Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

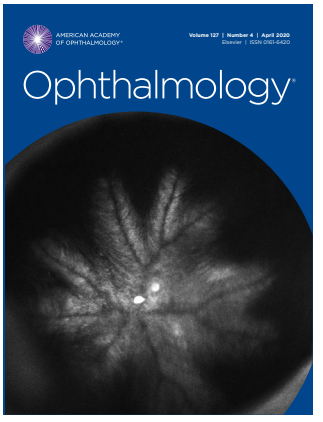
Private Equity Trends in Eye Care

April 2020

Chen et al. set out to identify temporal and geographic trends in private equity (PE) acquisitions in eye care in the United States. They concluded that PE-backed acquisitions of ophthalmic and optometric practices have rapidly increased since 2012, with some platform companies having already been sold or recapitalized to new investors.

For this cross-sectional study, the authors used PE acquisition and investment data from Jan. 1, 2012, to Oct. 20, 2019. They identified 228 ophthalmic and optometric practices that had been acquired by 29 PE-backed platform companies during that time. Of the 228 practices, 127 were comprehensive/multispecialty practices, nine were retina practices, and 92 were optometry-specific practices; they were associated with 1,466 clinical locations and involved 2,146 clinicians.

Acquisitions increased rapidly between 2012 and 2019: From 2012-2016, 42 practices were acquired; this grew to 186 from 2017-2019. Financing rounds of platform companies paralleled temporal acquisition trends. Three platform companies, comprising 60% of platforms formed before 2016, were subsequently sold or recapitalized to new PE investors by the end of the study period, with a median holding period of 3.5 years. Acquisitions occurred in 40 states, with a majority of PE firms developing multistate platform companies.



Of note, the authors found a slight decline in acquisition numbers in 2019 and a lower rate of platform formations. They speculate that this decline in PE interest may be due to expectations of limited profit potential due to current health care and market trends. Finally, they emphasize that future research should assess the impact of short-term PE investment on patient, provider, and practice metrics. *(Also see related commentary by David W. Parke II, MD, in the same issue.)*

Eye Injuries in the Iraq and Afghanistan Conflicts

April 2020

In an effort to inform future military surgical training requirements and medical planning, **Breeze et al.** compared incidences, ocular injury types, and treatment performed on U.S. and U.K. military service members and host nation civilians within the Iraq and Afghanistan conflicts. They found that eye injuries were more likely to have been treated definitively in U.S. deployed military treatment facilities, reflecting the absence of ophthalmologists in their U.K. counterparts.

For this retrospective cohort study, the authors evaluated data on 67,586 patients in the U.S. and U.K. military trauma registries who were treated at deployed military treatment facilities between March 2003 and October 2011. An adjusted multiple logistic regression model was performed using the main outcome measures of enucleation or evisceration and primary open globe repair as dependent variables and casualty nationality, location, and the presence of an ophthalmic surgeon as independent variables.

Of the 67,586 patients, 5,719 (8%) had sustained eye injuries. Of these, the most common were open globe injury without intraocular foreign body (3,201; 56%). Adnexal injuries were recorded in 1,265 patients (22%). The odds of undergoing evisceration or enucleation for open globe injury was highest in Iraqi and Afghani civilians (odds ratio [OR], 9.23; $p < 0.001$), but there was no evidence of a difference between U.S. and U.K. military service member casualties ($p = 0.38$). Primary repair of open globe injury was more commonly undertaken at U.S. medical facilities (OR 5.71; $p < 0.0001$), reflecting the presence of an ophthalmic surgeon at the U.S. facilities.

The authors emphasized that their findings support the inclusion of ophthalmologists in deployed coalition treatment facilities during future conflicts.

Medication Adherence and Visual Field Progression in CIGTS

April 2020

The Collaborative Initial Glaucoma Treatment Study (CIGTS) compared the effect of initial treatment with topical medications to that of trabeculectomy in 607 patients with newly diagnosed glaucoma. Of these, 307 were randomized to the medication arm of the study and underwent regular assessment of their medication adherence and disease progression. **Newman-Casey et al.** reported long-term data on these patients; they found a statistically and clinically significant association between medication nonadherence and visual field (VF) loss.

The patients were followed up at six-month intervals for an average of 7.3 years. Medication adherence was assessed via telephone calls in which patients were asked, "We want to get an idea of what medication taking is like for you. Did you happen to miss any dose of your [name of medication] yesterday (yes or no)?" The impact of medication adherence on mean deviation (MD) over time was assessed with a linear mixed regression model adjusting for the effects of baseline MD and age, cataract extraction, interactions, and time (through year 8, excluding time after crossover to surgery). Medication adherence was modeled as a cumulative sum of the number of prior visits at which a missed dose of medication was reported.

Adherence data were available for 306 of the 307 patients. Of these, 142 (46%) reported never missing a dose of medication, 112 (37%) reported missing medication at up to one-third of visits, 31 (10%) reported missing medication at one-third to two-thirds of visits, and 21 (7%) reported missing medication at more than two-thirds of visits.

Worse medication adherence was associated with loss of MD over time ($p = 0.005$). For patients who reported never missing a dose of medication, the average predicted MD loss over eight years was 0.62 decibels (dB), consistent with age-related loss (95% confidence interval [CI], 0.17-1.06; $p = 0.007$). Patients who reported missing medication doses at one-third of visits had a loss of 1.42 dB (95% CI, 0.86-1.98; $p < 0.0001$), and those who reported missing medication doses at two-thirds of visits showed a loss of 2.23 dB (95% CI, 1.19-3.26; $p < 0.0001$).

The authors noted that 79% of participants had five years of follow-up data, thus offering unique insights into the association between medication-taking behavior and the progression of VF loss. —*Summaries by Arthur Stone*

Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MHS

Predictors of Success in Selective Laser Trabeculoplasty

March/April 2020

In a large cohort of eyes undergoing selective laser trabeculoplasty (SLT), **Kuley et al.** sought to determine predictors of SLT success in lowering intraocular pressure (IOP) in patients with glaucoma. They found that greater pre-SLT IOP and angle pigment correlated positively with SLT success. Patient age, total SLT power, severity of glaucoma, and prior treatments were not associated with SLT success or failure.

For this retrospective case series, the authors evaluated 677 patients (997 eyes) who were treated at a single center by three glaucoma specialists between Jan. 1, 2012, and June 30, 2018. Baseline, demographic, procedural, and ophthalmic examination data were recorded at the time of the first SLT. IOP and medication data were recorded at all follow-up visits. SLT success was defined as IOP decrease greater than or equal to 20% from baseline at the three-, six-, and 12-month follow-up visits. Eyes were considered to have failed and were censored when additional SLT or glaucoma surgery was performed.

The patients' mean age was 70.2 (± 11.5) years. SLT success was achieved in 227 eyes (22.8%), while 770 (77.2%) failed to meet success criteria. Of the patients who did not achieve success, 523 failed due to insufficient reduction in IOP (<20% from baseline), and 46 failed due to requiring SLT or surgery. Pre-SLT IOP was 21.95 ± 5.2 mm Hg on 2.0 ± 1.2 medications in eyes with successful SLT, versus 19.0 ± 5.0 mm Hg ($p < 0.0001$) on 2.1 ± 1.3 medications ($p = 0.52$) in eyes with SLT failure.

At one year, mean IOP in eyes with SLT success was 14.7 ± 3.2 mm Hg on 2.0 ± 1.2 medications, compared to 16.3 ± 4.7 mm Hg ($p = 0.008$) on a mean of 1.9 ± 1.3 medications ($p = 0.37$) in eyes that failed SLT. Eyes with SLT success more often had greater angle pigment grading. There was no correlation between SLT outcomes and patients' age, glaucoma severity, total SLT power, type of glaucoma, visual field mean defect, or retinal nerve fiber layer thickness. —*Summary by Arthur Stone*

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Long-Term Outcomes for Idiopathic Macular Holes

April 2020

Elhusseiny et al. set out to evaluate long-term structural and visual outcomes in patients who underwent pars plana vitrectomy (PPV) for idiopathic full-thickness macular hole (MH). They found that visual acuity continued to improve at least three years after PPV and was maintained thereafter in a substantial percentage of the patients.

This retrospective case series involved 80 patients (87 eyes) who underwent PPV for idiopathic MH and had follow-up of at least five years' duration. The mean postoperative follow-up was 9.6 ± 4.3 years (median, 9 years; range, 5-22 years). Only cases of idiopathic MH were included in this case analysis; patients with traumatic, recurrent, persistent, and secondary MHs were excluded. The main outcome measure was postoperative best-corrected visual acuity (BCVA) and its correlation with different parameters evident on spectral-domain optical coherence tomography (SD-OCT).

Initial successful MH closure was achieved in 82 eyes (94%). Seven eyes (8%) experienced MH reopening and underwent reoperation. The mean BCVA for the entire cohort improved

from 0.20 ± 0.13 before surgery to 0.39 ± 0.23 at one year, 0.43 ± 0.26 at two years, 0.47 ± 0.29 at three years, and 0.50 ± 0.26 at five years. In addition, for patients with longer follow-up, BCVA was 0.53 ± 0.28 at eight years and 0.61 ± 0.27 at 10 years.

SD-OCT confirmed that postoperative integrity of the ellipsoid zone was established in 52 eyes (60%) and external limiting membrane integrity was restored in 54 eyes (62%). Cystoid spaces of variable severity were observed in 28 eyes (32%). Pre-op BCVA of 20/60 or better and post-op ellipsoid zone and external limiting membrane integrity were associated with better BCVA at follow-up. —*Summary by Jean Shaw*

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Corneal Hysteresis and Glaucoma Progression

April 2020

Wong et al. investigated the relationship between corneal hysteresis (CH) and displacement of the anterior lamina cribrosa surface (ALCS) in patients with glaucoma. They found that lower CH was associated with ALCS displacement over time, suggesting that it is a risk factor for glaucoma progression.

For this prospective observational case series, the researchers evaluated 96 patients (147 eyes) who either had glaucoma or were glaucoma suspects. The patients were followed for a mean of 3.5 years and 7.9 visits.

The researchers used the Ocular Response Analyzer (ORA) to measure CH and spectral-domain optical coherence tomography (SD-OCT) to assess mean ALCS depth and choroidal thickness. The rate of change in ALCS depth was calculated using linear mixed effect models.

Of the 147 eyes evaluated, 108 (73.4%) showed no significant ALCS displacement over time. However, 17 eyes (11.5%) showed posterior displacement, while 22 (15%) showed anterior displacement. Eyes with posterior displacement progressed more frequently than eyes with either anterior displacement or stable ALCS—and CH was significantly associated with a faster rate of posterior displacement during follow-up. Specifically, the researchers noted, for every 1 mm Hg decrease in CH, posterior displacement of the ALCS occurred at a rate of approximately 0.66 µm per year.

The results support the hypothesis that lower CH predisposes an eye to developing structural or functional glaucoma progression, the researchers said, as it serves as a marker for posterior ALCS displacement. Studies with a larger sample size and longer follow-up are needed.

Age at Time of Surgery for Intermittent Exotropia

April 2020

Repka et al. set out to determine the link between a child's age and the outcome of surgery for intermittent exotropia (IXT). They found that younger age at time of surgery is associated with better surgical outcomes.

For this secondary analysis of pooled data from a prospective randomized trial, the researchers evaluated 197 children between the ages of 3 and 11 (mean age, 6.2 years). All had basic-type IXT of 15 to 40 PD and at least 400 arcsec near stereoacuity. The children were randomly assigned to either 1) bilateral lateral rectus muscle recessions or 2) unilateral lateral rectus recession with medial rectus resection.

The results of this analysis revealed that the cumulative probability of having a suboptimal surgical outcome at the three-year post-op mark was 28% in children who were at least 3 but younger than 5 years old and approximately 50% for those who were age 5 or older. No other significant associations were found for other baseline factors, including magnitude of angle, control score, fixation preference, or near stereoacuity.

The authors caution that this analysis needs further confirmation from other studies. In particular, they said, the clinical question of whether early or delayed IXT surgery is associated with a better outcome needs to be addressed.

—*Summaries by Jean Shaw*

JAMA Ophthalmology

Selected and reviewed by Neil M. Bressler, MD, and Deputy Editors

Treat-and-Extend With Ranibizumab: Two-Year Results

March 2020

In a randomized clinical trial, **Kertes et al.** compared the efficacy of monthly intravitreal injections of ranibizumab to that seen with a treat-and-extend (T&E) approach for choroidal neovascularization (CNV) secondary to neovascular age-related macular degeneration. They found that, through 24 months, the T&E regimen resulted in clinically meaningful improvement in best-corrected visual acuity (BCVA) that was not worse than that achieved with monthly treatment.

For this trial, the researchers enrolled 580 treatment-naive patients with CNV. Patients were randomized 1:1 to receive intravitreal ranibizumab 0.5 mg in either a T&E or a monthly dosing regimen. The main outcome measure was mean change in BCVA from baseline to month 24. By the two-year mark, 466 (80.3%) of the 580 patients had completed the study, as 49 patients (19.5%) withdrew from the T&E arm and 65 (21.8%) withdrew from the monthly treatment arm.

At month 24, results were as follows:

- For the primary outcome, the mean (standard deviation) change in VA was not worse in the T&E treatment group (6.8 [14.1] letters) compared with the monthly treatment group (6.0 [12.6] letters; difference, 0.9; 95% confidence interval [CI], –1.6-3.3; $p = 0.21$).
- At month 24, a lower mean number of injections was reported for T&E treatment (17.6) than with the monthly dosing regimen (23.5; difference, 5.9; 95% CI, 5.4-6.5; $p < 0.001$).
- In the T&E arm, 73.7% (95% CI, 67.6%-79.3%) of the patients were able to extend their treatment interval to eight or more weeks during the 24 months of treatment, and 43.1% (95% CI, 36.6%-49.8%) of the patients reached the 12-week maximum extension interval.
- In the T&E group, 42.9% gained 10 or more letters from baseline, while

25.5% gained 15 or more letters. In contrast, 36.4% in the monthly treatment group gained 10 or more letters, while 23.1% gained 10 or more letters.

- With regard to letters lost, 9.5% in the T&E group lost 10 or more letters, while 6.5% lost 15 or more letters. The rates were similar in the monthly treatment group, as 9.8% lost 10 or more letters and 5.8% lost 15 or more letters.

The study has been extended to 36 months, with all participants receiving ranibizumab on a T&E basis.

Metastasis in Uveal Melanoma

March 2020

When it comes to predicting metastasis in patients with uveal melanoma, how do The Cancer Genome Atlas (TCGA) and American Joint Committee on Cancer (AJCC) classification systems compare? **Mazloumi et al.** set out to answer this question and found that the TCGA provides greater accuracy.

For this retrospective cohort study, the researchers evaluated 642 patients with uveal melanoma who were treated with plaque radiotherapy from Oct. 1, 2008, to Dec. 31, 2018. Patients without complete genetic analysis of both chromosomes 3 and 8 were excluded, as were those with iris melanoma.

Using AJCC classification, the 642 tumors were classified into four categories, 17 subcategories, and four stages (based on tumor largest basal diameter, thickness, location, and extraocular extension). Based on genetic results, they were then grouped into four TCGA classes. The mean follow-up time for the entire cohort was 43.7 months (range, 1.4-159.2 months); the main outcome was the value of the two methods for predicting uveal melanoma–related metastasis.

The researchers used univariate Cox regression and multivariate models to predict the likelihood of metastasis. At five years, TCGA classification showed a higher value for prediction of distant metastasis in all models: With univariate analysis, the Wald statistic was 94.8 for four TCGA classes (hazard ratio [HR], 2.8; 95% confidence interval [CI], 2.3-3.5; $p < 0.01$) and 67.5 for four AJCC categories (HR, 2.6; 95% CI, 2.1-3.2; $p < 0.01$). With multivariate analysis, the Wald statistic for TCGA was 61.5 (HR, 2.4; 95% CI, 1.9-2.9; $p < 0.01$) and 35.5 for AJCC classification (HR, 1.9; 95% CI, 1.5-2.4; $p < 0.01$).

The authors noted that follow-up data of five or more years were available on only 168 of the 642 patients. Nonetheless, they said, when genetic testing results are available, the TCGA system may be a more accurate way to identify those patients who are at high risk of metastasis.

Genetics of Pigmentary Glaucoma

March 2020

Despite evidence of familial aggregation, the sporadic nature of pigmentary glaucoma (PG) and its status as a relatively rare condition have stymied research on heritability. **Simcoe et al.** set out to elucidate the genetics of PG by calculating its single-nucleotide polymorphism (SNP) heritability and identifying other genetic associations. They found a possible genetic component and shared genetic risks with iris pigmentation and myopia.

For this genome-wide association study, the researchers included 227 affected individuals from Germany and 291 control participants from the United Kingdom. All were of European ancestry. Those with PG were younger (mean age, 58.7 years) than the control participants (mean age, 80.2 years). Main outcome measures were an estimate of SNP-explained heritability for PG, correlations of effect sizes between PG and iris pigmentation and myopia, and correlations of effect sizes between PG and other eye phenotypes.

Results of the analysis showed a heritability estimate of 45% (standard error, 0.22; $p = 6.15 \times 10^{-10}$). Some SNPs that have previously been linked to eye pigmentation and myopia correlated with those for PG. However, PG appeared to be genetically distinct from primary open-angle glaucoma and its endophenotypes.

The results point to some possible mechanisms that may contribute to PG, and the authors called for further research. *—Summaries by Jean Shaw*

Other Journals

Selected by Prem S. Subramanian, MD, PhD

Optic Disc Drusen and NA-AION

Journal of Neuro-Ophthalmology
Published online Jan. 16, 2020

Rueløkke et al. compared the prevalence of known risk factors for nonarteritic anterior ischemic optic neuropathy (NA-AION) in patients with the condition and in a subset of those with optic disc drusen (ODD-AION). They found that ODD may be a risk factor in the development of AION.

The researchers evaluated 27 patients with NA-AION; all were originally treated between 2008 and 2017. For this case-control study, the patients were questioned about their medical history and were asked about general vascular risk factors (diabetes, hypertension, dyslipidemia, and smoking) and other risk factors for NA-AION (sleep apnea, anemia at time of diagnosis, and ocular surgery before diagnosis). The patients were imaged with optical coherence tomography with enhanced depth imaging (EDI-OCT) to confirm the presence or absence of ODD.

All told, 14 patients had no ODD, and 13 had ODD-AION. Four of the 13 with ODD-AION (31%) had vascular risk factors; in contrast, 12 of the 14 with no ODD (86%) had vascular risk factors. Five patients with ODD-AION (38%) had previous ocular surgery, versus one patient with no ODD (7%).

Of note, during EDI-OCT screening for this study, two of the patients were found to have buried ODD and were reclassified. This finding implies that not all otherwise healthy NA-AION patients had originally undergone thorough screening, the authors said, and they added that cases of ODD-AION may be underdiagnosed. In particular, they noted that optic disc edema during the acute stage of the disease can mask ODD on EDI-OCT, and they suggested scanning during follow-up.

—Summary by Jean Shaw

EXTRA **MORE ONLINE.** For an additional summary, see this article online at aao.org/eyenet.