

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Effect of Medicaid Expansion on Rates of Dilated Eye Exams

July 2020

In the first study to do so, **Chen et al.** explored the effect of Medicaid expansion and the frequency of dilated eye exams among adults with diabetes. They found that even though the expansion initially resulted in many exams being performed, the effect was short-lived and became insignificant by 2017, despite little change in the number of insured members.

This retrospective review entailed a difference-in-differences (DiD) analysis of individual-level survey data for a nine-year period in the United States. Eligible for study entry were adults with previously diagnosed diabetes (18-64 years of age) whose household income was below 138% of the U.S. federal poverty level. Using data from the CDC's Behavior Risk Factor Surveillance System, the authors identified survey responders who had been asked about dilated eye exams in the period before and after Medicaid expansion. The main outcome measure was the DiD in the proportion of dilated eye exams received.

There were 52,392 survey responders, representing all 50 states and the District of Columbia. Medicaid expansion led to a 1.3% increase in the confidence interval and a 2.3% jump in the proportion of dilated eye exams, through four years after the expansion

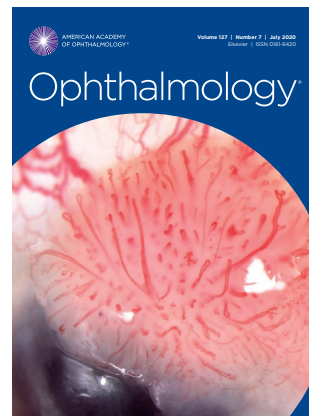
effort. The increase in exam rates was most significant within the two years following expansion. When excluding the states that were first to adopt the expansion, findings were similar.

Health care policymakers "should be aware that additional measures beyond expanding insurance coverage may be necessary to increase and sustain the rate of dilated eye examinations among diabetic populations," the authors said. Clearly, increasing the availability of insurance coverage may not be enough to boost access to regular eye care among diabetic patients. The authors concluded that continued improvement in this quality-of-care metric "requires further specific measures targeting insured, at-risk populations, such as new care-delivery models and education initiatives." (*Also see related commentary by Andrew Bindman, MD, in the same issue.*)

Ocular Findings and Conjunctival SARS-CoV-2

July 2020

Shortly after conjunctivitis was identified as a possible early symptom of COVID-19, reports of viral RNA in tears and conjunctival secretions of infected patients emerged. Working early in the pandemic, **Zhou et al.** studied the ocular traits and footprint of COVID-19, along with their relationship to disease duration. Although



they verified that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could be detected in conjunctival swabs, they noted that relatively few confirmed COVID-19 cases had ocular symptoms suggestive of conjunctivitis

or positive conjunctival swab results. Moreover, they found that neither factor correlated with disease duration.

This cross-sectional study was conducted in January and February of 2020 in Wuhan, China. The researchers recruited 121 patients treated at a university hospital for SARS-CoV-2 infection, which had been confirmed by at least one positive respiratory or another clinical specimen finding or a positive serological antibody result. A record review and external eye exam with penlight provided clinical information on ocular symptoms at onset and later in the disease. Physicians collected conjunctival and nasopharyngeal swabs from the affected eye of patients with ocular symptoms, and conjunctival swabs from a random eye in those patients without such symptoms, all on the same day.

The mean age of the 121 patients was 48 years (range, 22-89 years). SARS-CoV-2 RNA was found in three patients (2.5%); two of them had severe/critical disease and the other had mild/moder-

ate disease. Eight patients (6.6%) had ocular symptoms, including itching (n = 5), redness (n = 3), tearing (n = 3), discharge (n = 2), and foreign body sensation (n = 2). Seven of these eight patients had severe/critical disease. Only one patient had ocular symptoms plus a conjunctival swab that was positive for SARS; two patients without ocular symptoms had a positive conjunctival swab result.

There was no meaningful correlation between the presence of ocular symptoms and positive swab findings (odds ratio, 2.548; Fisher's exact test, $p = .39$). Neither the proportion of patients with ocular symptoms nor the proportion with positive swab results had a significant relationship with disease duration (Spearman rank correlation, 0.111 [$p = .22$] and 0.74 [$p = .42$], respectively). However, the difference in rates of positive SARS-CoV-2 test results with conjunctival swabs (2.5%) versus nasopharyngeal swabs (70.2%) was significant ($p < .001$). (Also see related commentary by Irene C. Kuo, MD, in the same issue.)

Facial Trauma Caused by Electric Scooter Accidents

July 2020

As electric scooters have become popular, injuries associated with their use have risen concurrently. However, little is known about ophthalmic trauma related to scooter use. Yarmohammadi et al. reported on patients who sustained facial injury after riding an electric scooter in the standing position. They noted many complex fractures involving multiple anatomic subunits—and the injuries tended to be severe and difficult to repair, likely due to the combination of speed impact, lack of restraint, diffuse impact, and coup/contrecoup forces.

For this study, the authors reviewed one-year data from two academic emergency departments. They gathered information on demographics, helmet use, drug/alcohol use at presentation, mechanism of trauma, type of facial injury, associated comorbidities, and need for hospitalization or surgical intervention.

Thirty-four patients presented with scooter-associated facial injury during the study period. Twenty-five (74%) were male; the patients' mean age was 36.7 years. None had been wearing a helmet. Nearly three-fourths were intoxicated/impaired from drugs or alcohol according to self-reports, physician observation, or toxicology results. The mean blood alcohol level of the tested intoxicated patients was 203.4 mg/dL. Nearly all patients (94%) had at least one facial fracture, and most (79%) involved anatomic subunits. Lateral orbital rim and orbital floor fractures were the most common, each occurring in at least half of the study population. Orbital roof and medial orbital wall fractures were each present in about 25%. An ophthalmic examination was performed in 26 patients, including all who had an orbital fracture.

Five patients had eyelid lacerations, and one had an intraretinal hemorrhage that did not impair vision. All but one patient had normal visual acuity. The exception was a patient with light perception and elevated intraocular pressure (>50 mm Hg) secondary to retrobulbar hemorrhage; lateral canthotomy and cantholysis were performed to decrease pressure and restore vision. No patient had extraocular muscle entrapment or globe rupture. Most patients (76%) were hospitalized; eight required surgery. About 20% had associated intracranial hemorrhage, and 12% had impaired neurologic status that required intubation. Most patients with hemorrhage had close monitoring but did not require neurosurgical intervention. A patient with cerebral contusion and extensive intracranial hemorrhage underwent craniotomy, had prolonged hospitalization, and required cognitive rehab in a skilled nursing facility.

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Risk of Progression to Advanced AMD in a U.K. Cohort

July 2020

Chakravarthy et al. set out to estimate the rates of progression to geographic

atrophy (GA) or choroidal neovascularization (CNV) in eyes with early or intermediate age-related macular degeneration (AMD). They found that progression to advanced AMD occurs frequently in these eyes, particularly when GA or CNV is present in the fellow eye.

For this retrospective cohort study, the researchers analyzed data extracted from a widely used electronic database in the United Kingdom. The data were collected between October 2000 and February 2016 at 10 retina clinics. The main outcome measure was the rate of progression to GA or CNV. A Cox proportional hazards model was used to estimate rates of progression. In addition, multivariate models were run; these included additional risk factors such as cardiovascular disease, hypertension, glaucoma, and smoking.

All told, records for 40,543 patients with early/intermediate AMD were included in the analysis. The patients were divided into four subgroups: 1) those with AMD in both eyes (early: early; n = 32,655); 2) those with AMD in one eye and CNV in the fellow eye (early:CNV; n = 7,069); 3) those with AMD in one eye and GA in the fellow eye (early:GA; n = 656); and 4) those with AMD in one eye and mixed GA/CNV in the fellow eye (early:mixed; n = 163).

Progression rates in study eyes, as expressed by 100 person-years, were as follows:

- In the early:early group, the rates of progression to GA or CNV were 2.0 and 3.2, respectively.
- In the early:CNV cohort, the rates of progression to GA or CNV were 4.1 and 15.2, respectively.
- In the early:GA group, the rates of progression to GA or CNV were 11.2 and 8.5, respectively.
- In the early:mixed cohort, the rates of progression to GA or CNV were 7.8 and 11.9, respectively.

With regard to other risk factors, age, female sex, and cardiovascular disease were associated with an increased risk of progression to advanced AMD. In contrast, diabetes and glaucoma were associated with a decreased risk of progression. —Summary by Jean Shaw

Which OCTA Scanning Protocol Is Best for PDR and NPDR?

July 2020

Although optical coherence tomography angiography (OCTA) can help detect microvascular changes indicative of diabetic retinopathy (DR), studies have failed to establish a protocol that optimally balances scan area and lesion detection and also works well in a busy clinical setting. **Zhu et al.** recently compared OCTA scan protocols; they found that 15×9-mm Montage imaging was significantly better than 6×6-mm Angio imaging for detecting DR lesions (with the exception of microaneurysms). However, they also found that 12×12-mm Angio scanning centered on the fovea and optic disc was comparable to 15×9-mm Montage imaging for discerning lesions without sacrificing sensitivity or speed.

For this study, the authors recruited 119 patients (176 scanned eyes) with proliferative DR (PDR; n = 80), non-proliferative DR (NPDR; n = 73), and diabetes mellitus without DR (n = 23). Eyes were imaged with swept-source (SS)-OCTA and multiple scan protocols in the following order: 3×3-mm Angio centered on the fovea; 6×6-mm Angio centered on the fovea and optic disc; 15×9-mm Montage; and 12×12-mm Angio centered on the fovea and optic disc.

Two ophthalmologists independently assessed the images for DR lesions, including microaneurysms, intraretinal microvascular abnormalities, neovascularization, nonperfusion, venous looping, and hard exudates.

Results were as follows:

- For neovascularization in the optic disc and elsewhere, the detection rate with 6×6-mm Angio centered on the fovea was approximately half that of 15×9-mm Montage (17.6% vs. 34.6%, respectively; $p < .05$).
- With 6×6-mm Angio centered on the fovea and optic disc, the rate was roughly two-thirds that of 15×9-mm

Montage (26.1% vs. 36.2%, respectively; $p < .05$).

- In detecting microaneurysms, 6×6-mm Angio centered on the fovea and the 6×6-mm Angio scan combination outperformed Montage imaging (85.2% vs. 79.0% and 84.8% vs. 79.0%, respectively; both $p < .05$).
- The 12×12-mm Angio images centered on the fovea and optic disc had detection rates comparable to those of 15×9-mm Montage images for all DR lesions ($p > .05$); however, the rates for nonperfusion and neovascularization were slightly higher with Montage images in patients who received both scans.

These findings support the use of widefield SS-OCTA for distinguishing PDR from NPDR, the authors said. They suggested that 12×12-mm Angio scans centered on the fovea and optic disc are a practical alternative to Montage imaging in busy clinical practices.

Elevated Expression of GHRH in Fibrous Inflammation of PDR

July 2020

Early in the pathogenesis of diabetic retinopathy (DR), immune cells become trapped in retinal capillaries, leading to retinal hypoxia, neovascularization, and eventually fibrovascular membranes (FVMs). Similarly, FVM development at the vitreoretinal interface is characteristic of proliferative diabetic retinopathy (PDR).

In a first-of-its-kind study, **Qin et al.** investigated whether the formation of FVMs in PDR also is linked to sustained inflammation. They found fibrinous inflammation in the FVMs of patients with active PDR. In addition, the authors found increased levels of growth hormone-releasing hormone (GHRH) and its receptor (GHRH-R) in the vitreous humor and their rich expression in polymorphonuclear leukocytes and other cells in PDR.

For this experimental study, the authors sampled vitreous humor, aqueous humor, and serum from the eyes of 36 patients: 12 with type 2 diabetes, 12 with PDR, and 12 with nondiabetic proliferative vitreoretinopathy (PVR) due to retinal detachment. The latter

served as controls. Age and sex distributions were similar for the three groups, but mean levels of hemoglobin A_{1c} and fibrinogen were much higher in patients with type 2 diabetes or PDR than in controls.

Six FVM samples were obtained from patients with PDR and three from patients with PVR. Histologic evaluation showed the following:

- In patients with PDR, the FVMs were composed of a mature region containing differentiated fibrocytes and rich blood vessels and an immature region with macrophage-like cells, numerous infiltrating polymorphonuclear leukocytes, and a fibrinogen-rich network.
- In those with PVR, the mature region of FVMs contained primarily differentiated fibrocytes, whereas the immature region contained mononuclear cells but no polymorphonuclear cells or fibrinogen-rich lattice.

With respect to GHRH and growth hormone (GH), the levels in PDR eyes were much higher in the vitreous humor (1.8-fold and 72.8-fold, respectively) and aqueous humor (2-fold and 4.9-fold, respectively) than in control eyes. In patients with type 2 diabetes, GH but not GHRH was elevated. Immunostaining for expression patterns in FVMs revealed GHRH and GHRH-R in polymorphonuclear leukocytes and vascular endothelial cells of patients with PDR. GHRH-R also was seen in fibrocytes of this group. Moreover, both were observed in polymorphonuclear cells that appeared to penetrate blood vessels.

In patients with PVR, GHRH-R was seen in fibrocytes and infiltrating mononuclear cells, and GHRH was detected in fibrocytes but not in infiltrating immune cells.

The authors hypothesize that GHRH and GHRH-R are involved in fibrinous inflammation in PDR by mediating the activities of polymorphonuclear leukocytes, vascular endothelial cells, and fibrocytes—potentially leading to generation and remodeling of FVMs. Further research may pave the way for therapies targeting GHRH and its receptor.

—Summaries by Lynda Seminara

Two-Year AMD Progression Predicts Late AMD and Long-Term Visual Loss

June 2020

Vitale et al. set out to determine whether patients with faster short-term worsening of age-related macular degeneration (AMD) would reach late AMD more quickly. They found that two-year progression along the 9-step Age-Related Eye Disease Study (AREDS) AMD severity scale correlated with poor clinical and visual outcomes by year 7.

This study focused on a cohort of 3,868 AREDS patients (7,736 eyes) who had at least one eye without late AMD or geographic atrophy (GA) at baseline. Two-year AMD progression was defined as an increase of ≥ 2 or ≥ 3 steps on the AMD scale. Year 7 outcomes were neovascular AMD, central GA, any GA, and best-corrected visual acuity (BCVA) loss of ≥ 2 or ≥ 3 lines.

Two-year progression of 2 steps or more occurred in 9% of eyes; progression of at least 3 steps occurred in 3.7%. By year 7, neovascular AMD was present in 6.7% of those eyes, 4.7% had central GA, 10% had any GA, and 37% and 20.9% had a loss in BCVA of ≥ 2 or ≥ 3 lines, respectively.

After adjusting for confounders and stratifying data by baseline AMD score, the authors noted that AMD progression of at least 2 steps in the first two years correlated with neovascular AMD by year 7; hazard ratios (HRs) ranged from 3.6 to 19.4. HRs for development of central GA or any GA ranged from 2.6 to 4.7 and from 1.6 to 16.9, respectively. HRs for decreased BCVA ranged from 1.3 to 2.8. The link to poor outcomes was stronger for two-year AMD progression of ≥ 3 steps than for ≥ 2 steps, and risk generally was higher for progressing eyes that had lower AMD scores at baseline. For external validation, the authors applied their analyses to a separate cohort of patients drawn from AREDS2; they noted similar predictor-outcome associations.

Clinical trials of AMD treatments, especially those targeting earlier disease stages, may be stymied by the need for large sample sizes and long follow-up times to account for slow infrequent progression to late AMD. Results of this study suggest that patients free of bilateral late AMD at baseline who have disease progression by year 2 are more likely than nonprogressing patients to have late AMD and visual loss by year 7. Further clinical studies in this at-risk subpopulation may help investigators detect meaningful treatment effects in smaller short-duration studies.

Eye Injuries and Fireworks: Prevalence and Trends

June 2020

Studies of the trends and national prevalence of firework-related ocular injuries are scarce. Shiuey et al. set out to characterize the firework-related ocular injuries treated in emergency departments (EDs) in the United States. During the 19-year study period, fireworks caused more than 34,000 ocular injuries, most of which occurred during celebrations of Independence Day and New Year's Day. The most common injury was ocular burn.

For this cross-sectional study, the authors gathered data from the National Electronic Injury Surveillance System (NEISS), a stratified probability sample of more than 100 hospital-affiliated U.S. EDs that represents more than 5,300 hospitals. Patients with an eye injury caused by fireworks from January 1999 through December 2017 were included. Outcomes of interest were the annual prevalence of these injuries and the firework types, stratified by such factors as demographics, diagnoses, and event date/location.

The 1,007 injuries identified in the NEISS database represented roughly 34,548 firework-related ocular injuries in U.S. EDs during the study period, or 1,840 injuries annually. Nearly 66% of patients were 18 years old or younger; 72% were male; and 51% were white. The most common injury was ocular burn (62.9%), followed by ocular foreign body (11.7%) and conjunctival irritation (9.6%). Ruptured globe

occurred in 2.8%, and other severe eye trauma was present in 4.6%. More than 90% of patients were treated and released, and 8.7% were admitted or were transferred to another facility.

Injuries were most often linked to firecrackers (19.2%) and bottle rockets (17.6%), followed by sparklers (8.7%), Roman candles (6.6%), and novelty devices (6.5%) such as poppers. Bottle rockets caused a disproportionately high number of severe injuries (odds ratio, 5.82; 95% CI, 2.72-12.46; $p < .001$). Injuries were most common on or near Jan. 1 and July 4, with 70.2% presenting in July, 7.4% in June, 10% in January, and 4.7% in December.

Is Visual Impairment a Risk Factor for Dementia in Women?

June 2020

Although some research shows a link between visual and cognitive impairment, robust longitudinal data are lacking. Tran et al. explored the relationship between visual status and the risk of incident dementia and found that the risk of dementia was two- to five-fold greater for visually impaired women. Severe visual impairment further amplified the risk.

This study was a secondary analysis of a prospective longitudinal cohort of women, in which the authors compared the likelihood of incident dementia or mild cognitive impairment (MCI) among women. Eligible participants were community-dwelling women (66-84 years of age) enrolled in one of two studies from the long-running Women's Health Initiative. Visual impairment was categorized as worse than 20/40, worse than 20/80, or worse than 20/100. Visual impairment also was assessed by self-reports. Cognitive impairment was determined by clinical assessment, cognitive testing, and centralized review and adjudication. The primary outcome was probable dementia; the researchers also evaluated incident MCI and a composite end point that included incident cases of probable dementia or MCI. Main outcome measures were hazard ratios (HRs) and 95% confidence intervals (CIs) for incident cognitive impairment.

Of the 1,061 participants (mean age, 73.8 years), 206 (19.4%) had self-reported visual impairment, and 183 (17.2%) had visual impairment established objectively. After adjustment for confounding factors, 42 (4%) were classified as having probable dementia. Twenty-eight women with MCI (2.6%) did not experience progression to dementia during the study period. The mean duration of follow-up after an eye examination was 3.8 years (range, 0-7 years).

Participants with objectively determined visual impairment were more likely to experience dementia. The highest risk was in those with a visual acuity (VA) of 20/100 or worse at baseline (HR, 5.66; 95% CI, 1.75-18.37). In contrast, dementia risk was lower among those with milder visual impairment (20/80 or worse: HR, 5.20; 95% CI, 1.94-13.95; 20/40 or worse: HR, 2.14; 95% CI, 1.08-4.21). Findings for MCI risk were similar: Those with the poorest VA had the highest risk of MCI (HR, 6.43; 95% CI, 1.66-24.85).

Identifying potentially modifiable risk factors for dementia is crucial to ensure effective interventions and other support, said the authors. Further research is needed to identify people at high risk for cognitive impairment and to study the effects of ophthalmic interventions on dementia incidence and cognitive trajectories.

—Summaries by Lynda Seminara

Other Journals

Selected by Prem S. Subramanian, MD, PhD

Fall-Related Eye Trauma Is on the Rise

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To better understand the epidemiology of eye trauma from falls, **Usmani et al.** reviewed records of patients who presented to U.S. emergency departments (EDs). They found that falls and associated eye injuries are on the rise, with the greatest increase in these eye injuries occurring in the elderly.

The authors gathered data from the Nationwide Emergency Department

Sample, which represents a 20% stratified sample of U.S. ED visits. Hospital characteristics were used as stratification criteria, and poststratification weighting was applied to estimate the number of nationwide ED visits. Falls involving eye trauma were identified by diagnostic codes. Multivariate regression was applied to explore relationships between fall-related factors.

During the 10-year study period, there was an increase in the incidence of eye trauma, from 30.7 to 33.8 per 100,000 persons. Although both children and adults \geq age 45 had a higher incidence of eye trauma with falls relative to adolescents or younger adults, only adults \geq 65 years had a disproportionately higher risk of a vision-threatening injury. In addition, substantially more of them required hospital admission. The most common ocular injuries were contusion of the orbital tissues (18.3%), eyelid or periocular laceration (18.1%), and orbital fractures (15.8%). Costs to treat these conditions in the study period, independent of other fall-related injuries, were estimated to exceed \$240 million.

The database-driven nature of this study did not allow the authors to identify specific impacts to quality of life as a result of the eye trauma, but severe effects of such injuries have been demonstrated elsewhere. The authors encourage ophthalmologists to collaborate with other specialists to devise strategies to identify and counsel at-risk groups and to reduce eye injury during unavoidable falls. Ophthalmologists should consider early referral of patients to low vision specialists and occupational therapists to reduce risk of falls. Particular emphasis should be given to the elderly, who have the highest risk of debilitating consequences of eye trauma; the authors encourage use of protective eyewear and polycarbonate glasses for these patients.

Influence of Disc Hemorrhage on Central VF Damage

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Previous studies have indicated a relationship between disc hemorrhage

(DH) and early central visual field (VF) damage. **Shukla et al.** set out to determine the effects of DH on the central VF and to further elucidate this relationship. They found a strong link between DH and the presence and progression of central VF defects.

For this study, the authors hypothesized that in addition to having more damage to the central VF, patients with DH would have faster central or global VF loss than would patients without DH. Cross-sectional and longitudinal analyses were performed on data from the African Descent and Glaucoma Evaluation Study cohort. Disc photographs were examined for the presence and specific location of DH, and VF damage was characterized by location within the central 10 degrees of the 24-2 field pattern. Pattern deviation and mean total deviation (MTD) were measured. Main outcomes were associations between DH and the presence of central VF damage and between DH and worsening VF.

In the cross-sectional analysis, DH was detected in 6.2% of the 355 eyes; it correlated with more severe central damage in the 24-2 field pattern (incidence rate ratio [IRR], 1.47) and in the 10-2 pattern (IRR, 1.81).

Results of the longitudinal analysis showed that eyes with DH progressed more rapidly than those without it, based on 24-2 global and 10-2 MTD rates ($p = .009$ and $p < .001$, respectively) but not according to 24-2 central MTD rates ($p = .338$).

Given the link between DH and the presence and progression of central VF damage, identification of DH “should prompt intensive central VF monitoring and surveillance with 10-2 fields to detect progression,” said the authors. They added that heightened awareness of this link should enable appropriate risk stratification and treatment escalation. Their suggestions for future work include more extensive measurements in 10-2 fields, particularly because research has shown that damage to this region may occur earlier. Frequent testing of more locations within the 10-2 and 24-2 grids may expedite the identification of VF decline.

—Summaries by Lynda Seminara