile esotropia. The angle of deviation before and 1, 3, and 6 months after botulinum toxin A injection or surgery, complications, pattern deviations, family history, abnormal head position, history of prematurity, intensive care unit admission were noted. A successful outcome was defined as ocular alignment of 10 PD or less. The study population consisted of 52 patients: 27 (52%) boys and 25 (48%) girls. In the botulinum toxin A group (n = 26), the mean age at admission was 14.0 ± 6.8 months, whereas the mean preoperative near and far angle of deviation were 41.92 ± 12.2 and 41.3 ± 13.0 PD, respectively. The mean age at the time of surgery was 40.6 ± 18.1 months. In the primary surgery group (n = 26), the mean age at admission was 34.0 ± 15.9 months. The mean preoperative near and far angle of deviation were 37.3 ± 8.0 and 35.3 ± 10.5 PD. The success rates 6 months after treatment in the botulinum toxin A group and the primary surgery group were 76.9% and 88.5% in near (P > .05) and 80.8% and 88.5% in far (P > .05), respectively. Three patients had transient ptosis and one had consecutive exotropia after botulinum toxin A injection. In infantile esotropia treatment, strabismus surgery after failed botulinum toxin A injection compared to primary surgery has statistically comparable surgical success rates. The main advantage of this study was reporting the course of deviation in patients who had unsuccessful ocular alignment after botulinum toxin A injections. However, there are some limitations, such as the study's retrospective nature and the lack of stereoacuity data of the patients

Incidence of Strabismus Post-Plaque Brachytherapy in Patients With Uveal Melanoma
Huang JJ, Saleem A, Liao EX, et al
Am J Ophthalmol 2024;262:161-169
The study aimed to assess the incidence and types of strabismus in patients with uveal melanoma who were treated with plaque brachytherapy. Conducted across multiple centers, the study reviewed 438 eyes from patients treated with iodine-125 or palladium-103 brachytherapy between October 2011 and May 2021. It found that strabismus developed in 2.5% of patients, with immediate postoperative strabismus in 1.1% of cases due to issues like slipped muscles or decompensated phorias, and late-onset sensory strabismus in 1.4%. Among the 438 patients, 81.1% had extraocular muscles disinserted during surgery, most commonly the lateral rectus. Strabismus surgery was the predominant treatment for those affected, although some received Fresnel prisms or convergence insufficiency exercises. The study is valuable for its comprehensive follow-up and detailed classification of strabismus types but is limited by its retrospective design and lack of extensive preoperative orthoptic evaluations. Clinically, the study underscores the need for vigilance regarding strabismus as a potential complication of brachytherapy, highlighting the importance of considering both surgical and non-surgical treatment options for affected patients.

Botulinum Toxin Injection for the Treatment of Third, Fourth, and Sixth Nerve Palsy: A Meta-Analysis

Khalili MR, Roshanshad A, Vardanjani HM
J Pediatr Ophthalmol Strabismus 2024;61(3):160-171
The efficacy of botulinum toxin injection for the treatment of third, fourth, and sixth nerve palsy was evaluated. PubMed, Scopus, EMBASE, Web of Science, and Google Scholar databases were searched. Data about the duration of palsy (acute vs chronic), cause of the palsy, type of toxin used, mean dose, and other background characteristics were collected. Outcome variables were success rate (defined by alleviation of diplopia or reduction in eye deviation) and standardized mean difference of prism diopter and abduction deficit before and after injection. The Joanna Briggs Institute checklist was implemented for the risk of bias assessment. The analysis included 38 articles, comprising 643 patients. The overall treatment success rate in acute and chronic nerve palsy was 79% and 33%, respectively. The success rate was not significantly different between different subgroups of age, type of botulinum toxin, pre-injection prism diopter, etiology of the palsy, duration of follow-up, and mean dose of botulinum toxin injection. However, in both acute and chronic palsy, diabetes etiology was accompanied by the highest success rate. Overall symptomatic response to botulinum injection was 84% (95% CI: 67% to 96%), whereas functional response was observed in 64% (95% CI: 47% to 79%) of the patients. The odds ratio for the success rate of treatment of palsies with botulinum toxin versus expectant management was 2.67 (95% CI: 1.12 to 6.36) for acute palsy and 0.87 (95% CI: 0.17 to 4.42) for chronic palsy. Botulinum toxin can be used for the treatment of acute third, fourth, and sixth nerve palsy, especially in patients with acute palsy and more severe tropia. There were three main limitations to the study. First, most of the included studies were case series with small sample sizes and there was no large randomized controlled trial evaluating the efficacy of the botulinum in a predefined control situation. Therefore, high-quality randomized controlled trials, which compare the efficacy of botulinum injection and its possible correlates with other treatment methods, are needed. Second, the number of studies of third and fourth nerve palsy was 17; as a result, subgroup analysis was not performed because it may yield misleading results due to the scarce studies in each subgroup. Finally, heterogeneous samples of patients with different etiologies and severities were included in most of the eligible studies. Also, a variety of definitions of response to treatment was used in the original studies.

Clinical spectrum and its association with recovery patterns in patients with acquired isolated ocular motor nerve palsies - an observational study
Agarwal D, Kasturi N, Kaliaperumal S
Strabismus 2024;32(3):210-216
The goal of this paper was to study the clinical spectrum and recovery patterns in patients of acquired isolated ocular motor nerve palsies (OMNPs). Patients above 5 years of age with various etiologies of OMNPs were included. Demographic and ocular details were recorded, and strabismus assessment was performed. Recovery patterns at 3 and 6 months were noted. OMNP was more common in adults, in the order VI > III > IV nerve. Ischemic cause (35%) was followed by idiopathic (26.3%). III nerve palsies were all unilateral, of which all ischemic palsies were pupil-sparing. By 6 months, >50 patients showing complete recovery had ischemic and idiopathic palsies. Smaller baseline deviation correlated with better recovery. Acquired isolated OMNPs are mostly ischemia-related, with >80% of cases fully recovering by 6 months. VI nerve palsy of ischemic or idiopathic etiology and small baseline deviation were associated with

self-recovery. The limitations of this study were having a very small pediatric population (only three cases), and also did not include combined cranial nerve palsies, which is a very common clinical entity

Divergence excess and basic exotropia types of intermittent exotropia: a major review; Part 2: non-surgical and surgical treatment options
Ma MM, Scheiman M
Strabismus 2024;32(3):159-194
This paper provides a comprehensive review of non-surgical and surgical treatment options for the IXT. They used Medline search involving combination of keywords including intermittent exotropia, divergence excess, basic exotropia, refractive error, glasses, spectacles, natural history, untreated, observe, occlusion, patch, overminus, overcorrecting minus, prism, vision therapy, orthoptic, antisuppression, fusion exercise, and surgery were used. All English articles from 01/01/1900 to 01/09/2020 were reviewed. The reference list of the identified articles was also checked for additional relevant articles. Studies focused on animal models or strabismus associated with neurologic disorders or injury were excluded. The following filters were used for surgical management due to the abundance of reports: full text, randomized controlled trial, review, in the last 5 years. Appropriate optical correction of refractive error is generally the starting point for all management approaches, but there is a lack of randomized clinical trial data regarding this treatment modality. Randomized clinical trial data indicate that both observation and occlusion are reasonable management options for children 3–10 years old, and there were insufficient data to recommend occlusion for children 12–35 months old. While overminus lenses were found to improve the control of IXT when assessed wearing overminus spectacles, this improvement did not persist after the treatment ended. The result of the only randomized clinical trial on the effectiveness of base-in prism indicated that this treatment is no more effective than nonprism spectacles for improving control. A recent randomized clinical trial showed that vision therapy/orthoptics is effective in improving the control of IXT when compared to observation alone. Surgery was found to alter a number of clinical characteristics of IXT, including reducing the distance and near angle of deviation, reducing photophobia, improving health-related quality of life, stereopsis, and the Newcastle Control Score. However, there are no randomized clinical trial data comparing surgery with a control group such as placebo or a no treatment observation group. The conclusion was that rigorously designed clinical trials to investigate the effectiveness of non-surgical and surgical treatments for intermittent exotropia are needed.

Relationships between fusional convergence, suppression depth, and exotropia control in intermittent exotropia
Kakeue K, Mihara M, Ataka H, et al
Strabismus 2024;32(3):139-148
The goal of the study is to assess the correlation between the contribution rates of fusional convergence from the dominant and non-dominant eye and suppression depth and exotropia control. This is a cross-sectional prospective study. The fusional convergence of 25 participants with intermittent exotropia (mean age 10.8 ± 3.4; range 6–18 years) was measured with an eye-tracking system. The contribution rate was defined based on the amplitude of fusional

convergence during refusion relative to the exo-deviation angle. The suppression depth was assessed, and exotropia control was evaluated using the intermittent exotropia Office Control Score. The correlations between the contribution rate from the dominant and non-dominant eyes and the suppression depth or control score were analyzed. There was a negative correlation between the dominant eye's contribution rate and the suppression depth in both eyes (r = −0.85, 95% confidence interval [CI]: −0.97 to − 0.20 in the fixated dominant eye and r = −0.91, 95%CI: −0.95 to − 0.40 in the fixated non-dominant eye). There was a negative correlation between the dominant eye's contribution rate and the control score at a 4-meter distance (r = −0.53, 95%CI: −0.76 to − 0.17). Suppression in intermittent exotropia patients could affect the fusional convergence in the dominant eye. The study has several limitations. Regarding methodology in the present study, eye movement recording was conducted to measure the contribution rate to fusional convergence at near distance. The majority of the participants with basic type exotropia had worse control at 4-meter than at near distance. The results for the contribution rates to fusional convergence, the suppression depth, and the phoria maintenance at near distance might have been different than their counterparts at 4-meter distance. Also, in some cases the eye defined as the dominant eye might have actually been the non-dominant eye, since individuals will sometimes change their dominant eye based on the viewing distance.

Prevalence and Incidence of Strabismus by Age Group in Japan: A Nationwide Population-Based Cohort Study
Miyata M, Kido A, Miyake M, et al
Am J Ophthalmol 2024;262:222-228
The study examined the prevalence and incidence of strabismus in Japan across various age groups and estimated the proportions of its subtypes. Using data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan from April 2009 to September 2020, the research found an overall prevalence of 2.154%, with a bimodal distribution peaking in school-aged children and individuals aged ≥75 years. Exotropia was the most common subtype (67.3%), followed by esotropia (26.0%) and cyclovertical strabismus (6.7%), which was rare in children but more prevalent in adults. The 1-year incidence of strabismus in 2019 was 321 per 100,000 person-years, with the incidence highest in early childhood and increasing with age. The study's strengths include its comprehensive nationwide data and detailed analysis, while its limitations involve potential misdiagnosis, incomplete subtype classification, and possible underrepresentation of very young children. The findings provide valuable insights into strabismus epidemiology, emphasizing age-related trends and subtype distribution, which can inform diagnostic practices and healthcare planning.

Evaluation of Macular Neurovasculature and Choroidal Blood Flow Following Inferior Oblique Myectomy Using Optical Coherence Tomography Angiography
Hashemi Javaheri Z, Sabermoghaddam AA, Abrishami M, Kiarudi MY, Motamed Shariati M
J Pediatr Ophthalmol Strabismus 2024;61(4):235-244
To evaluate the short-term effects of inferior oblique myectomy on the retinal neurovasculature, choroidal thickness, and choroidal vascularity index at the macula. Patients older than 5 years who were candidates for inferior oblique muscle myectomy surgery participated in the study.

Patients with any systemic or ocular disease that could affect the macular neurovasculature were not included in the study. After recording demographic data, including age and gender, and conducting a complete ophthalmic examination, macular optical coherence tomography (OCT), enhanced depth imaging OCT, and OCT angiography imaging were performed before (1 day to 1 week) and in the specific time intervals (1 week, 1 month, and 3 months) after the surgery for all participants. Eighteen patients (13 male and 5 female) who underwent inferior oblique muscle myectomy, with a mean ± standard deviation age of 24.22 ± 18.14 years were included in this study. The baseline mean ± standard deviation of subfoveal choroidal luminal area and subfoveal total choroidal area were 0.390 ± 0.03 and 0.539 ± 0.04 mm2 respectively. The changing pattern of the subfoveal choroidal vascularity index and subfoveal choroidal luminal area was statistically significant. Inferior oblique myectomy can lead to changes in choroid hemodynamics in the short term. However, these changes seem to be temporary. This study has some limitations. The sample size is relatively small. However, to obtain a more accurate conclusion about the effects of inferior oblique myectomy on the macular neurovasculature, we excluded patients with horizontal strabismus surgery from the study. Another limitation is the age range of the participants. Children older than 5 years participated in the study. Age could affect the neurovascular components of the eye and is potentially a confounding factor.

Strabismus Surgery

Efficacy of augmented-dosed surgery versus botulinum toxin A injection for acute acquired concomitant esotropia: a 2-year follow-up
Yu X, Pan W, Tang X, et al
Br J Ophthalmol 2024;108(7):1044-1048
104 patients with AACE who presented over a 1-year period were included, and followed for 2 years. The patients were not randomized but rather got to choose which treatment they received: botox injection vs augmented-dosed surgery. The authors also note that based on their clinical experience, augmented surgery was recommended rather than botox injection for one patient with a deviation angle larger than 50 PD. The surgery patients also got to choose between bilateral medial rectus recessions and unilateral recess/resect procedure. Also, patients treated with surgical intervention suffered from longer duration of AACE and larger esotropia deviation angle at distance. No patients in the surgery group relapsed with diplopia during the followup period, while 21 patients in the botox group experienced a recurrence of AACE. Of those, 17 chose to receive a second botox injection, 1 patient chose surgery, and 3 patients with diplopia relieved by rest chose observation. In the botox group, hours of near work per day were demonstrated to be a significant risk factor for relapse. While this study has several considerable limitations as described, it does provide evidence that specifically dose-augmented surgery achieves more stable and favorable outcomes (although BMR vs R+R is debatable, and no data on non-augmented surgery) compared to botox, but that botox can have some helpful effects in the right patients.

Outcomes for Intermittent Exotropia Using Three Common Surgical Approaches
Vadhul R, Rogers JD, Rogers DL
J Pediatr Ophthalmol Strabismus 2024;61(4):287-290
As with most problems in strabismus, there are multiple approaches to the surgical correction of intermittent exotropia (IXT), with the most common being bilateral lateral rectus recessions (BLR), unilateral lateral rectus recession and medial rectus resection (RR), and unilateral lateral rectus recession and medial rectus plication (RP). In this study, the authors review the surgical records of a single surgeon to ascertain the outcomes of each surgical approach. In all, 123 patients with basic IXT met inclusion criteria: 54 in the BLR group, 41 in the RR group, and 28 in the RP group. The average 1-year postoperative distance alignment values in primary gaze for the BLR, RR, and RP groups were 8.72, 7.46, and 12.83 PD of intermittent exotropia, respectively Post-hoc analysis revealed a significant difference in outcomes between BLR and RP (P = .02) and RR and RP (P = .02), with RP have greater post-operative IXT in both groups. The number of patients who requiring a second operation in the BLR, RR, and RP groups was 8 (15%), 5 (12%), and 6 (21%), respectively. This study is limited by the retrospective nature, the lack of randomization, and the fact that it is a single-surgeon study. Moreover, as the authors acknowledge, some studies have found contrasting results. Nonetheless, it is interesting to consider the optimal surgical approach to this common problem and calls for further investigation of plications.

Novel superior oblique anterior fiber plication with or without adjustable sliding knot for extorsion
Anderson M, Bothun ED
J AAPOS 2024 Jun;28(3):103927
To report a novel surgical technique for correcting excyclotropia, a superior oblique anterior fibers plication (SOAFP) with or without a hemi hangback anterior knot was introduced, allowing for postoperative adjustment. A retrospective interventional case series was conducted on patients undergoing SOAFP between January 1, 2019, and March 1, 2023, with at least one month of postoperative follow-up. Exclusion criteria included concurrent vertical or torsional strabismus surgery or evidence of preoperative orbital restriction. Ocular alignment was assessed using prism and alternate cover and double Maddox rod tests preoperatively, and at initial (1-5 days) and final (closest to 6-8 weeks) postoperative visits. Fourteen patients, aged 21-92 years, underwent SOAFP, with 18 eyes treated and 14 eyes receiving adjustable plications of 2-30 mm (mean, 8.93 ± 5.63 mm). SOAFP was the sole procedure in 12 eyes, while in 6 eyes it was combined with up to four horizontal rectus muscle recession, resection, or plication procedures. Preoperatively, the mean extorsion was 10.14° ± 7.01° (range, 2° to 30°). At the initial postoperative examination (1-5 days), the mean intorsional shift was 11.18° ± 7.37°, corresponding to 1.86° ± 1.04° of correction per millimeter of plication. Three eyes were adjusted after the initial visit to achieve a stronger plication effect targeting 5° intorsion. At the final visit, 61 ± 23 days postoperatively, the mean extorsion was 1.21° ± 2.29°, ranging from 5° of extorsion to 3° of intorsion. The mean final intorsional shift was 9.14° ± 7.53°, representing 1.16° ± 0.50° of correction per millimeter of plication. Of the 14 patients, 13 experienced improvement in diplopia. Limitations of the study include its retrospective design, small sample size, and short follow-up period. SOAFP allowed for targeted and easily adjustable correction of extorsion. Although no significant vertical or horizontal deviation was induced, there was an initial ipsilateral hyposhift and esoshift at distance and near. Therefore, it is recommended that SOAFP be performed on the ipsilateral eye of any small hypertropia (<4 PD).

Associations of strabismus surgery timing in childhood with mental health: a retrospective cohort study
Hidinger I, Kong L, Ely A
J AAPOS 2024 Jun;28(3):103929
To investigate the incidence of psychiatric diagnoses in relation to strabismus surgery timing among children with an early strabismus diagnosis who underwent surgery in childhood, a retrospective cohort study using TriNetX network data from 2003-2023 was conducted. Patients diagnosed with strabismus at ≤5 years of age and who had strabismus surgery before 18 years of age were included. Cohort 1 comprised patients who underwent initial strabismus surgery at ≤6 years of age, while cohort 2 included those with initial surgical intervention at ≥7 years of age. The incidence of mental health diagnoses from ages 7 to 18 was compared between cohorts. Results indicated that more patients in cohort 2 (123 of 693 patients, or 17.7%) were diagnosed with at least one mental health disorder compared to cohort 1 (59 of 688 patients, or 8.6%), with a risk ratio (RR) of 2.07 (95% CI, 1.546 to 2.77; P < 0.0001). Increased risk for specific psychiatric diagnoses was observed in cohort 2 versus cohort 1, including anxiety disorders (RR = 2.19; 95% CI, 1.225-3.922; P = 0.0065), attention-deficit/hyperactivity disorder (RR = 2.18; 95% CI, 1.499-3.175; P < 0.0001), conduct disorders (RR = 2.81; 95% CI,

1.425-5.556; P = 0.0018), and adjustment disorders (RR = 2.07; 95% CI, 1.103-3.876; P = 0.0204). However, no statistically significant difference was found between cohorts in depressive disorders (RR = 1.00; 95% CI, 0.419-2.392; P = 0.9974). Gender analysis showed that only males had a statistically significant increased rate of mental health diagnoses in cohort 2 versus cohort 1 (RR = 1.82; 95% CI, 1.284 to 2.577; P = 0.006). The strengths of the study include the use of a large database, while limitations include the retrospective nature of the study, which cannot assign causality, and the limited data available in the TriNetX database, such as race information. The impact on clinical practice suggests that children who undergo strabismus surgery at a later age after an early diagnosis may be more likely to experience mental health disorders during childhood, although it remains unclear whether these disorders result from delayed surgery or influence the decision to pursue surgery rather than continued conservative management.

Small tuck for superior oblique palsy
Bunyavee C, Miranda AR, Archer SM
J AAPOS 2024;28(4):103952
This study investigates the surgical outcomes of superior oblique (SO) tucks in patients with minimal or no SO tendon laxity, using smaller tucks compared to the standard 8-10 mm. The retrospective review included 27 patients treated by a single surgeon for SO palsy, with hypertropia in primary gaze being the primary outcome assessed at the first post-operative visit. Of the patients, 93.3% exhibited no SO tendon laxity during intraoperative exaggerated traction testing. An average SO tuck of 4.9 mm (range, 2-6 mm) was performed, with a median follow-up of 2 months. Significant improvements were noted in hypertropia in primary gaze at distance and near, hypertropia in the field of action of the SO, hypertropia in downgaze, lateral incomitance, and degree of subjective extorsion. However, the extent of SO tuck did not correlate with changes in hypertropia. The study's strengths include its focus on previously unreported data and outcomes, while limitations include a small sample size, short follow-up period, and retrospective design. The findings contribute evidence to the literature supporting the effectiveness of smaller SO tucks in improving ocular alignment for SO palsies with minimal to no SO tendon laxity.

Doses of medial rectus muscle recessions for divergence insufficiency-type esotropia
Miller AM, Holmes JM, Wu R, et al; Pediatric Eye Disease Investigator Group (PEDIG)
J AAPOS 2024 Jun;28(3):103905
The study evaluated whether doses of bilateral medial rectus recessions greater than those recommended by Parks's tables yielded better outcomes for adult-onset divergence insufficiency-type esotropia. Data from a prospective, observational study was analyzed, comparing the actual doses used (including any suture adjustments) to the standard doses recommended by Parks's tables. Success was defined as "rarely" or "never" experiencing diplopia in distance gaze and reading. Of the 42 patients included, 30 of 41 (73%) were classified as successful at 12 months, with 78% success in those receiving doses greater than Parks’s tables compared to 56% in those receiving doses according to Parks’s tables. The mean surgical dose was 1.0 mm greater than Parks’s tables for successful outcomes, compared with 0.7 mm for failures (mean difference = 0.3 mm; P = 0.13). Although the study's small

sample size limits its conclusions, it suggests that a surgical dose 1 mm greater than Parks's tables for each muscle is a reasonable approach for treating adult-onset divergence insufficiency-type esotropia.

Publication rates of registered strabismus trials from ClinicalTrials.gov
Meller L, Sambo AB, Nguyen N, Robbins SL, Granet DB
J AAPOS 2024 Jun;28(3):103936 This study investigated the characteristics and publication rates of registered strabismus trials from ClinicalTrials.gov, aiming to identify factors associated with publication. By examining trials completed before January 1, 2021, and verifying their publication status through PubMed, ClinicalTrials.gov, and Google Scholar, the researchers found that out of 117 trials, only 69 (59%) were published, with an average publication delay of 29 months. The study revealed that interventional trials were more likely to be published compared to observational trials. However, limitations include potential omissions of relevant trials and possible inaccuracies in ClinicalTrials.gov data. Despite the low publication rates and delays, it is noteworthy that most published studies are interventional, which may provide valuable insights into the safety and effectiveness of strabismus treatments.

Outcomes of Strabismus Surgery Following Teprotumumab Therapy
Hilliard G, Pruett J, Donahue SP, et al
Am J Ophthalmol 2024;262:186-191
The study assessed the outcomes of surgical treatment for strabismic diplopia in patients with Thyroid Eye Disease (TED) who had previously received teprotumumab. Conducted as a multicenter, retrospective case series involving 28 patients from seven academic centers, the research examined variables such as time since the last teprotumumab dose, prior orbital decompression, preoperative deviations, and postoperative outcomes. Results indicated that 57% of patients were diplopia-free after one surgery, with an overall success rate of 79% and 89% after additional surgery. For patients who had undergone prior orbital decompression, success rates were 64% after one surgery and 82% after a second. The study, notable for being the first to evaluate TED-related strabismus surgery outcomes following teprotumumab treatment, revealed that teprotumumab does not negatively impact surgical results. Despite its strengths, including data from multiple centers, the study has limitations such as its retrospective design, lack of long-term follow-up, and variability in surgical protocols. The findings support the continued use of teprotumumab and suggest that surgical approaches for TED-related strabismus remain effective.

A Comparison of Chemodnervation to Incisional Surgery for Acute, Acquired, Comitant Esotropia: An International Study
Cheung CSY, Wan MJ, Zurakowski D, et al
Am J Ophthalmol 2024;263:160-167
The study aimed to compare the effectiveness of botulinum toxin injections versus strabismus surgery for treating children with acute, acquired, comitant esotropia (ACE) and to identify predictors of treatment success. This international, multi-center, nonrandomized study gathered data through a cloud-based survey from 44 surgeons across 19 centers, analyzing outcomes for children treated with either intervention. Results indicated that at 6 and 12 months, success

rates were similar between the botulinum toxin (chemodenervation) and surgery groups. However, at 24 months, the surgery group had a significantly higher success rate (86.4%) compared to the chemodenervation group (52%). Treatment delay was associated with lower success rates, with the chemodenervation group generally receiving earlier intervention. Strengths of the study include its large, diverse dataset and the use of propensity matching to control for baseline differences. Limitations include the nonrandomized design, potential selection bias, and variability in treatment techniques. Clinically, while chemodenervation offers comparable short-term outcomes and is less invasive, strabismus surgery provides more durable results in the long term.

Combined recession and resection of the same lateral Rectus in the treatment of exotropia
Thouvenin D, Lequeux L, Bonifas C, Deboutte I
European Journal of Ophthalmology 2024;34(3):874-879
The authors propose that combined Recession-Resection of the Same Muscle (RRSM) may be a promising surgical treatment for exotropia that improves under general anesthesia, suggestive of an active divergence mechanism from overactive lateral rectus (LR) muscles. They designed this study as a retrospective review at a single center looking at a cohort of 100 patients with exotropia that decreased under general anesthesia who underwent the RRSM procedure by a single surgeon over a 16-month period and analyzed their surgical outcomes at 1 month and 6 months post-operatively. They excluded patients undergoing re-operations and those with pure convergence insufficiencies. All surgeries performed included a combined RRSM of one or two LR with a 10mm-recession and a “fine-tuned” resection of the LR based on Quantitative Forced Duction Test scores. Successful results were obtained (−8–+8 PD measured on Alternate Cover Test) among 83% of cases at distance fixation and 91% at near fixation after 6 months. No surgery-related complications or repeat surgeries were reported. The initial results of the study suggest the RRSM procedure may be a valid surgical treatment option for patients with exotropia due to overactive LR, as suggested by deviations that improve under general anesthesia. More long-term follow-up of patients is necessary to determine the success rates of this surgical procedure, and multicenter trials would be useful to confirm the generalizability of findings in different study populations.

Effect of vertical central plication on vertical deviations
Strube YNJ, Cheung K, Germano BR, Hopman WM, Wright KW
J AAPOS 2024 Apr;28(2):103861
The Wright central plication is a minimally invasive procedure used to correct small-angle strabismus. The purpose of this study was to evaluate the surgical effect of this surgery on vertical rectus muscles to correct vertical strabismus. This was a multicenter, retrospective review of surgical results. The study found that the mean vertical deviation change was 4.7 prism diopters and that 78% of patients had a final deviation of less than 5 PD. Patients with congenital SO palsy showed a very small response (1 PD), and patients with restrictive strabismus had a larger response (5.6 PD). A strength of this study was that it included 2 surgeons in different practices, so it is a little more generalizable. Limitations were the retrospective nature, exclusion of patients who were having concurrent surgery on other eye muscles, and lack of follow-up in many patients. This study is important as it provides a viable

option for treating small angle vertical strabismus and allows for the surgeon to know how much correction they should expect from the surgery.

A modified Nishida procedure for management of myopic strabismus fixus
Wen Y, Tang S, Shen T, Yan J
J AAPOS 2024;28(4):103962
Myopic strabismus fixus is characterized by large angle esotropia, hypotropia, and severe restrictions in eye movement. This study aims to compare outcomes in post-operative alignment and motility from two surgical techniques. This is a retrospective review of patients who underwent strabismus surgery at a single institution between January 2017 and June 2022. The modified Nishida procedure and medial rectus recession (Nishida-MRc) with or without traction suture (Ts) was compared to the half Jenson union and medial rectus recession (U-MRc) with or without traction suture. Success rate was defined as horizontal and vertical deviations <15 prism diopters. In this study, both techniques demonstrated comparable improvements in abduction and elevation limitations; however, extreme esotropia (>123°), had greater improvement in alignment with Nishida-MRc without traction suture and U-MRc with traction suture compared to U-MRc without traction suture. The Nishida-MRc procedure had more consistent and stable outcomes at 8 months post-operative with a trend toward fewer traction sutures. The strength of this study is consistent surgical technique and evaluation due to single surgeon. Limitations include retrospective design, small sample size, and inability to determine whether the amount of medial rectus recession or the placement of the scleral suture affected the amount of correction achieved. This study offers an alternative surgical technique for improved and stable outcomes in treating myopic strabismus fixus.

Long-term Motor and Sensory Outcomes After Unilateral Medial Rectus Recession-Lateral Rectus Resection for Infantile Esotropia
Mohan K, Sharma SK J Pediatr Ophthalmol
Strabismus 2024;61(2):106-113
Infantile esotropia is a frequent problem encountered in pediatric ophthalmology. Most commonly, this is treated with – at least initially – a bilateral medial rectus recession. Less commonly, it is treated with a unilateral medial rectus recession and lateral rectus resection; as such, there is a relative paucity of literature on outcomes from this surgical approach. The authors here seek to address this by performing a retrospective review of patients with infantile esotropia who underwent an initial unilateral MR recession and lateral rectus resection and had at least 10 years of follow up. A total of 100 patients were included, with a mean age at time of surgery of 2.2 years old. Overall, 54% were deemed to be a “surgical success” (orthotropic to <10 PD ET) at last follow up, with 34% having consecutive exotropia (i.e., any amount of XT) and 12% having residual, recurrent, or consecutive esotropia (ET>10 PD). Interestingly, the probability of surgical success was 94% at 10 year follow up, but dropped to 37% by 20 years. Age at time of surgery, duration of ET, presence of DVD, and magnitude of pre-operative deviation did not significantly influence the probability of surgical success. Although a retrospective study performed at a single institution, this still provides valuable data about a less commonly performed surgical procedure with an impressive length of follow up. It confirms what many of us have observed anecdotally – that infantile esotropes frequently developed

consecutive and recurrent deviations over the long term. This is valuable to pre-operative counseling and reinforces the need for long-term follow up.

A Comparative Analysis of Surgical Outcomes for Infantile Esotropia With and Without Prior Botulinum Toxin A Injection
Yigit DD, Kockar A, Gurez C, et al
J Pediatr Ophthalmol Strabismus 2024;61(4):245-251
Infantile esotropia typically necessitates early intervention, with some favoring surgery and others favoring botulinum toxin. In those receiving botulinum toxin, the second line treatment is usually surgery if the patient remains undertreated. Here, the authors look at surgical outcomes for infantile esotropia in patients who had primary surgical intervention versus patients who had surgery following failed treatment with botulinum toxin to ascertain if there are different outcomes between the two groups. In all, this single-institution retrospective review of patients with infantile esotropia examined 26 that had undergone botulinum toxin injection (3.0 units to both medial recti muscles) followed by surgery and 26 who had undergone primary surgery. The success rates 6 months post-operatively in the botulinum toxin + surgery group and the primary surgery group were 76.9% and 88.5% at near and 80.8% and 88.5% in far, respectively. These rates were not statistically different. Therefore, the authors conclude that surgical success rates in infantile esotropia are similar whether that surgery is done primarily or following a (failed) treatment with botulinum toxin. This is reassuring in that it suggests that surgery remains an equally effective second option in patients who may prefer to try botulinum toxin first. However, the success rates, while similar, do trend toward a higher success rate with primary surgery; there may be noise introduced in this, though, by the fact that the botulinum toxin group failed that treatment first, which could portend a more recalcitrant issue.

Zip-up Loop Myopexy in Heavy Eye Syndrome
Awadein A, Farag CS, Maher S
J Pediatr Ophthalmol Strabismus 2024;61(4):279-286
The loop myopexy, in which the bellies of the SR and LR are brought together to restore normal anatomic positioning, is a well-known surgical procedure for the correction of heavy eye syndrome. Here, the authors present a modification of the loop myopexy, which they term the “zip-up loop myopexy,” and retrospectively review the results of the procedure. Briefly, in this modification, the SR and LR muscle bellies are approximated using a suture 4-5 mm from the muscle insertion. According to the authors, the “muscles were then zipped together by 5-0 polyester sutures placed in an anteroposterior direction using a hand-over-hand technique.” This modified procedure has been performed on 8 patients average axial lengths of 33.2 mm, average preoperative horizontal angle of 78 PD, average preoperative vertical angle of 34 PD, and significant limitation of both abduction and elevation. In 7/8 patients, both the horizontal and vertical deviations were reduced to less than 8 PD with an average of 7-8 sutures. No complications occurred. Overall, this is an interesting and apparently effective modification to the loop myopexy that may be beneficial to patients with severe heavy eye syndrome.

Long-Term Effects of Botulinum Toxin A Versus Incisional Surgery for Management of Partially Accommodative Esotropia in Children: Comparison of Three Approaches

Wang Y, Jiang J, Li L
Am J Ophthalmol 2024;265:289-295
The study aimed to evaluate the effectiveness of three treatments for partially accommodative esotropia in children: bilateral medial rectus (MR) injection of botulinum toxin A (BTX-A), bilateral MR muscle recession surgery (BMR rc), and unilateral MR muscle recession combined with lateral rectus muscle resection surgery (R&R). This retrospective comparative clinical study reviewed 98 patients who received either BTX-A or surgical intervention between December 2014 and January 2023, assessing motor and sensory outcomes and tracking complications with a minimum follow-up of 12 months. Results showed that BTX-A had lower motor success rates at distance and near fixation compared to both R&R and BMR rc, particularly for children aged 2.5 years and older. Sensory outcomes were similar across groups, but BTX-A did not result in overcorrection, unlike BMR rc, which had a higher incidence of consecutive exotropia. The study's strengths include its large sample size, comprehensive follow-up, and inclusion of both motor and sensory outcomes, while its limitations involve potential biases inherent to retrospective designs and limited generalizability due to being conducted at a single institution. Clinically, BTX-A presents a viable, cost-effective option, especially for younger children, while surgical treatments generally offer higher motor success rates and fewer complications for older children.

Long-term comparison of horizontal rectus surgery with vertical tendon transposition and combined vertical tendon transposition and inferior oblique-weakening in V-pattern exotropia
Tellioğlu A, Yilmaz T, İnal A, et al
J AAPOS 2024;28(4):103958
This study compared the effectiveness of two surgical approaches for treating V-pattern exotropia: bilateral lateral rectus recession with vertical tendon transposition (LRVT) and LRVT combined with inferior oblique disinsertion (IO disinsertion). A retrospective chart review was conducted on patients with V-pattern exotropia and +1 or +2 inferior oblique overaction (IOOA) who underwent these surgeries and were followed for at least 3 years. Data collected included pre-operative, 6-month, and 3-year post-operative assessments, with surgical success defined as achieving less than 10 prism diopters of distance deviation in primary gaze. The results showed similar surgical success rates between the two groups (77.3% for LRVT alone and 73.9% for LRVT with IO disinsertion). Both groups had a reduction in the V-pattern, but the combination surgery achieved a statistically significant greater decrease of 5 prism diopters compared to LRVT alone. The study's strengths include its long follow-up period and comparison of two techniques, though limitations involve its retrospective nature and lack of pre- and post-operative torsion data. Clinically, this study highlights that combining LRVT with IO disinsertion may provide a more significant reduction in V-pattern exotropia than LRVT alone.

Outcomes for Intermittent Exotropia Using Three Common Surgical Approaches
Vadhul R, Rogers JD, Rogers DL
J Pediatr Ophthalmol Strabismus 2024;61(4):287-290 The purpose of this study was to compare a single surgeon’s surgical outcomes for treating intermittent exotropia using bilateral lateral rectus recession (BLR), unilateral lateral rectus recession and medial rectus resection (RR), and unilateral lateral rectus recession and medial rectus plication (RP). A retrospective

review of all surgeries for basic intermittent exotropia between 2015 and 2023 was performed. Only patients with initial correction using BLR, RR, or RP were included. Exclusion criteria included age older than 18 years, vertical deviation, any nonrefractive ocular diagnoses, prior ocular surgery, and inadequate follow-up. There were 460 patients identified; 123 met inclusion criteria with 54 in the BLR group, 41 in the RR group, and 28 in the RP group. The average pre-operative distance alignment (and standard error) values for the BLR, RR, and RP groups were 25.07 (7.35), 22.44 (5.95), and 23.84 (6.42) PD. At 1 year, the postoperative distance alignment values for the BLR, RR, and RP groups were 8.72 (7.89), 7.46 (6.31), and 12.83 (6.82) PD. A subanalysis found a significant difference between the BLR and RP (P = .02) and RR and RP (P = .02) groups. There was no difference between the BLR and RR groups (P = .57). This study of three surgical approaches for intermittent exotropia found RP had a significantly larger angle of exodeviation compared to BLR and RR at 1 year of follow-up. Both BLR and RR were equally effective approaches for treating intermittent exotropia. The retrospective nature of this study does impose several limitations. Patients were not randomized into their treatment groups. Rather, the surgeon performed each type of surgery during a distinct period in his career. This choice was based on what he believed to be the best initial surgical treatment for basic intermittent exotropia. Because surgical techniques were used in sequence and not randomized, not all groups have the same sample size. As this was a teaching institution, resident also assisted in performing some of these surgeries which could contribute to the variability also.

Nasal loop myopexy for management of exotropia-hypotropia complex associated with high myopia
Pawar N, Shyam P, Ravindran M
Strabismus 2024;32(3):206-209
Managing the exotropia-hypotropia complex in the context of high myopia demands a comprehensive approach that addresses both vertical and horizontal deviations. The surgical strategy employed in this case, which included loop myopexy, LR recession, and MR resection, achieved positive outcomes regarding alignment, elevation, and binocular vision. This is a single case report of a 24-year-old male with unilateral high myopia who presented with a large angle exotropia-hypotropia complex with limitation of elevation in abduction in his left eye. His ocular deviation was successfully managed through a nasal loop myopexy of the superior rectus (SR) and MR using a non-absorbable suture, combined with large LR recession and MR resection. Postoperatively, the patient had satisfactory ocular alignment with improved hypotropia and normal elevation in abduction, contributing to enhanced binocular vision and better cosmesis. A schematic of the procedure is published in the paper.

Short-term Effect of Strabismus Surgery on Choroidal Vasculature Guler
Alis M, Alis A, Kucuk A, Acikalin B
J Pediatr Ophthalmol Strabismus 2024;61(2):114-119
It is well-known that strabismus surgery can affect the anterior segment circulation of the eye. What is lesser-studied, however, is the degree to which strabismus surgery may affect choroidal vasculature and circulation, another potentially important consideration when performing said surgery. To investigate this, the authors performed OCTs on 42 eyes undergoing horizontal

strabismus surgery per-operatively, 1 day post-operatively, and 1 week post-operatively, collecting data on the choroidal area (TCA), stromal area (SA), luminal area (LA), and choroidal vascularity index (CVI). In sum, there was a statistically significant reduction in CVI and increase in TCA and SA on post-operative day one; these changes returned to their preoperative values by the post-op week one visit. This suggests, then, that strabismus surgery may transiently reduce choroidal vascularity. The clinical significance of this is unclear and is unlikely to change surgical practice given its transient nature. Moreover, given that the average age of patient at time of surgery was 16.7 years old, this is unlikely to apply to older patients, in whom changes in vasculature may be more concerning.

Biomechanics Explains Variability of Response of Small Hypertropia to Graded Vertical Rectus Tenotomy
Kim CZ, Lim S, Demer JL
Am J Ophthalmol 2024;265:21-27
The study investigated the variability in outcomes of graded vertical rectus tenotomy (GVRT) for treating small angle hypertropia associated with sagging eye syndrome and explored the utility of an adjustable technique under topical anesthesia to address this variability. Conducted using fresh bovine rectus muscle tendon specimens, the experimental study involved preconditioning and incrementally performing tenotomies at various percentages (25%, 50%, 75%, 90%, and 100%) while measuring remnant forces. The results showed that remnant force decreased linearly with increasing tenotomy percentage, from 4.23 ± 1.34 N to 0 N, but there was significant variability in responses, with coefficients of variation ranging from 27% to 49%. While the study provided detailed biomechanical data explaining the variability in clinical outcomes, it faced limitations such as using postmortem bovine tissue and potential variations in specimen preparation conditions. The findings underscore the considerable variability in the effects of graded tenotomy on tendon force, supporting the use of adjustable techniques for GVRT under topical anesthesia to better accommodate individual differences and potentially improve surgical outcomes for small angle vertical strabismus.

Medial Rectus Inferior Half Plication for the Treatment of Near Exotropia
Weatherby T, Marsh I
J Pediatr Ophthalmol Strabismus 2024;61(3):219-222
Near exotropia is a difficult condition to surgically manage because it is challenging to adequately reduce the near deviation without overcorrecting at distance. This was a retrospective analysis of the outcomes from a single surgeon performing a plication of the inferior half of the medial rectus muscle in 17 consecutive patients with near exotropia unresponsive to medial rectus bupivacaine injection Thirteen of 17 (76%) patients were asymptomatic after surgery with no diplopia for near fixation and with either a normal or slightly reduced prism fusion range enabling them to have comfortable binocular single vision. There was one minor surgical overcorrection with distance diplopia that disappeared within 2 weeks of surgery. Of the 4 of 17 (24%) patients who required further intervention, 3 required one further surgical procedure and 1 required an injection of bupivacaine into the contralateral medial rectus muscle to obtain a satisfactory alignment and control of symptoms. No patient needed more than two total operations. Limitations are are the small sample size, the lack of a control

group, and it being a retrospective study. It is also limited by the relatively short follow-up interval and so we are unable to comment on longer-term outcomes and risks of recurrence

Binocular Visual Deficits at Low to High Spatial Frequency in Intermittent Exotropia After Surgery
Yu X, Wei L, Chen Y, et al
Invest Ophthalmol Vis Sci 2024;65(10):41
Intermittent exotropia affects approximately 1% of the population and eye muscle surgery is the predominant treatment. Studies have shown that those with intermittent XT exhibit deficits in binocular function, even after repair. 13 patients with surgically aligned intermittent XT were compared to 13 normal controls. Binocular function was assessed using participants balance points, defined as the interocular contrast ratio (nondominant eye/dominant eye) using a binocular orientation task as three spatial frequencies. Patients with surgically corrected intermittent XT experience binocular imbalance across a wide range of spacial frequencies, with greater imbalance at higher frequencies. Overall, this study supports that binocular balance is disrupted in patients with surgically corrected intermittent exotropia, but it does not present any preoperative comparisons. Understanding changes in binocular function before and after strabismus surgery would provide useful information on the effect of eye muscle surgery on binocular function.

Trauma

Incidence and Outcomes of Eye Trauma Associated With Recreative Use of Nonpowder Toy Guns: A 12-Year Retrospective Study
Dentel A, Boulanger E, Chapron T, et al
Am J Ophthalmol 2024;265:73-79
The study investigated the outcomes of eye injuries caused by nonpowder toy guns (NPTGs). A retrospective case series analyzed 324 cases of ocular trauma from August 2010 to January 2023. The study found that foam bullets and dart blasters were the most common cause of injuries, while BB guns and airsoft guns led to more severe outcomes. Paintball guns often resulted in posterior segment lesions and required frequent surgeries. The study highlights the need for public health policies promoting protective eyewear to prevent these injuries, especially as injuries from foam bullets and dart blasters are on the rise.

Pediatric and Adolescent Traumatic Macular Hole: A Systematic Review
Helmy YAH, ElNahry AG, Zein OE, et al
Am J Ophthalmol 2024;265:165-175
The study is a systematic review aimed at evaluating the optimal management strategies for pediatric traumatic macular holes (TMH), given the lack of prospective randomized trials. It compares three approaches: early pars plana vitrectomy (PPV) within one month of trauma, delayed PPV beyond one month, and observation. The review analyzed data from multiple databases up to July 31, 2023, assessing visual acuity (VA), visual gain, and time to hole closure, while categorizing holes by size (small, medium, large). Findings indicate that for small TMH, final VA and visual gain were similar between PPV and observation groups. For medium TMH, observation led to better visual gain, although final VA was comparable. Large TMH showed similar outcomes between early and delayed PPV. Closure times were similar for small TMH in both approaches, with PPV generally having longer follow-up periods but similar or slightly better outcomes. The review highlights that PPV is effective in closing TMH and improving vision, especially for large holes, while the timing of surgery (early vs. delayed) may be flexible based on clinical judgment. Observation remains a viable option for smaller to medium-sized holes, particularly when immediate surgery is not feasible. The review underscores the need for more rigorous studies to clarify the optimal management and natural history of pediatric TMH.

A Comparative Analysis of Traumatic Retinal Detachment After Open and Closed Globe Injuries in Children
Wenzel DA, Gassel CJ, Druchkiv V, Neubauer J, Bartz-Schmidt KU, Dimopoulos S
Retina 2024;44(8):1422-1430
Traumatic retinal detachment is a serious complication of ocular trauma, and is often challenging to manage, whether associated with an open globe injury or closed globe injury. This study explored outcomes of traumatic retinal detachment in children with closed globe and open globe injuries seen at a tertiary center in Germany between 2002 and 2021. A total of 47 patients with traumatic RD, 25 from a closed-globe injury and 22 from and open-globe injury. The mean number of RD surgeries was similar in both groups, 1.68 in the closed globe group

and 2.23 in the open globe group. The number of non-RD surgeries (globe closure, phacoemulsification, etc) was significantly greater in the open globe group. Closed globe injury traumatic RD had significantly better preoperative log MAR VA and follow-up logMAR BCVA. Initial BCVA improvement was only seen in the closed globe group. In multivariable analysis, prognostic factors for favorable BCVA outcomes included higher preoperative BCVA, older age, and absence of proliferative vitreoretinopathy. Surgical treatment was different between the two groups, with scleral buckle being more common in the closed globe group and nearly all open globe injuries being treated with PPV with SO tamponade. Overall, this study shows challenges in treatment of pediatric traumatic RD and poor visual prognosis particularly in open globe injuries.

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Uveitis

None.

Vision Screening

Effectiveness of the Spot tm Vision Screener With Variations in Ocular Pigments Pophal CJ, Trivedi RH, Bowsher JD, et al
Am J Ophthalmol 2024;264:99-103
The study aimed to assess the effectiveness of the Spot Vision Screener in detecting Amblyopia Risk Factors (ARF) and refractive errors (myopia and hyperopia) in children, considering variations in ocular pigmentation. Involving 1,040 children from a pediatric clinic, the study categorized participants into three groups based on ocular pigment—darkly pigmented, medium pigmented, and lightly pigmented—and used the Spot Vision Screener prior to a complete eye examination by a blinded pediatric ophthalmologist. Results indicated that the Spot Vision Screener demonstrated excellent accuracy for myopia detection across all pigment groups, with sensitivities varying from 0.49 to 0.78, and good accuracy for hyperopia, with sensitivities ranging from 0.23 to 0.46. Specificities for both myopia and hyperopia were high across groups. The study's strengths include its large and diverse sample and robust diagnostic methods. However, its limitations include varying sensitivity based on ocular pigmentation, which could impact accuracy across different ethnic groups, and the lack of consideration for additional factors such as accommodation and pupil size. The findings endorse the use of the Spot Vision Screener but suggest that future advancements should address variations in sensitivity related to ocular pigmentation to enhance screening accuracy for diverse populations.

Association of Sociodemographic Characteristics with Pediatric Vision Screening and Eye Care: An Analysis of the 2021 National Survey of Children's Health
Antonio-Aguirre B, Block SS, Asare AO, et al
Ophthalmology 2024;131(5):611-621
The National Survey of Children’s Health (NSCH) is conducted annually by the census bureau to assess data on child health including vision. The current analysis was a cross-sectional study that focused on 2 vision related questions from the 2021 survey. They were both 2 part questions. The analysis looked at the responses to the following questions: 1) whether vision screening occurred in the past 2 years for children ages 6-17 years or ever for children < or equal to 5 years; 2) whether a child was referred to an eye doctor based on the vision screening;3) whether a child had an eye doctor visit in the past 2 years for ages 6-17 years or ever for children < or equal to 5 years; and if applicable the outcome of the visit. Results showed that 53.2% of children had a vision screening at least once if age less than 5 or within the past 2 years for 6-17 years. The study was able to provide a reasonable snapshot of the role of social determinants of health in access to pediatric eye care. The analysis showed that there was a significant gap in screening and effectively treating vision disorders in children. Some of these gaps were due to social, health, related and economic factors such as ethnicity, English language fluency and health insurance status. The study was possibly limited by nonresponse bias and the limitations of the questions asked . This study is significant in that it can provide data to determine access and utilization of pediatric eye care and highlight areas of education that can be undertaken to better serve the pediatric population.

Gaps in the Vision Screening Pathway for School-Aged US Children

Oke I, Slopen N, Galbraith AA, et al
JAMA Ophthalmol 2024;142(3):268-270
Variability in vision screening and vision screening policies can cause missed care for children with preventable vision loss. This cross-sectional study used a nationally representative survey of the US pediatric population (National Survey of Children's Health) to identify gaps in vision screening and associated factors. School-aged children (ages 6 to <18 years) participating in the 2021 survey were included. Of 30,173 children, vision screening within the last 2 years was reported by 18,494 participants (survey-weighted 61%). Of those screened, 5,134 (survey-weighted 30%) were referred for an eye exam and of those referred 4,823 (survey-weighted 92%) reported establishing care with a specialist. Children identifying as Hispanic, non-Hispanic Asian, non-Hispanic Black, residing in low-income households, and with a non-English primary household language were less likely to receive screening, more likely to be referred for an eye exam, and less likely to establish care with a specialist. Adolescents, children without health insurance, and children with caregivers with less than high school educations were also less likely to receive screening and more likely to be referred. This study showed that children from historically marginalized racial and ethnic groups, low-income households, and non-English speakers were less likely to receive screening, more likely to be referred, and less likely to establish care which may lead to racial, ethnic, and socioeconomic disparities in visual outcomes. This study was limited by the potential for recall bias.

Vision Testing for Adolescents in the US
Oke I, Slopen N, Hunter DG, Wu AC
JAMA Ophthalmol 2023;141(11):1068–1072
Investigators from Harvard Medical School and School of Public Health, Boston, MA, conducted a retrospective study to evaluate rates of vision testing for adolescents in the US and identify risk factors for not receiving testing. The primary outcome was the rate of vision testing in US adolescents, and the secondary outcome was site of testing. The authors conclude that rates of vision testing decreased with age in adolescents, primarily because of decreased testing in primary care clinics and schools. Adolescents from disadvantaged families were at increased risk for not receiving vision testing.

Visual Impairment

Comparison of Eye Tracking and Teller Acuity Cards for Visual Acuity Assessment in Pediatric Cortical/Cerebral Visual Impairment
Chang MY, Borchert MS
Am J Ophthalmol 2024;260:115-121 This study compares eye tracking and Teller acuity cards (TAC) for assessing visual acuity in children with cortical or cerebral visual impairment (CVI) to determine which method offers more reliable and valid results. The study involved 41 children with CVI from a pediatric neuro-ophthalmology clinic. Both methods were used to measure visual acuity, with 26 children undergoing TAC assessment by a masked examiner. Assessments were conducted at baseline and after one month. Test–retest reliability was measured with the intraclass correlation coefficient (ICC), and correlations between eye tracking, TAC, and Visual Behavior Scale (VBS) scores were analyzed with the Spearman correlation coefficient. Results showed that eye tracking had excellent test–retest reliability (ICC = 0.81, P < .0001), while TAC had fair reliability (ICC = 0.42, P = .04). There was a moderate correlation between eye tracking and TAC (r = 0.43, P = .03), a moderate correlation between TAC and VBS scores (r = 0.50, P = .009), and a strong correlation between eye tracking grating acuity and VBS scores (r = 0.72, P < .0001). Strengths of the study include high test–retest reliability for eye tracking and its strong correlation with pediatric neuro-ophthalmologic assessments. Eye tracking may offer more accurate measurement due to objective gaze direction determination. Limitations include a small sample size, variability in TAC results, and potential issues with visual field defects and strabismus. The study suggests that eye tracking is a more reliable and accurate method for assessing visual acuity in children with CVI compared to TAC. This finding could lead to the adoption of eye tracking in clinical settings for more precise evaluation of visual function and improve outcome measures in clinical trials for CVI. Further research is needed to validate these findings and explore eye tracking's potential for assessing additional visual and oculomotor parameters.

Distribution and causes of blindness and severe visual impairment in children at a tertiary referral centre in Rwanda
El-Khoury S, Strittmatter S, Tuyisabe T, Preussner PR, Abdelmassih Y
Br J Ophthalmol 2024;108(2):280-284
The authors reviewed the files of all patients below the age of 18 years that presented to a tertiary referral center in Rwanda in 2019 for this retrospective epidemiologic study. 11% of the presenting children (428/3939) had severe visual impairment or blindness (SVL/BL) in at least one eye. 39% were bilateral cases, and preschool children (<5 years old) accounted for 37% of all patients. The main diagnoses for bilateral cases for the entire cohort were cataract (18%), refractive error (18%), keratoconus (13%), congenital eye anomaly (9%), glaucoma (8%), cortical blindness (8%) and retinoblastoma (6%). For unilateral SVI/BL it was trauma (46%), cataract (8%), keratoconus (8%), infectious corneal disease (7%) and retinoblastoma (7%). Cataract and Keratoconus were identified as the two most important causes for unilateral as well as bilateral SVI/BL and the authors postulate that the high rates of keratoconus may be associated with the high prevalence of VKC in Rwanda. These data can help direct resources for addressing preventable and treatable causes of SVL/BL in Rwanda.