Reducing the Carbon Footprint of Cataract Surgery
July 2023

Cataract surgery, the most commonly performed ophthalmic operation, is a contributor to carbon emissions and overall waste. Sherry et al. reviewed published literature to explore the benefits and risks of sustainability methods used in health care, from which they created decision trees for surgeons. They found some strategies to be safe, cost-effective, and environmentally friendly and noted that others lacked risk-benefit data.

The authors began by generating a list of interventions relevant to cataract surgery—based on published literature and field observations. They applied the “rethink, reduce, reuse, recycle” framework to organize the potential interventions. Categories included advocacy, education, pharmaceuticals, supplies, waste, and process changes. They focused on environmental sustainability tactics that could be enacted by surgeons, nurses, pharmacists, and other clinical personnel. For each intervention, the authors reviewed published findings to ascertain any known impact on emissions, costs, safety, and clinical outcomes; they also documented gaps in the literature. In addition, they sought to capture health-system websites and reports that specified benefits or challenges of adopting a particular intervention.

The analyses showed evidence of the safety, cost-effectiveness, and/or environmental viability of various interventions. These include multipatient dosing of applicable intra- and perioperative medications; allowing post-op patients to take home their unfinished medicines; training staff to properly sort medical waste; reducing the amount of supplies used during surgery; and performing immediate sequential bilateral cataract surgery in appropriate patients. Benefits or risks were not stated for some strategies, such as switching single-use supplies to reusable materials or implementing a hub-and-spoke surgical model. Ophthalmology-specific details were unavailable for many advocacy and education strategies, but the risks of these should be minimal, said the authors.

“Which interventions will work best must be determined by the individual stakeholders at each hospital or health system,” noted the authors. They affirmed that, despite the literature limitations, there is ample evidence of the feasibility and cost-effectiveness of reducing emissions in the OR.

Racial Disparities Persist in Vision Care
July 2023

Inequities in the U.S. health system can undermine core American values. “It is essential for all domains of health care to identify relevant social determinants of health and to respond to the resulting health inequities accordingly,” said Chauhan et al., who analyzed responses to the U.S. National Survey of Children’s Health (NSCH) to explore the demographics of visual impairment and unmet vision-care needs. As suggested by results of previous studies, they found that Black and Hispanic children fared poorly.

The NSCH is a national, cross-sectional questionnaire that focuses on the physical and emotional health of children from birth to 17 years of age. For this study, 2016-2020 data were analyzed. The main outcome measures were vision impairment and unmet vision-care need. The prevalence of vision impairment was estimated from answers to the question “Does the child have blindness or problems with seeing, even when wearing glasses?” Respondents also were asked “During the past 12 months, was there any time when this child needed health care, but it was not received?” which was followed by an inquiry into the type of care that was lacking. Income, a key indicator of socioeconomic status (SES), was
factored into the study; based on the federal poverty level (FPL), income was classified as low SES (≤199% FPL) or high SES (≥200% FPL). Other demographic factors were sex, age group, and state of residence. Multivariable logistic regression was performed, and the analyses were weighted to generate nationally representative estimates. Hot deck imputation or sequential regression methods were applied when data on sex, income, or race/ethnicity were missing.

Rates of vision impairment were highest in southern states, including Louisiana (2.35%), Alabama (2.25%), and Mississippi (2.15%). Among 6- to 11-year-olds, the prevalence of unmet needs and vision impairment was greatest for Hispanics (OR, 2.00 and 1.60 [respectively] vs. Whites). Among older children (12-17 years), Hispanics were more likely than Whites to be visually impaired (OR, 1.91), and non-Hispanic Blacks had the highest level of unmet need (OR, 2.45 vs. Whites). Geographically, unmet needs were most pervasive in Georgia (1.05%), Wyoming (0.90%), and Texas (0.86%). In comparison to non-Hispanic Whites, non-Hispanic Blacks in the lowest SES (OR, 1.61) and highest SES (OR, 8.73) were significantly more likely to have unmet vision-related needs. Similarly, Hispanic children in these income categories were more likely than non-Hispanic Whites to be visually impaired (OR, 1.44 and 1.84, respectively). During the height of the Covid-19 pandemic, unmet needs climbed for all children but were most substantial for non-Hispanic Blacks and Hispanics, followed by non-Hispanic Asians.

“The clustering of unmet vision care and impairment in southern states merits further investigation,” said the authors. They hope their findings will result in targeted actionable plans to improve vision for all children.

**Low-Dose Atropine for Myopia Control**

*July 2023*

Bullimore and Brennan sought to predict the three-year efficacy of low-dose atropine by assessing results of the low-concentration atropine for myopia progression (LAMP) study and by reviewing a meta-analysis of 80 studies of axial length in untreated myopic children. They projected that three-year treatment with 0.05% atropine reduced axial length elongation (ALE) by 0.55 mm, which compares favorably with findings for higher atropine doses and other optical treatments for myopia.

In year 1 of the LAMP study, participants (N = 438) were assigned randomly to receive 0.05%, 0.025%, or 0.01% atropine or placebo; treatment assignments were continued through year 2. In year 3, half of the treated children stayed on their dose of atropine, and treatment was discontinued for the other half. The main outcome measures were changes in axial length and myopia progression. For this analysis, the authors focused on years 1 and 3.

In year 1, ALE was slowed by 0.21, 0.12, and 0.05 mm with atropine 0.05%, 0.025%, and 0.01%, respectively, compared with placebo. Myopia progression was reduced by 0.54, 0.35, and 0.22 D, respectively. In the same period, the placebo group had ALE of 0.41 mm and myopia progression of –0.81 D. During year 3, there were no significant dose-related differences in myopia progression. The three-year cumulative absolute reductions in ALE were 0.55, 0.31, and 0.16 mm with atropine 0.05%, 0.025%, and 0.01%, respectively. In pairwise comparisons for year 3, ALE and myopia progression were significantly greater for children who received 0.05% atropine than for those given 0.01% atropine. Although this suggests a greater rebound effect with 0.05% atropine, the authors considered the difference to be nominal clinically. The meta-analysis demonstrated that low-dose atropine slowed ALE by an average of 15%. As expected, the speed of myopia progression and ALE was faster after discontinuation of treatment.

These findings suggest that the efficacy of low-concentration atropine beyond one year of treatment exceeds that of some optical therapies and possibly even higher doses of atropine, said the authors. They concluded that an annual ALE slowing rate of 15% can be applied to predict three-year efficacy of low-dose atropine in the LAMP study.

**Predicting Two-Year Outcomes of Anti-VEGF Therapy for AMD**

*July 2023*

In the multicenter Comparisons of Age-Related Macular Degeneration (AMD) Treatments Trials (CATT), safety and efficacy were assessed for ranibizumab and bevacizumab. Given the wide variability of treatment responses, it is prudent to identify factors that may affect outcomes. In a secondary cohort analysis of CATT, Xue et al. looked at the early morphologic and functional responses to explore their potential for predicting two-year visual outcomes. They found that new elevation of the retinal pigment epithelium within three months of treatment coincided with significantly better BCVA gains within two years. Most of the early structural responses were not independent predictors of visual outcomes. The combination of baseline factors, early BCVA response, and morphologic findings within three months was moderately predictive of two-year visual outcomes.

The cohort comprised 1,185 patients with treatment-naïve neovascular AMD and baseline BCVA in the range of 20/25 to 20/320. Per the study protocol, participants were assigned randomly to receive a regimen of ranibizumab or bevacizumab. In the secondary analysis, the authors looked for links between two-year BCVA results and the morphologic and functional observations at baseline and three months. They applied univariable and multivariable regression models to assess the performance of each variable for predicting overall BCVA change and BCVA gains of at least three lines (the primary outcomes), using the R2 coefficient and area under the receiver-operating characteristic curve (AUC), respectively.

In multivariable analyses that included known significant baseline predictors of treatment outcomes (e.g., BCVA, macular atrophy, retinal pigment epithelium elevation [RPEE]) and an early favorable BCVA response, new RPEE within three months correlated...
significantly with higher BCVA gains by two years (10.2 letters vs. 3.5 letters for resolved RPEE; p < .001). This combination of significant predictors was found to moderately forecast the two-year BCVA (R^2 = 0.36). Baseline BCVA plus gains of at least three lines by month 3 predicted gains of this magnitude within two years (AUC, 0.83; 95% CI, 0.81-0.86).

No other three-month morphologic change was a significant predictor of two-year visual response, said the authors. They noted that "future research is needed to better understand the factors contributing to the variation in long-term vision outcomes with anti-VEGF therapy.”

American Journal of Ophthalmology
Selected by Richard K. Parrish II, MD

Regional Versus General Anesthesia in Open Globe Repair
July 2023

Although general anesthesia (GA) has been a mainstay in open globe repair, regional anesthesia with monitored anesthesia care (RA-MAC) has gained popularity as ophthalmologists perform more of these time-sensitive procedures in their own facilities. At a tertiary referral center, Fan et al. compared the clinical features and outcomes of open globe repair during GA versus RA-MAC. They found that RA-MAC was often chosen if the injury was mild, whereas GA was favored if VA was poor and the wound was severe. The improvement in VA was similar for both anesthesia cohorts.

This study was based on medical records of patients with open globe injury treated at Bascom Palmer Eye Institute from January 2015 to October 2020. The facility had no predefined anesthesia protocol for open globe repair, but RA-MAC usually was the first choice and, if warranted, could be switched to GA at the discretion of the surgeon. The main outcome measure was VA at the last follow-up visit.

The records of 507 adult patients (507 eyes) were reviewed. Globe repair was safely accomplished during RA-MAC in 462 patients (91%) and during GA in 45 patients (9%). RA-MAC was selected for 96% of zone 1 repairs (240/251 patients) and for 92% of zone 2 repairs (156/170 patients) (p < .001); it was also used for 76% of zone 3 repairs (65/86 patients).

Globe injuries were more severe in the GA cohort. Accordingly, RA-MAC was linked to better presenting VA, shorter and more anterior wounds, and less time in the OR. The VA improvement after repair was comparable for the two groups: .52 logMAR with RA-MAC and .46 logMAR with GA (p = .68). At the authors’ facility, use of RA-MAC in open globe repair has grown from 64% before 2000 to 91% since 2015.

These findings indicate that RA-MAC may be a viable alternative to GA in the setting of open globe repair, said the authors, particularly if given to patients who are likely to cooperate during the procedure.

Subthreshold Amblyopia
July 2023

While compiling a database of patients with amblyopia who visited Boston Children's Hospital during a five-year period, Michalak et al. noted that a substantial number of cases did not meet the VA threshold for this disorder. The authors found that although most 12-month treatment outcomes were unremarkable for patients with “subthreshold amblyopia,” nearly half of them subsequently had 20/20 vision in both eyes, as well as stereopsis improvement.

Included in the analysis were 2- to 12-year-olds who had a new diagnosis of amblyopia between 2010 and 2014. BCVA was better than 20/40 in at least one eye but was not correctable to 20/20; no patient had a structural abnormality. The main outcome measure was amblyopia resolution, defined as VA of 20/20 or better in both eyes.

Among 2,311 new diagnoses of amblyopia, 464 (20.1%) were considered subthreshold. The median age of this subgroup was 6.3 years, and 49.6% were female. Nearly 62% had an amblyogenic factor, and the remainder did not meet the quantitative criteria for amblyopia. Almost all subthreshold cases (97.5%) received treatment, consisting of eyeglasses (94%), patching (38%), and/or atropine (6%).

Approximately 69% of the subthreshold cohort returned for follow-up (median time, 3.1 years). Twenty percent experienced full resolution within 12 months. By the final visit, resolution was complete in 152 patients (47.8%); this included five of eight patients who received observation only. Among those with complete resolution, median stereopsis improved from 4.50 (first visit) to 3.91 (final visit).

In the univariate analysis, factors correlating with amblyopia resolution were longer follow-up time, no previous amblyopia treatment, no mechanism meeting amblyopia criteria, better log stereopsis at initial and final visits, and greater self-reported use of glasses. In the multivariate analysis, the only factor with a significant link to resolved subthreshold amblyopia was longer duration of follow-up (OR, 1.38; p < .001), indicating that this cohort may benefit from extended monitoring and extra encouragement to adhere to treatment.

Most studies of amblyopia involved patients with worse baseline VA; hence, information on the management and outcomes of subthreshold amblyopia is lacking. The authors recommend research to explore the natural history of subthreshold amblyopia and to determine whether good outcomes can be achieved by observation alone.

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

Smartphone-Based ROP Screening
June 2023

Telemedicine screening programs for retinopathy of prematurity (ROP) are effective, but they require expensive widefield digital fundus imaging (WDFI) and thus may not be accessible in low-income countries. Smartphone-based fundus imaging (SBFI) systems are inexpensive but have a narrower field of view and lack testing in real-world telemedicine settings. In a study conducted in India, Young et al.
looked at the efficacy of ROP screening with SBFI and the accuracy of grading by artificial intelligence (AI) versus humans. They found SBFI systems to be highly sensitive for detecting ROP requiring treatment and noted that both types of grading were effective.

This prospective cross-sectional study was part of a teleophthalmology program in India. From January 2021 to April 2022, premature infants who met normal ROP screening criteria were enrolled. Both eyes of each infant underwent WDFI as well as imaging via one of two smartphone-based ophthalmoscopy devices (Make-In-India RetCam or Keeler Monocular Indirect Ophthalmoscopy). The images were obtained by trained technicians, usually general nurses. For every image, two masked readers evaluated the zone, stage, plus, and vascular severity. The smartphone-obtained images were stratified into three datasets: training (70%), validation (10%), and test (20%). These datasets were used to train a ResNet-18 deep-learning architecture for classification of disease (normal, preplus, or plus), which was applied to derive patient-level predictions of referral-warranted ROP (RW-ROP) and treatment-requiring ROP (TR-ROP). Main outcome measures were 1) the sensitivity and specificity of RW-ROP and TR-ROP detection by human and AI graders and 2) area under the receiver–operating characteristic curve (AUC) for human-graded vascular severity scores, which ranged from one to nine. The sensitivity and specificity of the two SBFI systems were compared using Pearson χ² testing.

The study population comprised 156 infants (312 eyes; mean gestational age, 33.0 weeks). There was no significant difference in sensitivity or specificity between the two smartphone systems, so their findings were combined. SBFI was only moderately sensitive for detecting more-than-mild ROP (59%). However, as a screening tool, using the cutoff of at least RW-ROP (i.e., type II ROP and/or preplus or worse), its sensitivity was 100%. SBFI plus human grading detected TR-ROP with sensitivity of 100% and specificity of 83.49%. The AUCs for human-graded severity were .95 for RW-ROP and .96 for TR-ROP. With SBFI plus AI grading, sensitivity and specificity were 100% and 58.6% (respectively) for detecting TR-ROP and were 80.0% and 59.3% (respectively) for detecting RW-ROP.

These findings suggest that the combination of SBFI and AI may be effective for detecting TR-ROP. Use of these low-cost methods would increase the global reach of ROP screening.

Discharge Disparities After Ocular Injury From Firearms
June 2023

Building on evidence of racial, ethnic, and insurance-related disparities in trauma care, Mike et al. were eager to learn whether such inequity extends to the discharge practices for patients who sustain a firearm-related ocular injury. Their review of more than 8,700 cases, representing roughly 900 U.S. care centers, showed substantial differences in discharge patterns. Patients who were older, Medicare-insured, and White were more likely than others, including Blacks and Hispanics, to be released to an advanced care facility (ACF).

The study was a retrospective analysis of the U.S. National Trauma Data Bank for the period 2008–2014. The data were scanned to identify patients who were hospitalized for a firearm-associated ocular injury, determined from ICD-9-CM diagnostic and E-codes. The collected data included demographics, injury type and severity, and insurance status. Statistical analyses were conducted through 2021. The primary outcome measure was the likelihood of discharge to an ACF.

Altogether, 8,715 relevant patients were identified. Most (85.7%) were male, 35% were African American, and approximately 47% were White. The mean age was 33.8 years. Payments for the trauma care were received from government insurance plans (31.5%), patients themselves (29.4%), or commercial health plans (22.8%). The most common discharge dispositions were home (48.8%) and ACF (20.5%). According to multivariate analysis, factors linked to the highest odds of ACF placement were hospital stay ≥6 days (OR, 3.05; p < .001), age ≥65 years (OR, 2.94; p < .001), associated traumatic brain injury (OR, 2.32; p < .001), severe traumatic brain injury (OR, 2.10; p < .001), and very severe injury (OR, 2.22; p < .001). White patients had the highest odds of release to an ACF, regardless of insurance status (OR range, 2.17–2.80; p < .001). Black patients on Medicare (OR, 3.31; p < .001) or who self-paid (OR, 2.05; p < .001) were more likely than others to be discharged home. The racial and ethnic disparities in discharge patterns were apparent regardless of age, injury severity, or geographic location.

The authors noted that more research is needed to confirm or refute the findings and to explore reasons for the disparities. (Also see related commentary by Albert Y. Wu, MD, PhD, and Anne Xuan-Lan Nguyen, in the same issue.)

Cost Utility of Bevacizumab Versus Aflibercept for RVO-Related Macular Edema
June 2023

Using a Markov process and a microsimulation cohort of patients with characteristics similar to those of SCORE2 participants, Kymes et al. conducted a cost-utility comparison of bevacizumab and aflibercept for treatment of macular edema (ME) caused by retinal vein occlusion (RVO). For the first year of treatment, they found that the costs of aflibercept exceeded those of bevacizumab by more than $18,000.

The simulated cohort included 5,000 patients who were evaluated 100 times, each with a different set of demographic and clinical characteristics, which were selected randomly and were based on the SCORE2 trial. Cohort members had a diagnosis of ME caused by central or hemiretinal RVO. The authors chose utility as the quality-of-life parameter because of its value in quantifying patients’ perceptions of the importance of functional limitations. Data were collected for a five-year period (through October 2019) and were analyzed subsequently. Incremental cost-utility data were compared for bevacizumab and aflibercept, each as first-line treatment.
According to the analysis, the cost of treatment for the first year was $18,127 higher with aflibercept. For the same period, the gain in quality-adjusted life-years was .026 with bevacizumab and .020 with aflibercept. Given these findings and the similar clinical efficacy of the two drugs, bevacizumab appeared to have superior cost utility. At the current prices, aflibercept would be considered more cost-effective than bevacizumab only if it could achieve nearly perfect vision for the patient.

The authors acknowledged that some patients with RVO-related ME may derive a greater benefit from initial treatment with aflibercept as opposed to bevacizumab. To better understand the optimal use of these drugs for this condition, the authors suggest including anatomic as well as patient-centered outcomes in future research. (Also see related commentary by Sean T. Berkowitz, MD, MBA, and Avni P. Finn, MD, MBA, in the same issue.)

Other Journals
Selected by Prem S. Subramanian, MD, PhD

Macular Perfusion and Neuronal Loss in TBI
*Investigative Ophthalmology & Visual Science*
2023;64(4):35

Traumatic brain injury (TBI) may cause structural and functional damage to the visual system, with retinal ganglion cell (RGC) degeneration often occurring in the absence of vision-related symptoms. This degeneration correlates with diminished retinal blood flow, but whether the perfusion reductions precede or follow neurodegeneration has been unclear. To learn more, Hepschke et al. analyzed ophthalmic data for patients with TBI, hypothesizing that perfusion reductions would precede and predict neurodegeneration. Instead, they found that in patients with reduced visual function after TBI, macular perfusion remained normal until the ganglion cell layer (GCL) thinned—indicating that the perfusion changes are secondary to local GCL loss.

Included in this prospective single-center case series were patients admitted to the hospital after acute TBI (moderate or severe) who underwent early ophthalmic examinations, including OCT and OCT angiography. The exams were conducted within 14 days of injury, as well as two to six months later. Measurements included thickness of the GCL and density of the superficial vascularplexus (SVP) and intermediate capillary plexus. Only patients with complete datasets for both eyes were included. Excluded from the analysis were patients who had any direct penetrating or nonpenetrating injury to the eye, those with a pre-existing pathology of the retina or optic nerve, and patients who were unable to cooperate for the exams.

Twenty-one adults met the inclusion criteria (mean age, 38 years). At initial examination, macular structure and perfusion were normal in all patients. At this point, visual function was abnormal for three patients; the observed neurodegeneration and loss of perfusion in these patients coincided with the visual function deficits. At the follow-up visit, nine of the 21 patients had reduced macular GCL thickness. Perfusion in the SVP correlated strongly with local GCL thickness; the sum of vessel density was the metric with the strongest association (p < .0001).

Per the authors, this is the largest published study of patients with moderate or severe TBI that includes comprehensive ophthalmic data. “We have shown for the first time that macular SVP retinal perfusion after anterior visual pathway damage reduces in proportion to the structural loss of macular RGC, rather than directly in response to injury,” said the authors. They emphasized that this can occur independently of detectable changes in visual function.

**XEN 45 Gel Stent: Long-Term Effectiveness**
*Clinical Ophthalmology*
2023;17:1223-1232

Marcos-Parra et al. reviewed three-year data to analyze the safety and effectiveness of the XEN 45 Gel Stent (Allergan), with or without concomitant phacoemulsification (phaco), for reducing IOP and medication burden in patients with open-angle glaucoma (OAG). In both surgical groups, these parameters were reduced significantly, and the safety profile was good. After the first post-op week, there was no significant difference in the IOP-lowering effect of XEN-solo and XEN-phaco.

This single-center study involved patients with OAG who received the XEN 45 stent alone or in conjunction with cataract surgery. The same surgeon performed the implantations while the patients were under local anesthesia. The stent was placed in the superior nasal quadrant using a standard anterior segment technique. During the procedure, a 27-gauge needle was used to inject 0.1 mL of mitomycin C (0.01%) subconjunctivally, under the Tenon capsule. The main outcome measure was the mean change in IOP from baseline to 36 months posttreatment for XEN-solo and XEN-phaco. Secondary end points included the mean change in number of glaucoma medications and the incidence of adverse events.

Among the 154 eyes included in the analysis, 37 (24%) received XEN-solo and 117 (76%) underwent XEN-phaco. Overall, the mean IOP was lowered from 19.1 ± 5.0 mm Hg at baseline to 14.9 ± 3.8 mm Hg at month 36 (p < .0001). In the XEN-solo and XEN-phaco groups, IOP was reduced from 21.2 ± 6.2 mm Hg and 18.4 ± 4.3 mm Hg, respectively, to 14.3 ± 4.0 mm Hg (p < .0004) and 15.2 ± 3.7 mm Hg, respectively (p = .0009). The overall number of glaucoma medications was reduced from 2.1 ± 0.8 to 0.2 ± 0.6 (p < .0001).

Thirty-six eyes (23.4%) required a needling procedure, and 33 (21.4%) experienced bleb fibrosis; these were the most common complications. The frequency of surgical revision was significantly greater in the XEN-solo group.

The authors concluded that the XEN 45 implant lowers IOP and decreases medication burden long term, whether used by itself or with cataract surgery. They noted that some doubts remain, including the cost-effectiveness of this procedure and the influence of different concentrations of mitomycin C on clinical outcomes.