A PUBLICATION BY REVIEW of OPHTHALMOLOGY

RETINA SPECIALIST

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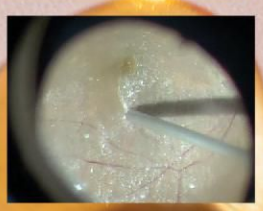
Do *vitamins* have an *effect* on *GA?*

The latest research shows potential for slowing progression - **Page 16**

Also Inside

Online Video



- *A new approach to managing lamellar hole- associated epiretinal proliferation* – **Page 12**

Ken is a real patient with GA, and Dr. Arshad Khanani is his retina specialist who treats his GA with IZERVAY.

Moments like this deserve your protection.

Ken loves to golf—Dr. Khanani loves to keep him golfing for longer.

Dr. Arshad Khanani is a compensated physician.

INDICATION

IZERVAY™ (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

- Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

References: 1. Holz FG, Strauss EC, Schmitz-Valckenberg S, van Lookeren Campagne M. Geographic atrophy: clinical features and potential therapeutic approaches. *Ophthalmology*. 2014;121(5):1079-1091. **2.** Izervay. Package insert. Northbrook, IL: Astellas Pharma US, Inc.; 2025. **3.** Syfovre. Package insert. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2025. **4.** Astellas Pharma US, Inc. Izervay. Data on File.

Protect healthy retinal cells for longer with IZERVAY[1,2]

Only IZERVAY showed efficacy at one year in two Phase 3 trials[2,3]

In 2 clinical trials of 624 people, IZERVAY was proven to reduce the annualized rate of GA lesion growth by 18%-35% in one year compared to those who were not treated.[2]

Demonstrated safety through 2 years in the GATHER trials[2]

Consistent real-world safety across more than 400k vials distributed.[2,4*]

izervay™ (avacincaptad pegol intravitreal solution) 2 mg

Treat GA to help preserve vision for longer[1,2]

Scan to explore IZERVAY:
The #1 prescribed FDA-approved treatment for new GA patients[4†]

*As of 08/25. Based on samples and commercially distributed vials.
†Based on Symphony data from 3/24-7/25. May not represent entire population.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Neovascular AMD

- In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

Increase in Intraocular Pressure

- Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration.

Please see Brief Summary of Prescribing Information for IZERVAY on the following page.

MAT-US-IZE-2025-00719 11/25

astellas

IZERVAY™ (avacincaptad pegol intravitreal solution)
Rx only
Brief Summary: This information is not comprehensive. Visit IZERVAYecp.com to obtain the FDA-approved product labeling or call 800-707-4479.

1 INDICATIONS AND USAGE
IZERVAY is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

2 DOSAGE AND ADMINISTRATION
2.1 General Dosing Information
IZERVAY must be administered by a qualified physician.
2.2 Recommended Dosage
The recommended dose for IZERVAY is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days).

4 CONTRAINDICATIONS
4.1 Ocular or Periocular Infections
IZERVAY is contraindicated in patients with ocular or periocular infections.
4.2 Active Intraocular Inflammation
IZERVAY is contraindicated in patients with active intraocular inflammation.

5 WARNINGS AND PRECAUTIONS
5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.
5.2 Neovascular AMD
In the GATHER1 and GATHER2 clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.
5.3 Increase in Intraocular Pressure
Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

6 ADVERSE REACTIONS
The following potentially serious adverse reactions are described elsewhere in the labeling:

- Ocular and periocular infections
- Active intraocular inflammation
- Endophthalmitis and retinal detachments
- Neovascular AMD
- Increase in intraocular pressure

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
The safety of avacincaptad pegol was evaluated in 733 patients with AMD in two sham-controlled studies (GATHER1 and GATHER2). Of these patients, 292 were treated with intravitreal IZERVAY 2 mg (0.1 mL of 20 mg/mL solution). Three hundred thirty-two (332) patients were assigned to sham.
Adverse reactions reported in ≥2% of patients who received treatment with IZERVAY pooled across GATHER1 and GATHER2, are listed below in Table 1.

Table 1: Common Ocular Adverse Reactions (≥2%) and greater than Sham in Study Eye

Adverse Drug Reactions	IZERVAY N=292	Sham N=332
Conjunctival hemorrhage	13%	9%
Increased IOP	9%	1%
Blurred Vision*	8%	5%
Choroidal neovascularization	7%	4%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

* Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy Risk Summary
There are no adequate and well-controlled studies of IZERVAY administration in pregnant women. The use of IZERVAY may be considered following an assessment of the risks and benefits.
Administration of avacincaptad pegol to pregnant rats and rabbits throughout the period of organogenesis resulted in no evidence of adverse effects to the fetus or pregnant female at intravenous (IV) doses 5.5 times and 3.4 times the human exposure, respectively, based on Area Under the Curve (AUC), following a single 2 mg intravitreal (IVT) dose (see Data).
In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15%-20%, respectively.
Animal Data
An embryo fetal developmental toxicity study was conducted with pregnant rats. Pregnant rats received daily IV injections of avacincaptad pegol from day 6 to day 17 of gestation at 0.1, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. An increase in the incidence of a non-adverse skeletal variation, described as short thoracolumbar (ossification site without distal cartilage) supernumerary ribs, was observed at all doses evaluated. The clinical relevance of this finding is unknown. Plasma exposures at the high dose were 5.5 times the human AUC of 999 ng·day/mL (23976 ng·hr/mL) following a single 2 mg IVT dose.
An embryo fetal developmental toxicity study was conducted with pregnant rabbits. Pregnant rabbits received daily IV injections of avacincaptad pegol from day 7 to day 19 of gestation at 0.12, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. Plasma exposure in pregnant rabbits at the highest dose of 1.2 mg/kg/day was 3.4 times the human AUC of 999 ng·day/mL (23976 ng·hr/mL) following a single 2 mg IVT dose.
8.2 Lactation
There is no information regarding the presence of avacincaptad pegol in human milk, or the effects of the drug on the breastfed infant or on milk production. Many drugs are transferred in human milk with the potential for absorption and adverse reactions in the breastfed child. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IZERVAY and any potential adverse effects on the breastfed infant from IZERVAY.
8.4 Pediatric Use
Safety and effectiveness of IZERVAY in pediatric patients have not been established.
8.5 Geriatric Use
Of the total number of patients who received IZERVAY in the two clinical trials, 90% (263/292) were ≥65 years and 61% (178/292) were ≥75 years of age. No significant differences in efficacy or safety of avacincaptad pegol were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

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EDITORIAL

By Jason Hsu, MD

Novel tech: A self-contained implantable biofactory

Recently, revakinagene taroretcel-lwey (Encelto, Neurotech) was FDA-approved as the first-ever treatment for slowing the progression of macular telangiectasia type 2 (Mac Tel). The device contains genetically modified cells that release ciliary neurotrophic factor. With any new therapy comes a myriad of questions and concerns. Some have likened Encelto to the complement inhibitors for geographic atrophy, as both slow down progression but don't reverse it. The rate of ellipsoid zone loss with Encelto was more favorable, ranging from 31 to 55 percent over 24 months in two parallel Phase III trials, compared to around 20 percent with the complement inhibitors.[1] However, neither therapy has demonstrated definitive functional vision preservation. Encelto showed significant reductions in retinal sensitivity loss in one of the two Phase III trials. Otherwise, visual acuity, reading speed and visual function questionnaires were similar between the treated and sham groups.

The other concern that has been voiced is that Mac Tel is slowly progressive and few patients complain of any deficits. I agree many patients fall into this category, but in speaking to some in more detail, I realize that many are just doing their best to adapt to their slowly changing reality. The majority of my patients have been referred in because they were noticing difficulties with vision in one eye. While we bank on the other eye carrying them through, what if it, too, goes down the tubes? We've then lost our opportunity to save vision.

Finally, there's the surgical aspect that we must consider, including the risks involved and, ultimately, cost. The data seems to be showing better efficacy with earlier treatment, but is it risky to put this into someone's better-seeing eye, especially if the patients who really want it are the ones who have already lost significant central vision in the first eye? While the device seemed to have low rates of adverse events, there are still the usual risks of surgery. It's also important to consider the issues with miosis and dark adaptation which are related to the release of CNTF. On the flip side, this can be a one-and-done procedure, unlike complement inhibitors that require repeated intravitreal injections. Compared to gene therapy where there's no kill switch, the device can be removed if there are adverse reactions.

We're in an exciting time with new treatment options becoming available for both established and new indications. It's great to be able to offer something now for our Mac Tel patients. While it won't be for everyone, my sense is that some patients could see a lot of potential upside in being able to slow down the disease.

REFERENCE

1. Chew EY, Gillies M, Jaffe GJ, et al. Cell-based ciliary neurotrophic factor therapy for macular telangiectasia type 2. NEJM Evid 2025;4:8:EVIDoa2400481.

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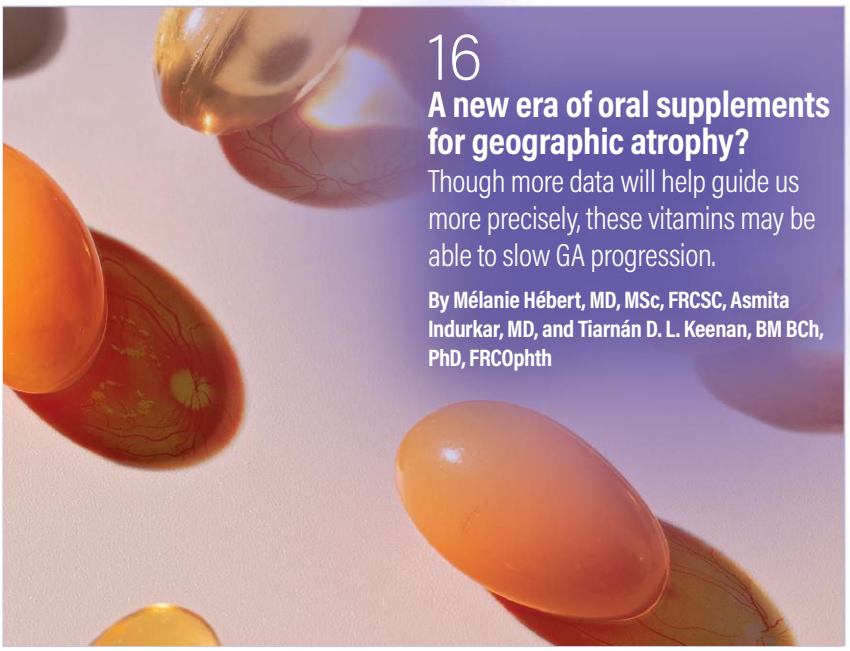
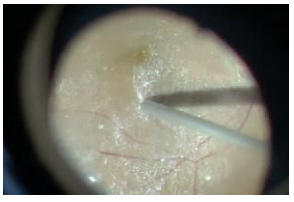
FEATURES



DEPARTMENTS



The **first and only** FDA-approved treatment for adults with idiopathic macular telangiectasia type 2 (MacTel)[1]

ENCELTO™

(revakinagene taroretcel-lwey)

implant, for intravitreal use

Proven to **slow disease progression** in two phase 3 studies[1,2]*

*Based on two phase 3, randomized, multicenter, sham-controlled studies (Study A and Study B). Both studies evaluated the rate of ellipsoid zone (EZ) area loss (macular photoreceptor loss) in 228 adults with MacTel type 2 over 24 months. Results for ENCELTO: 54.8% reduction in retinal degeneration in Study A (P<0.0001); 30.6% reduction in Study B (P=0.0186).[1,2]

The permanent J-code for ENCELTO is now available: J3403

Scan the QR code for more information about accessing ENCELTO

INDICATIONS AND USAGE

ENCELTO is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENCELTO is contraindicated in patients with active or suspected ocular or periocular infections, and in patients with known hypersensitivity to Endothelial Serum Free Media (Endo-SFM).

WARNINGS AND PRECAUTIONS

ENCELTO implantation surgery and/or implantation related procedures have been associated with the following:

Severe Vision Loss

Severe vision loss defined as three or more lines of visual acuity loss [≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters] has occurred following ENCELTO implantation. Monitor patients for signs and symptoms of vision loss and manage as clinically indicated.

Infectious Endophthalmitis

Infectious endophthalmitis may occur following ENCELTO implantation. Signs and symptoms of infectious endophthalmitis include progressively worsening eye pain, vision loss, or scleral and conjunctival injection. To mitigate the risk of endophthalmitis, use proper aseptic surgical technique for ENCELTO implantation. Monitor patients for signs or symptoms of infectious endophthalmitis. Remove ENCELTO implant if infectious endophthalmitis occurs and manage symptoms according to clinical practice.

Retinal Tear and Detachment

Retinal tears and retinal detachment may occur following ENCELTO implantation. Signs and symptoms of retinal tears include acute onset of flashing lights, floaters, and/or loss of visual acuity. Signs and symptoms of retinal detachment may include progressive visual field loss and/or loss of visual acuity. Use standard vitreoretinal surgical techniques during ENCELTO implantation to minimize the risk of retinal tears and retinal detachment. Monitor for any signs or symptoms of retinal tear and/or retinal detachment. Treat rhegmatogenous retinal detachment and retinal tears promptly. Remove ENCELTO implant, if vitrectomy with a complete gas fill or silicone oil fill is required.

Vitreous Hemorrhage

Vitreous hemorrhage, which may result in temporary vision loss, has occurred following ENCELTO implantation. Patients receiving antithrombotic medication (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous hemorrhage. To reduce the risk of vitreous hemorrhage, interrupt antithrombotic medications prior to the ENCELTO implantation. Vitrectomy surgery may be necessary to clear severe, recurrent, or non-clearing vitreous hemorrhage. If the patient has a late onset vitreous hemorrhage (greater than one year following ENCELTO implantation surgery), examine the ENCELTO implantation site for possible implant extrusion. If implant extrusion has occurred, surgically reposition ENCELTO.

Implant Extrusion

Implant extrusion through the initial scleral wound has occurred following ENCELTO implantation. Signs and symptoms of implant extrusion include recurrent uveitis, vitreous hemorrhage, eye pain more than one year after implantation, or visibility of titanium fixation loop under the conjunctiva. To reduce the risk of implant extrusion, carefully follow the specific surgical steps for ENCELTO implantation.

Evaluate patients after 6 months to confirm proper positioning of ENCELTO and then annually. If ENCELTO begins to extrude, surgically reposition ENCELTO to a proper scleral wound depth either in the same site or in the opposing inferior quadrant of the vitreous cavity.

Cataract Formation

Cataract formation, including cataract cortical, cataract nuclear, cataract subcapsular, cataract traumatic, and lenticular opacities, has occurred following ENCELTO implantation. To reduce the risk of ENCELTO-related cataract formation or progression, carefully follow the specific surgical steps for ENCELTO implantation.

Suture Related Complications

Suture related complications, including conjunctival erosions due to suture tips and suture knots, have occurred following ENCELTO implantation.

To mitigate the risk of suture related complications, carefully follow the specific surgical steps for ENCELTO implantation and manage suture-related complications as clinically indicated.

Delayed Dark Adaptation

Delayed Dark Adaptation, a delay in the ability to adjust vision from a bright lighting condition to a dim lighting, has occurred following ENCELTO administration which remained unchanged for the duration of study follow up. Advise patients to take caution while driving and navigating in the dark.

ADVERSE REACTIONS

The most common adverse reactions (≥2%) reported with ENCELTO were conjunctival hemorrhage, delayed dark adaptation, foreign body sensation, eye pain, suture related complications, miosis, conjunctival hyperemia, eye pruritus, ocular discomfort, vitreous hemorrhage, blurred vision, headache, dry eye, eye irritation, cataract progression or formation, vitreous floaters, severe vision loss, eye discharge, anterior chamber cell, iridocyclitis.

Please see Brief Summary of full Prescribing Information on adjacent pages.

References: 1. ENCELTO [prescribing information]. Cumberland, RI. Neurotech Pharmaceuticals, Inc. **2.** Data on file. Neurotech Pharmaceuticals, Inc. Cumberland, RI.

neurotech

BRIEF SUMMARY OF PRESCRIBING INFORMATION
This Brief Summary does not include all of the information needed to use ENCELTO™ safely and effectively.
See full Prescribing Information for ENCELTO.

ENCELTO (revakinagene taroretcel-lwey) implant, for intravitreal use

Initial U.S. Approval: 2025

INDICATIONS AND USAGE

ENCELTO is indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

DOSAGE AND ADMINISTRATION

Recommended Dose

For intravitreal implantation only

- ENCELTO is administered by a single surgical intravitreal procedure performed by a qualified ophthalmologist.
- The recommended dose is one ENCELTO implant per affected eye. Each ENCELTO implant contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF) (NTC-201-6A cell line), a neurotrophic factor.

CONTRAINDICATIONS

ENCELTO is contraindicated in patients with:

- Active or suspected ocular or periocular infections.
- Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

WARNINGS AND PRECAUTIONS

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Severe vision loss defined as three or more lines of visual acuity loss [≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters] has occurred following ENCELTO implantation. Monitor patients for signs and symptoms of vision loss and manage as clinically indicated.

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Vitreous hemorrhage, which may result in temporary vision loss, has occurred following ENCELTO implantation. Patients receiving antithrombotic medication (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous hemorrhage. To reduce the risk of vitreous hemorrhage, interrupt antithrombotic medications prior to the ENCELTO implantation. Vitrectomy surgery may be necessary to clear severe, recurrent, or non-clearing vitreous hemorrhage. If the patient has a late onset vitreous hemorrhage (greater than one year following ENCELTO implantation surgery), examine the ENCELTO implantation site for possible implant extrusion. If implant extrusion has occurred, surgically reposition ENCELTO.

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Evaluate patients after 6 months to confirm proper positioning of ENCELTO and then annually. If ENCELTO begins to extrude, surgically reposition ENCELTO to a proper scleral wound depth either in the same site or in the opposing inferior quadrant of the vitreous cavity.

Cataract Formation

Cataract formation, including cataract cortical, cataract nuclear, cataract subcapsular, cataract traumatic, and lenticular opacities, has occurred following ENCELTO implantation. To reduce the risk of ENCELTO-related cataract formation or progression, carefully follow the specific surgical steps for ENCELTO implantation.

Suture Related Complications

Suture related complications, including conjunctival erosions due to suture tips and suture knots, have occurred following ENCELTO implantation.

To mitigate the risk of suture related complications, carefully follow the specific surgical steps for ENCELTO implantation and manage suture-related complications as clinically indicated.

Delayed Dark Adaptation

Delayed Dark Adaptation, a delay in the ability to adjust vision from a bright lighting condition to a dim lighting, has occurred following ENCELTO administration which remained unchanged for the duration of study follow up. Advise patients to take caution while driving and navigating in the dark.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

ADVERSE REACTIONS (cont'd)

Clinical Trials Experience (cont'd)

The safety data described in this section reflects exposure to ENCELTO in two clinical trials, Study 1 (NTMT-03-A) and Study 2 (NTMT-03-B) and are pooled for analysis. A total of 117 patients received ENCELTO, and 111 patients underwent a sham procedure and were followed for a duration of 24 months.

Serious adverse reactions occurred in six patients (5%) including suture related complications (n=5) and implant extrusion (n=1).

Table 1 lists the most common adverse reactions that occurred in ≥2% patients and with higher frequency in ENCELTO group compared to Sham group in Study 1 and Study 2.

Table 1. Adverse Reactions occurring in ≥2% of Patients and with higher frequency in ENCELTO group compared to Sham group in ENCELTO studies*

Adverse Reactions	ENCELTO (N=117) n (%)	Sham (N=111) n (%)
Conjunctival hemorrhage	36 (31)	29 (26)
Delayed dark adaptation	27 (23.1)	1 (1)
Foreign body sensation in eyes	18 (15)	15 (13.5)
Eye pain	18 (15)	10 (9)
Suture related complication**	18 (15.4)	3 (2.7)
Miosis	18 (15.4)	0 (0.0)
Conjunctival hyperemia	13 (11)	9 (8)
Eye pruritus	10 (9)	4 (3.6)
Ocular discomfort	10 (9)	1 (1)
Vitreous hemorrhage	10 (8.5)	0 (0.0)
Vision blurred	8 (7)	4 (4)
Headache	8 (7)	1 (1)
Dry eye	7 (6)	2 (2)
Eye irritation	6 (5.1)	2 (2)
Cumulative cataract incidence	6 (5)	0 (0)
Vitreous floaters	6 (5)	0 (0.0)
Severe visual loss>15 letters***	4 (3)	0 (0)
Eye discharge	4 (3.4)	1 (0.9)
Anterior chamber cell	4 (3.4)	0 (0.0)
Iridocyclitis	3 (2.6)	0 (0)

*Pooled data from Study 1 and Study 2; Adverse reaction rates were comparable between the two studies

**Suture related complications include exposed suture, foreign body sensation, conjunctival wound dehiscence, painful sutures, suture irritation, suture granuloma, scleral wound opening, and itchy suture

***Includes one case of visual loss due to cataract formation which remained unresolved at the end of the study

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no data on the use of ENCELTO in pregnant women. Endogenous CNTF is naturally found in maternal plasma, placental cells, and umbilical cord blood. It is not known if the use of ENCELTO increases CNTF above naturally occurring levels in these tissues.

In animal reproduction studies, subcutaneous administration of rhCNTF to pregnant rats and rabbits demonstrated no evidence of teratogenic effects on the fetus. However, when administered to rabbits at a dose level of 10ug/kg/day, a decrease in implantations and live fetuses was observed. When administered to rats at a dose level of 100ug/kg/day a decrease in corpora lutea was observed.

The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Data

Animal Data

See *Risk Summary* for details on data.

Lactation

Risk Summary

There is no data on the presence of ENCELTO in human milk, its effects on the breastfed infant, or its impact on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ENCELTO and any potential adverse effects on the breastfed infant from rhCNTF or from the underlying maternal condition.

Pediatric Use

The safety and effectiveness of ENCELTO have not been established in pediatric patients.

Geriatric Use

There were 38 patients (32%) 65 years of age and older and two patients (1%) 75 years of age and older in Study 1 and Study 2 who received ENCELTO. Clinical studies of ENCELTO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

Manufactured for:
Neurotech Pharmaceuticals, Inc.
Cumberland, RI 02864

ENCELTO™ (revakinagene taroretcel-lwey) implant, for intravitreal use | neurotech

US-EO-PM-250200024 04/2025

A routine case of AMD or something more?

An older woman presents with nyctalopia and findings atypical of AMD, prompting genetic testing.

By Dany Hage MD, Jennifer R. Chao, MD, PhD, and Alyssa C. Bonnell, MD

Dany Hage MD

Jennifer R. Chao, MD, PhD

Alyssa C. Bonnell MD

A 60-year-old woman was referred for evaluation of macular drusen. The patient reported she was diagnosed with nonexudative age-related macular degeneration four years prior to presentation. On questioning, she reported progressive nyctalopia but denied other visual changes, including metamorphopsia.

Examination findings

Best-corrected visual acuity of the right eye was 20/50 and left eye was 20/20. Intraocular pressures were normal in both eyes. Pupils were equal, round and reactive without a relative afferent pupillary defect.

Slit lamp biomicroscopy was unremarkable in both eyes. Dilated fundoscopic examination in both eyes revealed few macular drusen and retinal pigment epithelial mottling. There was mild vascular attenuation. There were few drusen in the periphery *(Figure 1A and 1B)*.

Work up

Fundus autofluorescence demonstrated hyper- and hypoautofluorescent changes throughout the posterior pole and mid-periphery *(Figure 1C and 1D)*. Optical coherence tomography was notable for scattered sub-RPE deposits in both eyes *(Figure 2)*. On comparison with imaging obtained four years prior to presentation to our service, there was mild blunting of the foveal contour in the right eye and progression of the sub-RPE deposits in both eyes *(Figure 2B and 2D)*. Neither eye developed cystoid macular edema, subretinal fluid or hemorrhage.

Diagnosis

We observed that the pattern of macular drusen and fundus autofluorescence was slightly atypical for AMD. A few of the mid-peripheral autofluorescent changes had an irregular pisciform fleck-like appearance. These examination findings, coupled with the patient's report of progressive nyctalopia, prompted consideration of a macular dystrophy. The patient was subsequently referred for genetic testing.

Genetic testing revealed two variants in the *ABCA4* gene. Mutations in this gene are associated with Stargardt disease. The first variant was a known pathogenic splice-site variant, c.4253+43G>A, that has been identified as a hypomorphic allele.[1] The second variant was a likely pathogenic missense variant, c.2965G>A, p.(Val989Ile). Further genetic testing of her children revealed that her two variants were inherited separately and in *trans* configuration. When considering the correlation between genotype and phenotype, patients with hypomorphic and missense mutations are often found to have a milder form of Stargardt disease. Therefore, these genetic findings may explain why the patient presented with a later age of onset and a milder form of the disease than is typically seen. Ultimately, the patient was diagnosed with late-onset Stargardt disease.

Management

There's currently no treatment available to reverse the effects of Stargardt disease. However, understanding the etiology of the patient's macular degeneration has allowed us to recommend that the patient limit vitamin A supplementation, which is known to be associated with Stargardt disease progression. Another benefit of this diagnosis is that she may now be eligible for ongoing and upcoming clinical trials.

Discussion

Stargardt disease is the most common inherited juvenile macular dystrophy in the United States.[2,3] It has an estimated prevalence of 1 in 10,000 and displays an autosomal recessive mode of inheritance.[3] There is a variable age of onset among

BIOS

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tients; however, it classically presents in childhood or early adulthood.[3] Less commonly, late-onset Stargardt, as seen in our case, can develop in late adulthood and often has a better visual prognosis with sparing of the fovea in many cases.[3]

Stargardt disease (STGD1) is caused by mutations in the *ABCA4* gene, which encodes an ATP-binding cassette transporter that's expressed in the outer segment of photoreceptors and in low concentrations throughout the RPE.[4,5] The transporter is involved in clearing toxic byproducts of retinoid metabolism; therefore, dysfunction of the transporter leads to the accumulation of bisretinoids and A2E, which in turn causes dysfunction of the RPE, deposition of fluorescent lipofuscin and photoreceptor death.[4,5]

The classic presentation of Stargardt disease includes progressive loss of central vision, decreased color vision and slowed dark adaptation. Fundus examination may appear normal early in the disease course. However, over time, yellow pisciform flecks of lipofuscin deposition can be seen throughout the posterior pole and mid-periphery, as well as pigmentary mottling and macular atrophy.[6]

Similarly, patients with AMD often experience loss of central vision, metamorphopsia and decreased color and contrast sensitivity.[7] The hallmarks of AMD include drusen and pigmentary changes throughout the macula, as well as geographic atrophy in the later stages of the disease.[7] While the pathogenesis of AMD is multifactorial, dysfunction of the RPE and choroid ultimately leads to photoreceptor degeneration and central vision loss.[8]

Catherina H.Z. Li, MD, and colleagues recently analyzed 71 patients in the Netherlands with late-onset Stargardt disease.[9] They found that the median age was 55 years; the most frequent allele was c.5603A→T (p.Asn1868Ile); and that none

(Continued on page 14)

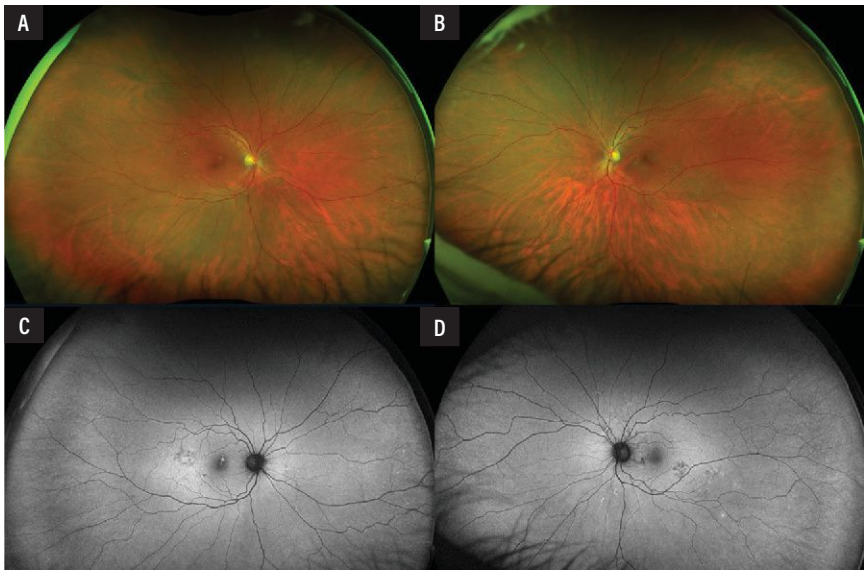


Figure 1. Optos pseudocolor fundus photography of the right and left eyes demonstrating drusen around the central and temporal macula, and throughout the periphery (A, B). Vessels appear mildly attenuated. Fundus autofluorescence of the right and left eyes demonstrating hyper- and hypoautofluorescent changes throughout the macula and mid-periphery (C, D).

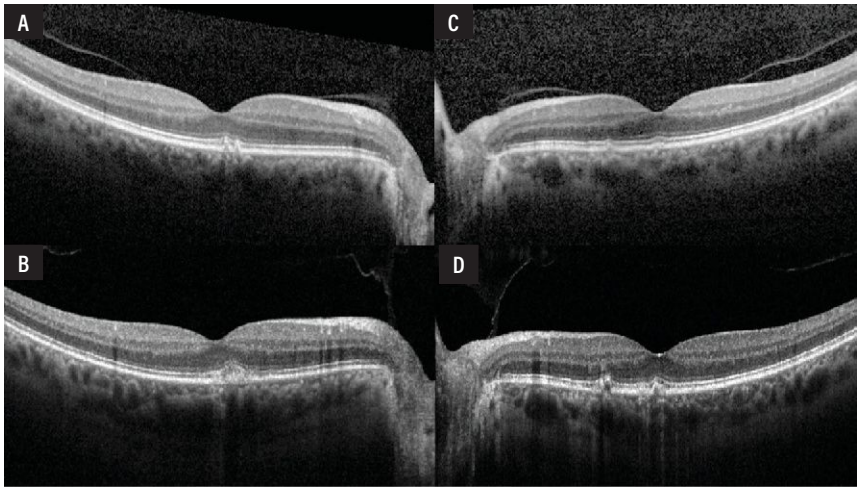


Figure 2. Optical coherence tomography of the right and left eyes on initial evaluation when she was first diagnosed with AMD (A, B), compared to the first presentation to our service four years later (C, D). There are sub-RPE deposits in both eyes with evidence of progression over time. In the right eye there is mild blunting of the foveal contour (C). There is no cystoid macular edema, subretinal fluid or hemorrhage in either eye.

LHEP embedding with a backflush needle

Surgeons describe a new twist on an old procedure that may offer new benefits.

Masaki Fukushima, MD and Kotaro Tsuboi, MD, PhD

Masaki Fukushima, MD

Kotaro Tsuboi, MD, PhD

The concept of lamellar macular hole was first reported by Gass et al. in 1976.[1] Subsequently, OCT illustrated that a thick proliferative tissue often accompanies LMH on the macula, which was named lamellar hole-associated epiretinal proliferation. In eyes with LMH, removing LHEP doesn't necessarily result in improved postoperative vision and a full-thickness macular hole is sometimes developed postoperatively.

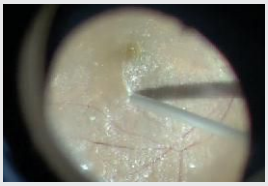
Dr. Fumio Shiraga reported that embedding LHEP into the hole achieved favorable outcomes.[2] In the original method, LHEP is peeled from the ILM using microforceps and embedded into the hole while keeping it attached to the edge of the hole. This technique requires precise handling of the microforceps. If the LHEP is gripped too deeply, it may damage the underlying sensory retina or ILM, potentially causing scotomas. Additionally, LHEP is sticky and may adhere strongly to the microforceps' tips, leading to unintentional removal from the hole's edge.

Here, we describe a new method we've developed that uses a backflush needle instead of the forceps to achieve successful LHEP embedding.[3]

View the Video

Drs. Fukushima and Tsuboi demonstrate their embedding technique using a backflush needle.

Go to https://vimeo.com/1137001573 or scan the QR code.



Surgical technique

After a core vitrectomy, we use triamcinolone acetonide to visualize a thin preretinal membrane on the macula *(Figure*

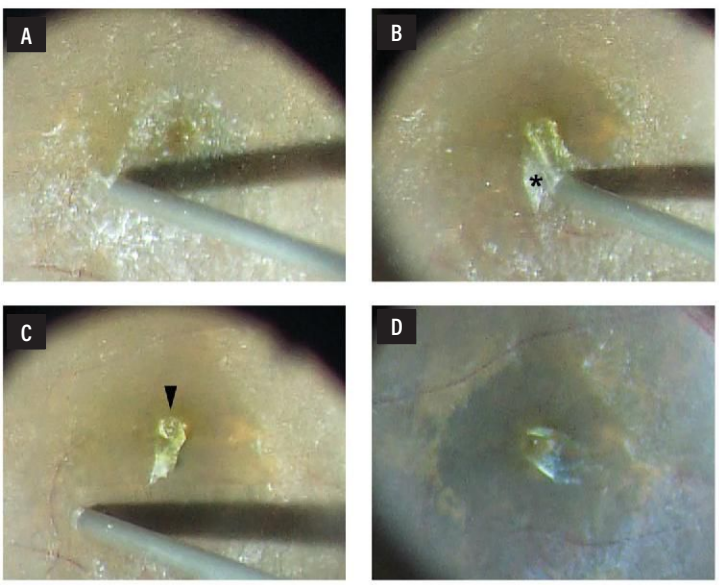


Figure 1. (A) The membrane is visualized with triamcinolone acetonide. (B) The thin preretinal membrane, a non-yellowish tissue (asterisk), is peeled centripetally using a 25-gauge disposable Shiraga backflush instrument with an extendible brush tip (D.O.R.C./Zeiss) and passive aspiration. (C) The thin preretinal membrane is selectively removed by passive aspiration, but the LHEP, which appeared as a yellowish tissue (arrowhead), remains adjacent to the hole. (D) Staining of the ILM with BBG reveals that the entire ILM is stained, suggesting that the ILM in the area of the thin preretinal membrane peeling remains intact.

BIOS

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1A), which we peeled using a silicone-tipped backflush needle with "passive" aspiration (the irrigation pressure was set to 20 mmHg). We then gently peel the thin preretinal membrane centripetally and remove it, leaving the LHEP adjacent to the hole *(Figure 1 B, C)*. Although we selectively remove the thin preretinal membrane by passive aspiration, the LHEP remains on the edge of the hole because of its strong adhesion.

We then peel the ILM using Brilliant blue G. The entire ILM is stained without any damage *(Figure 1D)*, suggesting that the ILM in the area of the thin preretinal membrane peeling remains intact. We then embed the remaining LHEP into the hole, followed by a fluid-air exchange to conclude the surgery. The technique has three advantages:

1. It simplifies the peeling process, eliminating the need for advanced microforceps skills.
2. Passive aspiration selectively removes the thin preretinal membrane while preserving the LHEP at the LMH edge.
3. The technique minimizes retinal damage, as shown by uniform internal limiting membrane staining after membrane peeling.

Important considerations

To avoid excessive aspiration near the macula, we've found it's safer to turn off IOP control in the Constellation system (Alcon), which is the device we use. Starting the peeling process about two disc diameters away from the macula and using BBG or triamcinolone for better visualization can help, though the method may not work for LMH cases with thick ERM.

Final thoughts

In summary, the LHEP embedding technique using a backflush needle offers a simpler, safer and more controlled alternative to traditional microforceps-based methods. By relying on passive aspiration to selectively peel the thin preretinal membrane while preserving and embedding the LHEP, this approach maintains ILM integrity and enhances reproducibility among surgeons. RS

REFERENCES

1. Gass JDM. Lamellar macular hole: A complication of cystoid macular edema after cataract extraction. Archives of Ophthalmology 1976;94:793-800.
2. Shiraga F, Takasu I, Fukuda K, et al. Modified vitreous surgery for symptomatic lamellar macular hole with epiretinal membrane containing macular pigment. Retina 2013;33:1263-1269.
3. Fukushima M, Hayashi A, Kusaka S, et al. Use of a backflush needle with a silicone tip cannula to embed lamellar hole-associated epiretinal proliferation. Retina 2023;43:12:2204-2207.

A routine case of AMD or something more?

(Continued from page 11)

of the patients in the study had two severe variants.[9] Most patients were found to have flecks in their fundi, foveal-sparing retinal atrophy and preserved central vision.[9] Additionally, they found that 22 percent of their patients had been previously diagnosed with AMD with geographic atrophy.[9] While exceedingly rare, late-onset Stargardt disease should remain on the differential for a patient with AMD, especially in cases with atypical fundoscopic findings or symptoms, such as progressive nyctalopia beyond what is observed with normal aging.

Multimodal imaging, including fundus photography, FAF and OCT, can be used in conjunction with fundoscopic examination to improve recognition of late-onset Stargardt. In general, flecks are often irregularly shaped, whereas drusen are round.[9] Flecks have a less prominent yellow tint, while drusen tend to be brighter; flecks are also more hyperautofluorescent on FAF.[9]

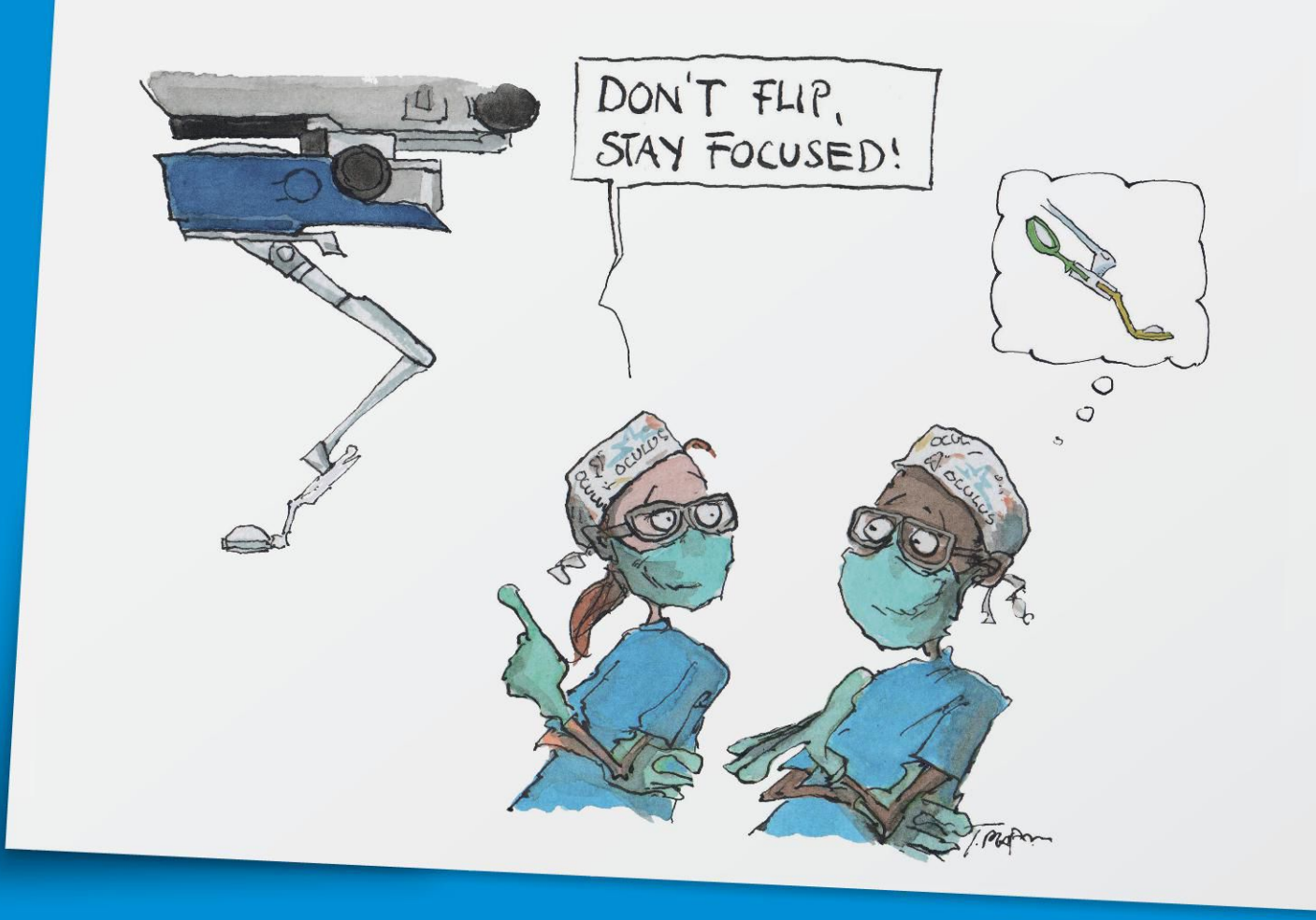
Drusen are often concentrated around the macula, as opposed to flecks, which can be found throughout the posterior pole and mid-periphery.[9] On OCT, drusen are defined as being under the RPE, while flecks may be situated within the photoreceptor layers.[9] Additionally, foveal involvement is common in AMD, whereas late-onset Stargardt tends to spare the fovea.[9]

Bottom Line

While late-onset Stargardt disease and AMD may have similar clinical presentations, it's important to distinguish between them to inform genetic and prognostic counseling, as well as to provide accurate guidance on vitamin A supplementation and eligibility for clinical trial participation. RS

REFERENCES

1. Zernant J, Lee W, Nagasaki T, et al. Extremely hypomorphic and severe deep intronic variants in the ABCA4 locus result in varying Stargardt disease phenotypes. Cold Spring Harb Mol Case Stud 2018;4:4:a002733.
2. Fujinami K, Zernant J, Chana RK, et al. Clinical and molecular characteristics of childhood-onset Stargardt disease. Ophthalmology 2015;122:2:326–34.
3. Tanna P, Strauss RW, Fujinami K, et al. Stargardt disease: Clinical features, molecular genetics, animal models and therapeutic options. Br J Ophthalmol 2017;101:1:25–30.
4. Lenis TL, Hu J, Ng SY, et al. Expression of ABCA4 in the retinal pigment epithelium and its implications for Stargardt macular degeneration. Proc Natl Acad Sci U S A 2018;115:47:E11120–E11127.
5. Allikmets R, Singh N, Sun H, et al. A photoreceptor cell-specific ATP-binding transporter gene (ABCR) is mutated in recessive Stargardt macular dystrophy. Nat Genet 1997;15:3:236–46.
6. Cremers FPM, Lee W, Collin RWJ, et al. Clinical spectrum, genetic complexity and therapeutic approaches for retinal disease caused by ABCA4 mutations. Prog Retin Eye Res 2020;79:100861.
7. Bressler SB, Do DV, Bressler NM. Age-related macular degeneration: Drusen and geographic atrophy. In: Albert DM, Miller JW, Azar DT, Blodi BA, eds. Albert and Jakobiec's Principles and Practice of Ophthalmology. 3rd ed. Philadelphia: Saunders; 2008.
8. Fleckenstein M, Schmitz-Valckenberg S, Chakravarthy U, et al. Age-related macular degeneration: A review. JAMA 2024;331:2:147–57.
9. Li CHZ, Pas JAAH, Corradi Z, et al. Study of late-onset Stargardt type 1 disease: Characteristics, genetics, and progression. Ophthalmology 2024;131:1:87–97.



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A new era of oral supplements for geographic atrophy?

Though more data will help guide us more precisely, these vitamins may be able to slow GA progression.

By Mélanie Hébert, MD, MSc, FRCSC, Asmita Indurkar, MD, Tiarnán D. L. Keenan, BM BCh, PhD, FRCOphth

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Tiarnán D. L. Keenan, BM BCh, PhD, FRCOphth

Take-home points

- Recent analyses of the AREDS1 and -2 datasets measured rates of geographic atrophy progression in each eye and related them to the randomizations in the clinical trials for robust assessment of treatment effects.
- Oral micronutrient supplementation slowed GA progression towards the central macula, likely by augmenting the natural phenomenon of foveal sparing.
- For extrafoveal GA, the AREDS2 supplements slowed the rate of progression to the fovea by approximately half; this was accompanied by supportive results according to GA area and visual acuity, particularly in relevant GA subgroups.
- Given their excellent safety profile, convenient administration and low cost, patients with extrafoveal GA may benefit from AREDS2 oral supplements.
- For slower progression, all patients with GA may also benefit from a healthy lifestyle, particularly a Mediterranean-type diet rich in vegetables and fruit, with less red meat, and avoiding cigarette smoking and heavy alcohol consumption.
- Since these were post hoc analyses, we're planning a new dedicated randomized clinical trial of oral supplementation for extrafoveal GA, as part of the AREDS3 program.

AREDS2 oral supplements are well known to decrease the risk of progression to advanced age-related macular degeneration, particularly neovascular AMD.[1-3] They're recommended by the American Academy of Ophthalmology for patients with intermediate or advanced AMD in at least one eye.[4] We hadn't previously analyzed in detail whether they might also be helpful in slowing GA enlargement. We recently had the opportunity to address this important question, with the availability of GA data from reading center grading of all AREDS1/2 participants.[5] Specifically, we calculated the GA enlargement rate for all eyes in these two large datasets with long follow-up time. Importantly, we can relate these enlargement rates to the underlying randomizations in the trials. Because of these robust randomizations, we're justified in inferring causality and treatments effects, which isn't true for observational data.

We used GA area as one outcome measure, in line with many recent clinical trials. However, for extrafoveal GA, the area metric has the problem that it treats all macular locations as equally important, whereas we know that the fovea and nearby paracentral areas are most important for visual acuity and quality of life.[6,7] We therefore used GA proximity to the foveal center-point as a second outcome measure *(Figure 1)*. For eyes with extrafoveal GA, time-to-fovea is increasingly recognized as an important metric,[8] and slower change in proximity over time can indicate greater tendency to foveal sparing. Foveal sparing is an important protective phenomenon, whereby GA expansion near and into the fovea is usually much slower than expan-

BIOS

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Disclaimer

This research was supported by the Intramural Research Program of the National Institutes of Health (NIH). The contributions of the NIH authors were made as part of their official duties as NIH federal employees, are in compliance with agency policy requirements, and are considered Works of the United States Government. However, the findings and conclusions presented in this paper are those of the authors and don't necessarily reflect the views of the NIH or the U.S. Department of Health and Human Services.

sion elsewhere, leading to beneficial GA configurations (e.g., horseshoe and donut) where the GA wraps around the fovea but doesn't involve it until much later *(Figure 1)*.[9] These configurations are usually compatible with good visual acuity.[10] Therefore, strategies to enhance foveal sparing would be very valuable, as they could keep eyes in these beneficial GA configurations for longer.

AREDS results

The AREDS randomization is shown in Figure 2A. In eyes with extrafoveal GA, for rate of progression towards the fovea, the oral antioxidant component (comprising vitamin C, vitamin E, and beta-carotene) had a significant treatment effect *(Table 1)*.[5] Participants randomly assigned to the antioxidants had a progression rate that was 36 percent slower than those randomly assigned to no antioxidants. Interestingly, no significant treatment effect was detected for area-based progression overall, although a beneficial treatment effect was present for the subgroup of eyes with early GA (particularly those with extrafoveal GA). In fact, in that subgroup of eyes with early extrafoveal GA, the rate of visual acuity decline was twice as slow in participants randomized to antioxidants vs no antioxidants. The zinc component had no significant beneficial or harmful effect for either the area or proximity outcome measure.

AREDS2 results

Almost all AREDS2 participants were also assigned to take the AREDS supplements, so AREDS2 participants with extrafoveal GA were presumably already benefiting from the antioxidant component taken by all participants. In these analyses of the AREDS2 randomization *(Figure 2B)*, we were therefore looking for any additional treatment effect. Interestingly, we saw a similar pattern of results to AREDS. In eyes with extrafoveal GA, for rate of progression towards the fovea, we did observe an additional significant treatment effect for the lutein/zeaxanthin component *(Table 2)*.[5] Participants randomly assigned to the lutein/zeaxanthin component (and to no beta-carotene) had a progression rate that was 35 percent slower than those randomly assigned to no lutein/zeaxanthin. This was accompanied by a borderline significant difference for visual acuity, with slower decline in acui-

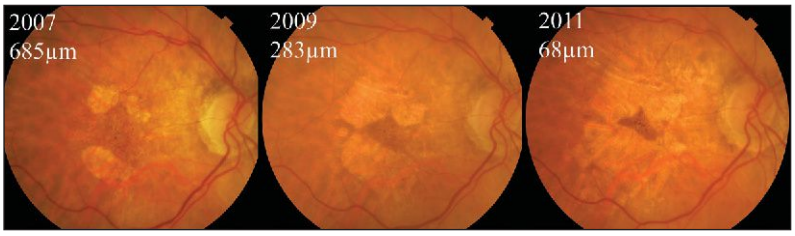

Figure 1. Color fundus photographs showing the progression of extrafoveal geographic atrophy towards the fovea over time. Geographic atrophy proximity (i.e., the shortest distance between the foveal center-point and the nearest pixel of GA) decreased gradually over time from 685 mm (2007) to 68 mm (2011). ***(This figure was published in: Keenan TDL, et al. Oral Antioxidant and Lutein/Zeaxanthin Supplements Slow Geographic Atrophy Progression to the Fovea in Age-Related Macular Degeneration. Ophthalmology 2025;132:1:14-29. Copyright Elsevier (2025))***

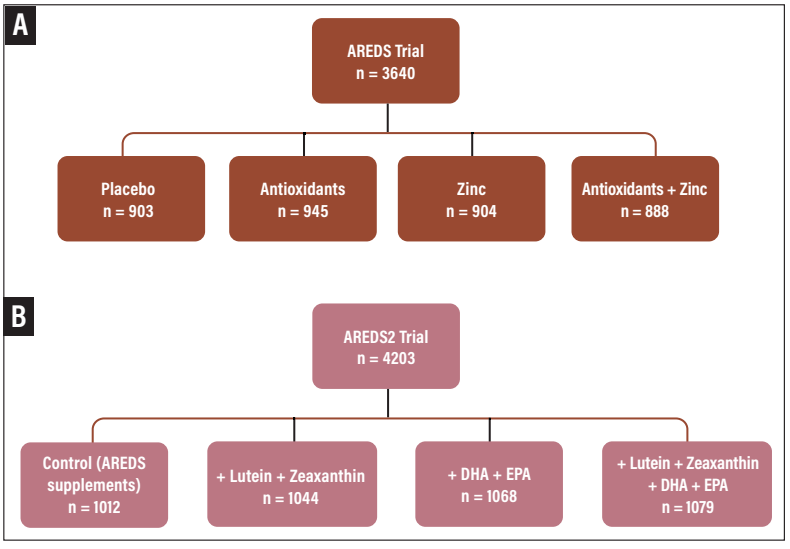

Figure 2. Randomization schemes. A) Age-Related Eye Disease Study: Participants were randomized 1:1:1:1, using a 2x2 factorial design, to oral antioxidants (vitamin C, vitamin E, and β-carotene) only, zinc only, both antioxidants and zinc, or placebo. B) AREDS2: Participants were randomized, 1:1:1:1, using a 2x2 factorial design, to oral lutein/zeaxanthin only, docosahexaenoic acid (DHA) plus eicosapentaenoic acid only, both lutein/zeaxanthin and DHA/EPA, or placebo. All participants were also offered the original AREDS formulation to take alongside the randomly assigned primary treatment.

Table 1. Geographic atrophy proximity-based progression and area-based progression in the Age-Related Eye Diseases Study (AREDS), according to randomized assignment

Randomized assignment (main effects)	Proximity-based progression rate			Area-based progression rate		
	n (eyes)	Estimate (µm/year)	P	n (eyes)	Estimate (µm/year)	P
No antioxidants	109	72.9	**0.012**	206	0.255	0.63
Antioxidants	99	50.7		186	0.261	
No zinc	87	57.9	0.28	166	0.261	0.58
Zinc	121	67.4		226	0.255	

Bold font: P-value significant at the 0.05 threshold

ty in those assigned to lutein/zeaxanthin. Again, no significant treatment effect was detected for area-based progression. The docosahexaenoic acid/eicosapentaenoic acid component had no significant beneficial or harmful effect for either the area or proximity outcome measure.

Putting together the results from both trials

The combined results suggest that the modern AREDS2 supplement (which includes the same vitamin C, vitamin E, and lutein/zeaxanthin doses) should slow GA progression towards the fovea by as much as half. Therefore, patients with extrafoveal GA should benefit from AREDS2 supplements *(Figure 3)*. The supplements may substantially slow GA expansion towards and into the fovea, presumably by enhancing foveal sparing. Together with their oral administration, high convenience, low cost and excellent safety profile, this makes the supplements an attractive option, with very few downsides. Importantly, approximately two-thirds of cases arise as extrafoveal GA,[11] so this is a common form of disease.

However, as these results come from post hoc analyses, we need to replicate them in a new dedicated trial. We're therefore planning a prospective trial of oral supplements for extrafoveal GA, as part of the AREDS3, and hope to begin enrolling participants for this in the near future. In the meantime, the results represent the only large-scale data available examining GA progression according to oral supplement use by randomization.

Biological plausibility and a unifying explanation

Multiple points support the idea of a genuine treatment effect. First, not all post hoc analyses are created equal. These results come from randomized data, so they represent a high level of evidence quality. By contrast, observational data on supple-

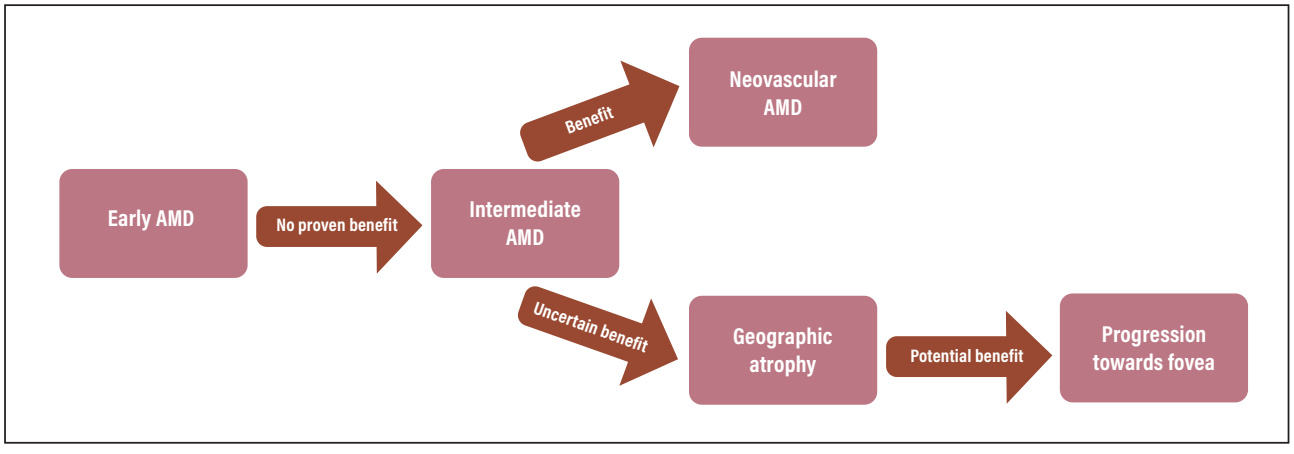

Figure 3. Diagram illustrating the potential benefits of oral micronutrient supplementation for different stages of age-related macular degeneration.

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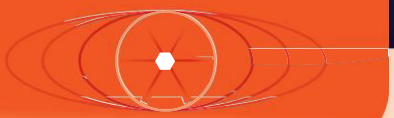

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REFERENCES: 1. TRIESENCE Prescribing Information. Harrow IP, LLC; 2023. **2.** Dyer D, Callanan D. Clinical evaluation of the safety and efficacy of preservative-free triamcinolone (Triesence® [triamcinolone acetonide injectable suspension] 40 mg/mL) for visualization during pars plana vitrectomy. *Retina*. 2009;29(1):38–45. doi:10.1097/IAE.0b013e318188c6e2. **3.** Thorne JE, Sugar EA, Holbrook JT, et al; Multicenter Uveitis Steroid Treatment Trial Research Group. Periocular triamcinolone vs intravitreal triamcinolone vs intravitreal dexamethasone implant for the treatment of uveitic macular edema: the POINT trial. *Ophthalmology*. 2019;126(2):283–295. doi:10.1016/j.ophtha.2018.08.021. **4.** Maia M, Farah ME, Belfort RN, et al. Effects of intravitreal triamcinolone acetonide injection with and without preservative. *Br J Ophthalmol*. 2007;91(9):1122–1124. doi:10.1136/bjo.2006.112466.

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- Hypersensitivity to triamcinolone or any component of this product.

DOSAGE AND ADMINISTRATION:

- Initial recommended dose for all indications except visualization: 4 mg (100 microliters of 40 mg/mL suspension) with subsequent dosage as needed over the course of treatment.
- Recommended dose for visualization: 1 to 4 mg (25 to 100 microliters of 40 mg/mL suspension) administered intravitreally.

WARNINGS AND PRECAUTIONS

- TRIESENCE® is a suspension; it should not be administered intravenously.
- Ophthalmic effects: May include cataracts, infections, and glaucoma. Monitor intraocular pressure.
- Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia: Monitor patients for these conditions and taper doses gradually.
- Infections: Increased susceptibility to new infection and increased risk of exacerbation, dissemination, or reactivation of latent infection.
- Elevated blood pressure, salt and water retention, and hypokalemia: Monitor blood pressure and sodium, and potassium serum levels.
- GI perforation: Increased risk in patients with certain GI disorders.
- Behavioral and mood disturbances: May include euphoria, insomnia, mood swings, personality changes, severe depression, and psychosis.
- Decreases in bone density: Monitor bone density in patients receiving long term corticosteroid therapy.
- Live or live attenuated vaccines: Do not administer to patients receiving immunosuppressive doses of corticosteroids.
- Negative effects on growth and development: Monitor pediatric patients on long-term corticosteroid therapy.
- Use in pregnancy: Fetal harm can occur with first trimester use.
- Weight gain: May cause increased appetite.

ADVERSE REACTIONS

- Based on a review of the available literature, the most commonly reported adverse events following ocular administration of triamcinolone acetonide were elevated intraocular pressure and cataract progression. These events have been reported to occur in 20-60% of patients.
- Less common reactions occurring in up to 2% of patients include: endophthalmitis (infectious and non-infectious), hypopyon, injection site reactions (described as blurring and transient discomfort), glaucoma, vitreous floaters, detachment of retinal pigment epithelium, optic disc vascular disorder, eye inflammation, conjunctival hemorrhage and visual acuity reduced. Cases of exophthalmos have also been reported.

DRUG INTERACTIONS

- *Anticoagulant Agents* – Corticosteroids may enhance or diminish the anticoagulant effect of anticoagulant agents. Coagulation indices should be monitored.
- *Antidiabetic Agents* – Corticosteroids may increase blood glucose concentrations. Dose adjustments of antidiabetic agents may be required.
- *CYP 3A4 Inducers and Inhibitors* – CYP 3A4 inducers and inhibitors may respectively increase or decrease clearance of corticosteroids, necessitating dose adjustment.
- *NSAIDs* – Concomitant use of NSAIDS, including aspirin and salicylates, with a corticosteroid may increase the risk of GI side effects.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Two prospective case control studies showed decreased birth weight in infants exposed to maternal corticosteroids in utero. Triamcinolone acetonide was shown to be teratogenic in rats, rabbits, and monkeys at inhalation doses of 0.02 mg/kg and above and in monkeys, triamcinolone acetonide was teratogenic at an inhalation dose of 0.5 mg/kg (1/4 and 7 times the recommended human dose). Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Mothers

Corticosteroids are secreted in human milk. The risk of infant exposure to steroids through breast milk should be weighed against the known benefits of breastfeeding for both the mother and baby.

Pediatric Use

The efficacy and safety of corticosteroids in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. The adverse effects of corticosteroids in pediatric patients are similar to those in adults.

Geriatric Use

No overall differences in safety or effectiveness were observed between elderly subjects and younger subjects, and other reported clinical experience with triamcinolone has not identified differences in responses between the elderly and younger patients.

PATIENT COUNSELING INFORMATION

Patients should discuss with their physician if they have had recent or ongoing infections or if they have recently received a vaccine.

Patients should be advised of common adverse reactions that could occur with corticosteroid use such as elevated intraocular pressure, cataracts, fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite, and weight gain.

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ment use, even from clinical trials, suffer from high risk of confounding and poor ascertainment of actual supplement use; it's therefore impossible to make claims of efficacy or lack of efficacy from them. Second, a similar pattern of results was seen independently in AREDS and AREDS2, which is unlikely to occur by chance.

Third, the results are biologically plausible. For example, lutein/zeaxanthin are abundant in the central macula (given sufficient dietary or supplement intake, since these important carotenoids can't be synthesized by the body) but virtually absent in the peripheral macula.[12] Therefore, it seems likely that, if their presence and antioxidant activity are able to slow GA progression, this effect would be observed preferentially at the central macula, where they're located. This effect would be captured well by the proximity measure but very poorly by the GA area measure, which is dominated by the more peripheral macula. These ideas are also supported by the subgroup analyses.

Fourth, the visual acuity data provide some support for the structural data. We had minimal expectation that slowing GA progression to the fovea would be accompanied by slower decline in acuity, since progression fell well short of actual center-point involvement in most cases. Despite this, significant or numerical differences were seen for some important comparisons.

Finally, in separate analyses of the same datasets according to dietary intake, as opposed to supplement use, we found similar associations, with strong associations between healthier diet and slower GA progression.[13-15] In this way, both observational data on dietary intake and randomized data on oral supplementation point to the importance of antioxidants in slowing GA progression. In fact, in analyses that considered diet and randomized supplement intake together, the results for extrafoveal GA even demonstrated a degree of redundancy. With increasing oral supplementation by randomization, the associations between a healthier diet and slower progression to the fovea were fewer and weaker.[15] It's very difficult to explain these results in the absence of a genuine treatment effect of oral supplements.

One potential limitation of these analyses is the use of color fundus photography, which was the gold standard for grading GA area and proximity at the time of the trials. However, levels of inter-grader agreement for measuring GA area on the AREDS2 CFP images have been analyzed in detail, and had low mean difference, narrow limits of agreement and no systematic bias.[16] Although fundus autofluorescence and/or OCT imaging are now typically used, several studies have shown high levels of correlation between CFP and FAF images in measuring GA area and progression.[17-19] In previous large-scale analyses of the AREDS2 dataset itself, measurements of GA progression rates were extremely similar between the two modalities, with no significant difference.[17] In fact, the evaluation of foveal involvement was considered

Table 2. Geographic atrophy proximity-based progression and area-based progression in the Age-Related Eye Disease Study 2 (AREDS2), according to randomized assignment.

Randomized assignment (main effects)	Proximity-based progression rate			Area-based progression rate		
	n (eyes)	Estimate (μm/year)	P	n (eyes)	Estimate (μm/year)	P
No lutein/zeaxanthin	411	105.3	**0.017**	629	0.282	0.83
Lutein/zeaxanthin	382	84.5		581	0.280	
No lutein/zeaxanthin†	174	114.4	**0.011**	274	0.306	0.64
Lutein/zeaxanthin†	151	80.1		231	0.298	
No DHA/EPA	359	97.9	0.58	569	0.278	0.60
DHA/EPA	434	93.0		641	0.284	

** All participants also assigned to receive AREDS supplements*

† Considering only those participants in the secondary randomization study population who were randomly assigned to no β-carotene (analyzed because lutein/zeaxanthin and β-carotene compete for intestinal absorption)

DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid

Bold font: P-value significant at the 0.05 threshold

superior on CFP than on FAF. The central masked reading center grading and the repeated-measures regression (based on measurements at multiple time-points per eye) also mitigate this concern, through increased precision and power. Most importantly, even if the use of CFP were associated with slightly lower inter-grader agreement for GA measurements, this would apply to all randomized treatment arms. The randomization is key here and means that the results can't be explained by the grading approach.

Lifestyle factors and geographic atrophy progression

More broadly, outside oral supplement use, our analyses strongly suggest that lifestyle factors are important not just for risk of GA occurrence but also for rate of GA progression.[14] Analyses of the AREDS1/2 datasets have shown consistently that a Mediterranean-type diet is associated with slower GA area-based progression and slower progression to the fovea; for extrafoveal GA, this is accompanied by a slower decline in visual acuity.[13,15] The most important components include vegetables, fruit, and less red meat. Cigarette smoking is associated with faster GA area-based progression, and, in men, heavy alcohol consumption is also associated with faster area-based progression.[11,20] Overall, patients with GA may therefore benefit from both a healthy lifestyle and oral micronutrient supplementation.

Bottom line

Patients with extrafoveal GA should be counselled on the potential benefit of AREDS2 supplements in slowing GA progression to the fovea. In analyses that related GA progression rates back to the clinical trial randomizations, the AREDS2 supplements appear to slow progression to the fovea by approximately half, likely by augmenting the natural protective phenomenon of foveal sparing. Slowing the GA time-to-fovea in this way should help preserve visual acuity and quality of life. Patients with GA should also be advised on the likely importance of lifestyle factors in slowing progression, particularly adopting a healthy diet and avoiding smoking.

REFERENCES

1. Age-Related Eye Disease Study Research G. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol 2001;119:1417-36.
2. Age-Related Eye Disease Study 2 Research G. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: The Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA 2013;309:2005-15.
3. Age-Related Eye Disease Study 2 Research G, Chew EY, Clemons TE, et al. Secondary analyses of the effects of lutein/zeaxanthin on age-related macular degeneration progression: AREDS2 report no. 3. JAMA Ophthalmol 2014;132:142-9.
4. Vemulakonda GA, Bailey ST, Kim SJ, et al. Age-related macular degeneration preferred practice pattern. Ophthalmology 2025;132:P1-P74.
5. Keenan TDL, Agron E, Keane PA, et al. Oral antioxidant and lutein/zeaxanthin supplements slow geographic atrophy progression to the fovea in age-related macular degeneration. Ophthalmology 2025;132:1:14-29. .
6. Schmitz-Valckenberg S, Nadal J, Fimmers R, et al. Modeling visual acuity in geographic atrophy secondary to age-related macular degeneration. Ophthalmologica 2016;235:215-24.
7. Kunzel SH, Broadbent E, Moller PT, et al. Association of lesion location and functional parameters with vision-related quality of life in geographic atrophy secondary to age-related macular degeneration. Ophthalmol Retina 2024;8:794-803.
8. Zhang C, Kahan E, Begaj T, et al. Geographic atrophy natural history versus treatment: Time to fovea. Ophthalmic Surg Lasers Imaging Retina 2024;55:576-585.
9. Shen LL, Sun M, Ahluwalia A, et al. Natural history of central sparing in geographic atrophy secondary to non-exudative age-related macular degeneration. Br J Ophthalmol 2022;106:689-695.
10. Sunness JS, Rubin GS, Zuckerbrod A, Applegate CA. Foveal-sparing scotomas in advanced dry age-related macular degeneration. J Vis Impair Blind 2008;102:600-610.
11. Keenan TD, Agron E, Domalpally A, et al. Progression of geographic atrophy in age-related macular degeneration: AREDS2 report number 16. Ophthalmology 2018;125:1913-1928.
12. Owsley C, Swain TA, McGwin G Jr, Clark ME, Kar D, Curcio CA. Biologically guided optimization of test target location for rod-mediated dark adaptation in age-related macular degeneration: Alabama Study on Early Age-related Macular Degeneration 2 baseline. Ophthalmol Sci 2023;3:100274.
13. Agron E, Mares J, Chew EY, Keenan TDL, Group AR. Adherence to a Mediterranean diet and geographic atrophy enlargement rate: Age-Related Eye Disease Study 2 report 29. Ophthalmol Retina 2022;6:762-770.
14. Keenan TDL. Geographic atrophy in age-related macular degeneration: A tale of two stages. Ophthalmol Sci 2023;3:100306.
15. Agron E, Vance E, Domalpally A, Chew EY, Keenan TDL. Relationships between diet and geographic atrophy progression in the Age-Related Eye Diseases Studies 1 and 2. Nutrients 2025;17.
16. Danis RP, Domalpally A, Chew EY, et al. Methods and reproducibility of grading optimized digital color fundus photographs in the Age-Related Eye Disease Study 2 (AREDS2 report number 2). Invest Ophthalmol Vis Sci 2013;54:4548-54.
17. Domalpally A, Danis R, Agron E, et al. Evaluation of geographic atrophy from color photographs and fundus autofluorescence images: Age-Related Eye Disease Study 2 report number 11. Ophthalmology 2016;123:2401-2407.
18. Yaspan BL, Williams DF, Holz FG, et al. Targeting factor D of the alternative complement pathway reduces geographic atrophy progression secondary to age-related macular degeneration. Sci Transl Med 2017;9.
19. Khanifar AA, Lederer DE, Ghodasra JH, et al. Comparison of color fundus photographs and fundus autofluorescence images in measuring geographic atrophy area. Retina 2012;32:1884-91.
20. Duic C, Vance E, Agron E, Keenan TDL, Group AR. Alcohol consumption and risk of age-related macular degeneration and geographic atrophy progression: AREDS2 report 34. Ophthalmol Retina 2024;9:3:200-211.

How social determinants of health shape outcomes in retinal disease

Examining the socioeconomic and structural drivers that influence access, treatment and vision outcomes.

By Ranveer Palia, MSc, Sunny Lang Qin, MD, Jaron Kai Pruett, MD, and Sally S. Ong, MD


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Take-home points

- Socioeconomic barriers reduce timely screening and treatment in diabetic retinopathy, leading to worse vision outcomes.
- Lower socioeconomic status and minority status are linked to poorer visual outcomes in retinal vein occlusion.
- Delayed care due to social disadvantage results in more severe detachments and worse prognosis in rhegmatogenous retinal detachment.
- Partnerships between retina specialists and federally qualified health centers can bridge systemic gaps in access and advance equity in vision health for underserved communities.

A 46-year-old African-American man with poorly controlled type 1 diabetes presented to clinic with blurry vision. He was diagnosed with proliferative diabetic retinopathy in both eyes, complicated by diffuse capillary nonperfusion involving the macula *(Figure 1)*. His visual acuity measured 20/200 in the right eye and 20/400 in the left. The consulting physician at the time recommended treatment, but the patient was lost to follow-up.

Two years later, the patient presented to our clinic with worsening vision, now reduced to hand motions in both eyes. Examination showed bilateral fovea-involving tractional retinal detachments *(Figure 2)*. Further questioning revealed that the patient was unemployed, faced housing and food instability, and depended on public and Medicaid transportation to get to medical appointments. Surgical intervention was recommended; however, the patient's prognosis for visual recovery was dismal, and his case illustrates how much worse outcomes can be when patients are lost to follow-up, often due to challenges related to social determinants of health.

Unfortunately, stories like this one aren't uncommon in retinal practice. Retinal diseases remain a leading cause of vision loss and blindness worldwide. While risk factors such as diabetes, hypertension, aging, smoking and trauma are well established, outcomes are also shaped by SDOH. These include factors such as income, access to care, health literacy, transportation, food insecurity and social support.[1] Healthy People 2030 has defined SDOH as "the conditions in the environments where people are born, live, learn, work, play, worship and age," and further grouped SDOH into five domains: economic stability; education access and quality; health-care access and quality; neighborhood and built environment; and social and community context.[2] Together, these conditions often determine whether patients can obtain timely diagnosis, initiate treatment and adhere to follow-up schedules.

There's growing recognition that SDOH play a pivotal role in ophthalmology, influencing disparities in diagnosis, treatment

BIOS

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access, adherence and long-term outcomes. Two patients with the same disease severity may have vastly different prognoses depending on the social and economic contexts in which they live.

In this article, we highlight how SDOH affect the care and prognosis of three key retinal diseases: diabetic retinopathy, retinal vein occlusion and rhegmatogenous retinal detachment. Through these examples, we highlight how non-biological factors drive disease burden and outcomes, and why addressing them is critical to reducing inequities.

Diabetic retinopathy

Diabetic retinopathy is one of the leading causes of vision loss globally, with an estimated 9.6 million people living with diabetic retinopathy in the United States, yet awareness and access to medical care remain uneven across populations.[3] Growing evidence highlights that SDOH are critical drivers of outcomes for patients at risk of or living with DR. Studies using national data demonstrate both the scale of the disease and the disparities in its recognition and treatment. For example, an analysis of National Health and Nutrition Examination Survey data found that awareness of DR was low overall, and that minority status, unemployment and food insecurity significantly influenced whether patients knew about the disease.[4]

Similarly, population-level analyses of the National Health Interview Survey showed that unemployment, disability and residence in the Southern United States were associated with higher DR burden, underscoring the role of geography and economic stability.[5] Large-scale surveys have also demonstrated that individuals facing social vulnerabilities such as unemployment and poor self-rated health were less likely to undergo recommended eye exams, further linking structural disadvantage to gaps in preventive care.[6,7]

Specific SDOH drivers have been extensively studied. Food insecurity not only worsens diabetes control but also reduces the likelihood of patients pursuing vision care, with both food and housing instability associated with lower odds of DR screening.[8,9] Economic stability plays a similar role: Unemployment, disability, and financial hardship decrease access to preventive care.[5,6] Race, ethnicity and cultural factors introduce additional disparities, with minority populations less likely to undergo guideline-based monitoring, while childcare responsibilities and perceived provider bias further reduce

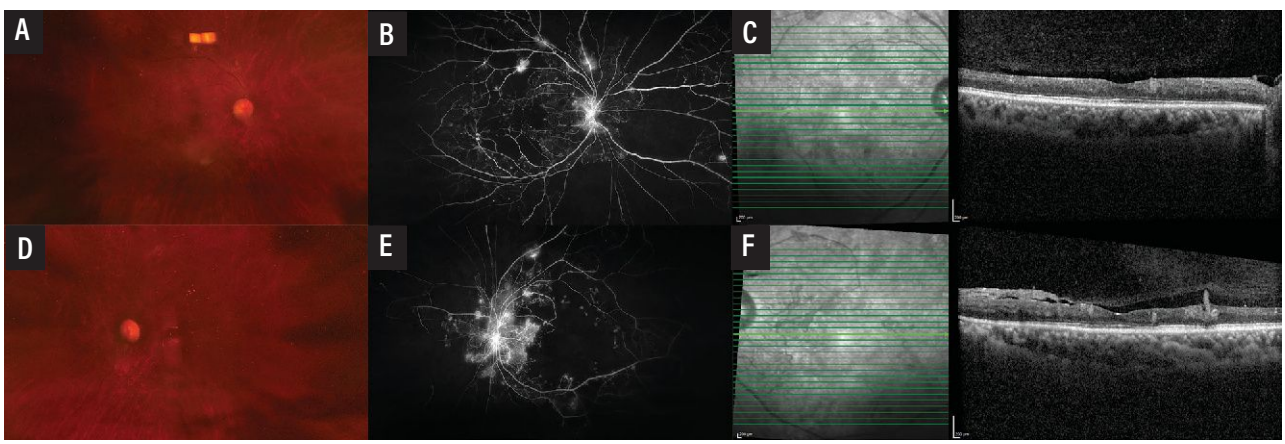

Figure 1. Multimodal imaging of the patient in 2023 when he presented with visual acuities of 20/200 in the right eye and 20/400 in the left eye. Color photos of the right (A) and left (D) eyes show neovascularization of the disc and elsewhere, and severe vascular attenuation. Fluorescein angiograms of the right (B) and left (E) eyes confirm presence of neovascularization of the disc and elsewhere as well as diffuse capillary nonperfusion affecting the macula worse in the left eye. Optical coherence tomography of the macula of the right (C) and left (F) eyes demonstrate diffuse retinal thinning.

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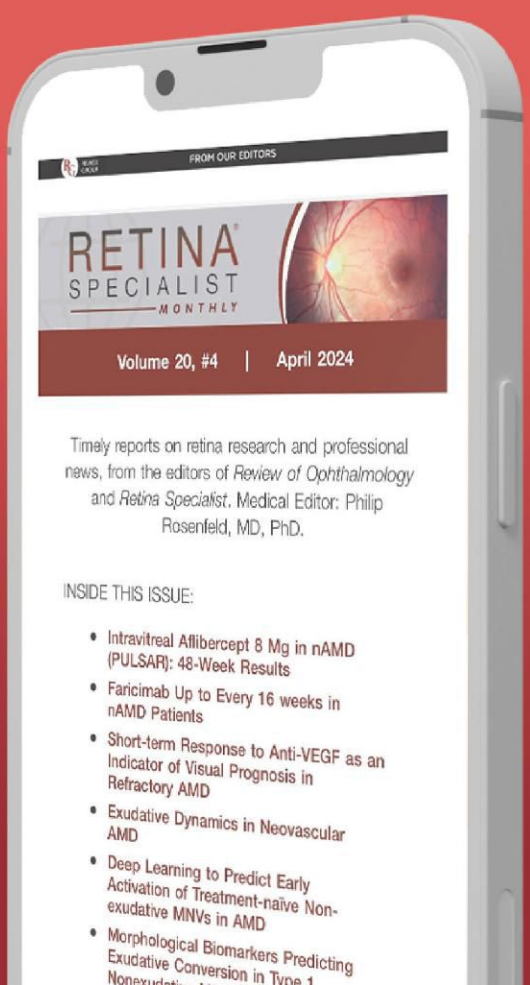

access.[7,10-11]

Access to health care and insurance coverage remain central issues: Insurance status and higher education improve the odds of completing annual exams, while lack of coverage, financial insecurity and transportation barriers increase the risk of advanced complications.[12-14] Broader reviews emphasize that systemic issues—including language barriers, limited provider availability and fragmented coverage—continue to shape inequities in vision care.[15,16]

The implications of these findings are clear. Tailoring prevention strategies by employment status, geography or disability may improve screening rates, and increasing awareness of DR in underserved communities could provide an entry point for preventive diabetes care.[3-4] Structural barriers must also be addressed through expanded insurance coverage, transportation support and multilingual resources.[15] At a systems level, incorporating SDOH into electronic health records may allow clinicians to anticipate patient needs and design interventions accordingly.[16] In parallel, culturally sensitive approaches are essential for reducing disparities in racial and ethnic minority groups.[10,11]

Retinal vein pcclusion

Central and branch retinal vein occlusions are important causes of vision loss with an estimated 16.4 million adults being affected by retinal vascular occlusions globally (2.5 million by CRVO and 13.9 million by BRVO).[17] It's well known that predisposing factors for RVO include many of the same risks as those for cardiovascular and cerebrovascular disease, namely hypertension, obesity, hyperlipidemia and diabetes mellitus.[18-21] In the United States, these systemic risk factors have been shown to be both more prevalent and worse-controlled among patients with markers of low socioeconomic status, possibly placing these patients at increased risk of vision-threatening illness.[22] However, further work is needed to determine whether this directly translates into a higher incidence or prevalence of RVOs in socially and economically disadvantaged populations.

While this has yet to be demonstrated, a recent retrospective study found that among patients presenting with BRVO with cystoid macular edema who were treated with intravitreal anti-VEGF injections, those with higher socioeconomic deprivation scores had thicker final central macular thickness.[23] Additionally, non-White patients had worse initial and final best corrected visual acuity. Both these results point to disparities in visual outcomes associated with lower socioeconomic status among patients with RVOs.

More recently, an analysis of over 600 cases of RVO from the National Institutes of Health's All of Us database further highlighted the role of social determinants in disease risk. In addition to confirming traditional medical risk factors mentioned above, the study found that patients who identified as Black and those with opioid use were independently associated with an increased risk of both BRVO and CRVO, highlighting the need for further investigation into how social and behavioral factors contribute to RVO.[24]

Rhegmatogenous retinal detachment

Rhegmatogenous retinal detachment is the most common form of RD, with an estimated incidence of 6.3 to 17.9 per 100,000 persons.[25] Multiple studies have demonstrated that socioeconomic factors significantly impact how patients present with RRD and their subsequent outcomes. Research consistently shows that socioeconomically disadvantaged patients are more likely to present with severe disease, including worse visual acuity and fovea-involving detachments.[26]

Large-scale studies from major U.S. academic centers have found that factors such as older age, male gender, minority race and lower income are independently associated with more severe presentation.[26,27] Patients with public insurance (Medicare/Medicaid) or no insurance have worse baseline visual acuity and higher rates of fovea-involving

detachments compared to those with private insurance.[26-28] Neighborhood-level factors, including area deprivation indices and transportation barriers, also predict worse baseline severity even after controlling for individual characteristics.[27] International studies from Scotland and other countries have reported similar patterns, with retinal detachment severity correlating inversely with socioeconomic status.[25,29]

Beyond initial presentation, socioeconomic disadvantage affects surgical outcomes. Patients from disadvantaged backgrounds face higher reoperation rates and worse long-term visual outcomes, even after accounting for baseline disease severity.[26,28] These disparities persist across different health-care systems and geographic regions.

These disparities matter because RRD outcomes have been shown to be closely linked to baseline visual acuity and foveal status.[30] Delays in presentation allow progression to foveal involvement, where subfoveal fluid can cause irreversible photoreceptor damage.[31-33] Socioeconomic barriers to timely care—including limited health-care access, transportation challenges and delayed symptom recognition—directly compromise visual outcomes in this sight-threatening condition.

Bottom line

Diabetic retinopathy, retinal vein occlusion and rhegmatogenous retinal detachment are all vision-threatening conditions for which outcomes can be heavily impacted by SDOH, which include socioeconomic status, access to high quality education and health care, safe and healthy environments, and social connectedness.[2] Evidence demonstrates that patients facing financial hardship, unemployment, food and housing insecurity, transportation barriers or systemic inequities are more likely to present with advanced disease, have lower rates of preventive screening, and experience worse visual outcomes.[4-6,8-9,12-14,26-28]

Addressing these disparities requires multi-level interventions. At the patient level, culturally sensitive education, awareness campaigns, and navigation support can encourage timely care and adherence to screening guidelines. At the system level, telehealth initiatives and integration of SDOH into electronic health records can mitigate barriers, particularly for historically underserved populations. Another promising system-level strategy involves leveraging federally qualified health centers, which are uniquely positioned to extend vision care to communities most affected by social and structural inequities.

FQHCs serve over 30 million Americans, most of whom are uninsured or publicly insured, and yet fewer than 3 percent of patients receive vision services, even though they face disproportionately higher rates of diabetic retinopathy, glaucoma and vision

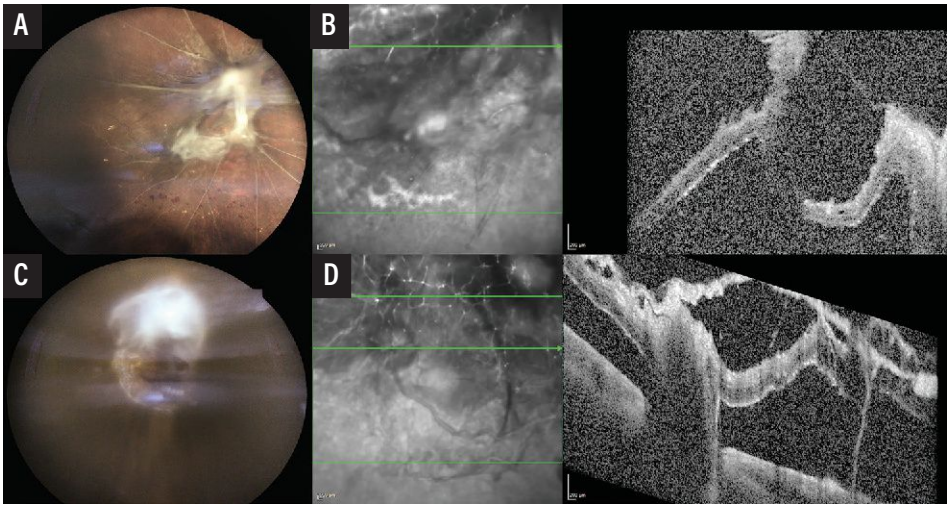

Figure 2. The patient was lost to follow-up and returned two years later with worsening vision in both eyes to hand motions. Fundus photos of the right (A) and left (C) eyes show progressive proliferative diabetic retinopathy with bilateral fovea-involving tractional retinal detachments with thick fibrovascular membranes extending from the optic nerve head to both the superotemporal and inferotemporal arcades. Optical coherence tomography of the right (B) and left (D) eyes through the macula confirm tractional retinal detachments, showing the retinal layers pulled anteriorly in a tent-like configuration with complete loss of the normal foveal contour.

impairment.[35] Many patients and providers alike are unaware that FQHCs can be powerful partners in preventing vision loss. Retina specialists and ophthalmology practices can help change this by building closer relationships with local FQHCs—offering on-site or teleophthalmology screening, rotating clinics or streamlined referral networks. Such collaborations can bring retinal expertise directly to patients who might otherwise never see a specialist, while connecting those identified with eye disease to the enabling services FQHCs already provide like transportation, translation and case management.[36,37]

Beyond improving access, these partnerships can foster awareness within the community that vision care is an important part of comprehensive health care. Moreover, investing in FQHC-based vision programs isn't only the ethical thing to do but also yields long term economic benefits. FQHCs prevents avoidable blindness, which reduces long-term health costs and helps maintain the independence and productivity of those most affected by social and structural inequities.[36,37] By engaging with FQHCs, retina specialists have an opportunity not only to treat disease but to transform the systems that determine who gets to keep their sight, bringing us closer to equitable vision care for all.

REFERENCES:

1. Braveman P, Gottlieb L. The social determinants of health: It's time to consider the causes of the causes. Public Health Rep 2014;129(Suppl 2):19-31.
2. Centers for Disease Control and Prevention. Social determinants of health. Public Health Gateway. Published May 15, 2024. Accessed November 4, 2025. https://www.cdc.gov/public-health-gateway/php/about/social-determinants-of-health.html
3. Lundeen EA, Burke-Conte Z, Rein DB, et al. Prevalence of diabetic retinopathy in the US in 2021. JAMA Ophthalmol 2023;141:8:747–754.
4. Nwanyanwu K, Andoh J, Chen E, et al. Social determinants associated with diabetic retinopathy awareness: National Health and Nutrition Examination Survey (2001–2008). Am J Ophthalmol 2025;278:389-401.
5. Zaman M, Zajner C, Xie J, et al. Association between sociodemographic factors and self-reported diabetic retinopathy: A cross-sectional, population-based analysis. Am J Ophthalmol 2025;271:138-148.
6. Silverberg EL, Sterling TW, Williams TH, et al. Associations between social determinants of health and self-reported diabetic retinopathy: Exploratory analysis. Int J Environ Res Public Health 2021;18:2:792.
7. Besagar S, Yonekawa Y, Sridhar J, et al. Association of socioeconomic, demographic, and health care access disparities with severe visual impairment in the US. JAMA Ophthalmol 2022;140:12:1219-1226.
8. Talebi R, Yu F, Tseng VL, Coleman AL. Association between food insecurity and chronic eye disease in the National Institutes of Health's All of Us Research Program. Ophthalmol Sci 2024;5:3:100697.
9. Ravindranath R, Bernstein IA, Fernandez KS, et al. Social determinants of health and perceived barriers to care in diabetic retinopathy screening. JAMA Ophthalmol 2023;141:12:1161-1171.
10. Chaudhury AS, Ige M, Marwah S. Race, social determinants of health, and the quality of diabetic eye care. JAMA Ophthalmol 2024;142:10:961-970.
11. Huang BB, Saseendrakumar R, Delavar A, Baxter SL. Racial disparities in barriers to care for patients with diabetic retinopathy in a nationwide cohort. Transl Vis Sci Technol 2023;12:3:14.
12. Jotte A, Vander Kooi W, French DD. Factors associated with annual vision exams among diabetic adults: Analysis of the 2019 National Health Interview Survey. Clin Ophthalmol 2023;17:613-621.
13. Andersen JA, Gibbs L. Does insulin therapy matter? Pharmacies' role in managing diabetes care outcomes. Prim Care Diabetes 2018;12:3:224-230.
14. Chan AX, McDermott JJ, Lee TC, et al. Associations between healthcare utilization and access and diabetic retinopathy complications using all US nationwide surgery data. PLoS One 2022;17:6:e0269231.
15. Solomon SD, Shoge RY, Ervin AM, et al. Improving access to eye care: A systematic review of the literature. Ophthalmology 2022;129:10:e114-e126.
16. Lee TC, Saseendrakumar BR, Nayak M, et al. Social determinants of health data availability for patients with eye disease. Ophthalmol Sci 2022;2:2:100151.
17. Laouri, M, Chen, E, Looman, M, & Gallagher, M. The burden of disease of retinal vein occlusion: Review of the literature. Eye 2011;25:8:981–988.
18. Kolar P. (2014). Risk factors for central and branch retinal vein occlusion: A meta-analysis of published clinical data. Journal of Ophthalmology 2014:2014:724780. doi: 10.1155/2014/724780. Epub 2014 Jun 9
19. Yau JW, Lee P, Wong TY, Best J, & Jenkins A. Retinal vein occlusion: An approach to diagnosis, systemic risk factors and management. Internal Medicine Journal 2008;38:12:904–910.
20. Okonkwo ON, Adenuga OO, Nkanga D, Ovienria W, et al. Prevalence and systemic associations of retinal vascular occlusions in Sub-Saharan Africa. Annals of African Medicine 2023;22:3:279–285.
21. Fiebai B, Ejimadu, CS, Komolafe RD. Incidence and risk factors for retinal vein occlusion at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria. Nigerian Journal Of Clinical Practice 2014;17:4:462–466.
22. Powell-Wiley, TM, Baumer Y, Baah, FO, Baez, AS, et al. Social determinants of cardiovascular disease. Circulation Research 2022;130:5:782–799.
23. Woldetensaye AG, Selander JM, Huang H, Patel PV, et al. The impact of social determinants of health on presentation, treatment, and outcomes in branch retinal vein occlusion with cystoid macular edema. Ophthalmic Surgery, Lasers & Imaging Retina 2023;54:7:411–416.
24. McDermott JJ, Lee TC, Chan AX, Ye GY, et al. Novel association between opioid use and increased risk of retinal vein occlusion using the National Institutes of Health All of Us Research Program. Ophthalmology Science 2022;2:1:100099.
25. Mitry D, Charteris DG, Fleck BW, Campbell H, Singh J. The epidemiology of rhegmatogenous retinal detachment: Geographical variation and clinical associations. Br J Ophthalmol 2010;94:6:678-684.
26. Xu D, Uhr J, Patel SN, Pandit RR, Jenkins TL, Khan MA, Ho AC. Sociodemographic factors influencing rhegmatogenous retinal detachment presentation and outcome. Ophthalmol Retina 2021;5:4:337-341.
27. Ong SS, Tran D, Westlund E, et al. Neighborhood-level social determinants of health and presenting characteristics for rhegmatogenous retinal detachments. JAMA Ophthalmol 2024;142:9:845–854.
28. Rahman S, Sharma N, Valentim CCS, et al. Rhegmatogenous retinal detachment: Variations in clinical presentation and surgical outcomes by socioeconomic status and race. Ophthalmic Surg Lasers Imaging Retina 2022;53:10:538-545.
29. Mitry D, Charteris DG, Yorston D, et al. The epidemiology and socioeconomic associations of retinal detachment in Scotland: A two-year prospective population-based study. Invest Opthalmol Vis Sci 2010;51:4963.
30. Saidkasimova S, Mitry D, Singh J, et al. Retinal detachment in Scotland is associated with affluence. Br J Ophthalmol 2009;93:1591e1594.
31. Wykoff CC, Smiddy WE, Mathen T, Schwartz SG, Flynn HW Jr, Shi W. Fovea-sparing retinal detachments: Time to surgery and visual outcomes. Am J Ophthalmol 2010;150:2:205-210.e2.
32. Chang CJ, Lai WW, Edward DP, Tso MO. Apoptotic photoreceptor cell death after traumatic retinal detachment in humans. Arch Ophthalmol 1995;113:7:880-886.
33. Kubay OV, Charteris DG, Newland HS, Raymond GL. Retinal detachment neuropathology and potential strategies for neuroprotection. Surv Ophthalmol 2005;50:5:463-475.
34. Bai P, Burt SS, Woodward MA, et al. Federally Qualified Health Centers as a model to improve vision health: A systematic review. JAMA Ophthalmol 2025;143:3:242-251.
35. Ong SS. Expanding vision services at Federally Qualified Health Centers. JAMA Ophthalmol 2025;143:3:251–253.
36. Bastos de Carvalho A, Lee Ware S, Belcher T, et al. Evaluation of multilevel barriers and facilitators in a large diabetic retinopathy screening program in Federally Qualified Health Centers: A qualitative study. Implement Sci Commun 2021;2:1:54.
37. Yadlapalli N, Hollinger R, Berzack S, et al. Potential gaps in eye care based on evaluation of Federally Qualified Health Centers. JAMA Ophthalmol 2024;142:11:1018–1026.

Retinal microvascular metrics: The emerging role of swept-source OCT angiography

The challenges and potential of SS-OCTA in diagnosing and managing retinal disease.

By Kailynn M. Barton, BS, Shivesh H. Shah, BA, Chong Chen, MD and John B. Miller, MD

Take-home points

- Ultrahigh-speed SS-OCTA offers repeated B-scan imaging between 100 to 400 kHz to evaluate retinal microvasculature density, flow and signal voids.
- The non-invasive nature of SS-OCTA and high speeds provide a valuable alternative to other imaging modalities such as fluorescein angiography.
- Applications of SS-OCTA are broad, with current research evaluating longitudinal progression of various retinal diseases.
- Challenges in SS-OCTA include minimizing artifacts and creating comprehensive artificial intelligence models to evaluate standardized retinal microvascular metrics.
- Pediatric RDs have diverse etiologies and prognoses—partner with the family to align expectations and clarify treatment goals.

Ultrahigh-speed swept-source optical coherence tomography angiography has gained increased attention for its ability to characterize retinal blood flow metrics with high precision. It offers a more non-invasive approach than fluorescein angiography, and faster scan rates compared to spectral-domain OCTA.[1] SS-OCTA has demonstrated utility across a wide range of retinal diseases, including diabetic retinopathy, age-related macular degeneration and retinal vein occlusion. Though primarily limited to larger centers at this time, SS-OCTA offers substantial potential for broader clinical implementation for retinal evaluation.

The field of retinal imaging has rapidly advanced in the past two decades, with ongoing efforts aimed at streamlining image analysis with higher accuracy. We aim to provide a brief overview of retinal microvascular metrics evaluated through ultrahigh-speed SS-OCTA—emphasizing relevant technical specifications, the potential for, and challenges of, clinical application, and potential future advancements.

Technical considerations

In brief, optical coherence tomography angiography is an imaging modality that relies on capturing repeated brightness scan (B-scan) images to quantify changes due to blood flow in comparison to surrounding static tissue, while still evaluating the structural characteristics of traditional OCT.[2] Early SS-OCTA prototypes were limited by relatively low B-scan acquisition rates, which constrained their ability to perform the repeated scans required for angiographic signal detection. Since the introduction of ultrahigh-speed SS-OCTA by Fujimoto's group in 2010,[3,4] this imaging modality has been frequently studied for its clinical utility in a variety of retinal diseases. Using a tunable swept laser detected by a photodiode, modern ultrahigh-speed SS-OCTA can achieve scan rates between 100 to 400 kHz. This scan rate offers an improvement


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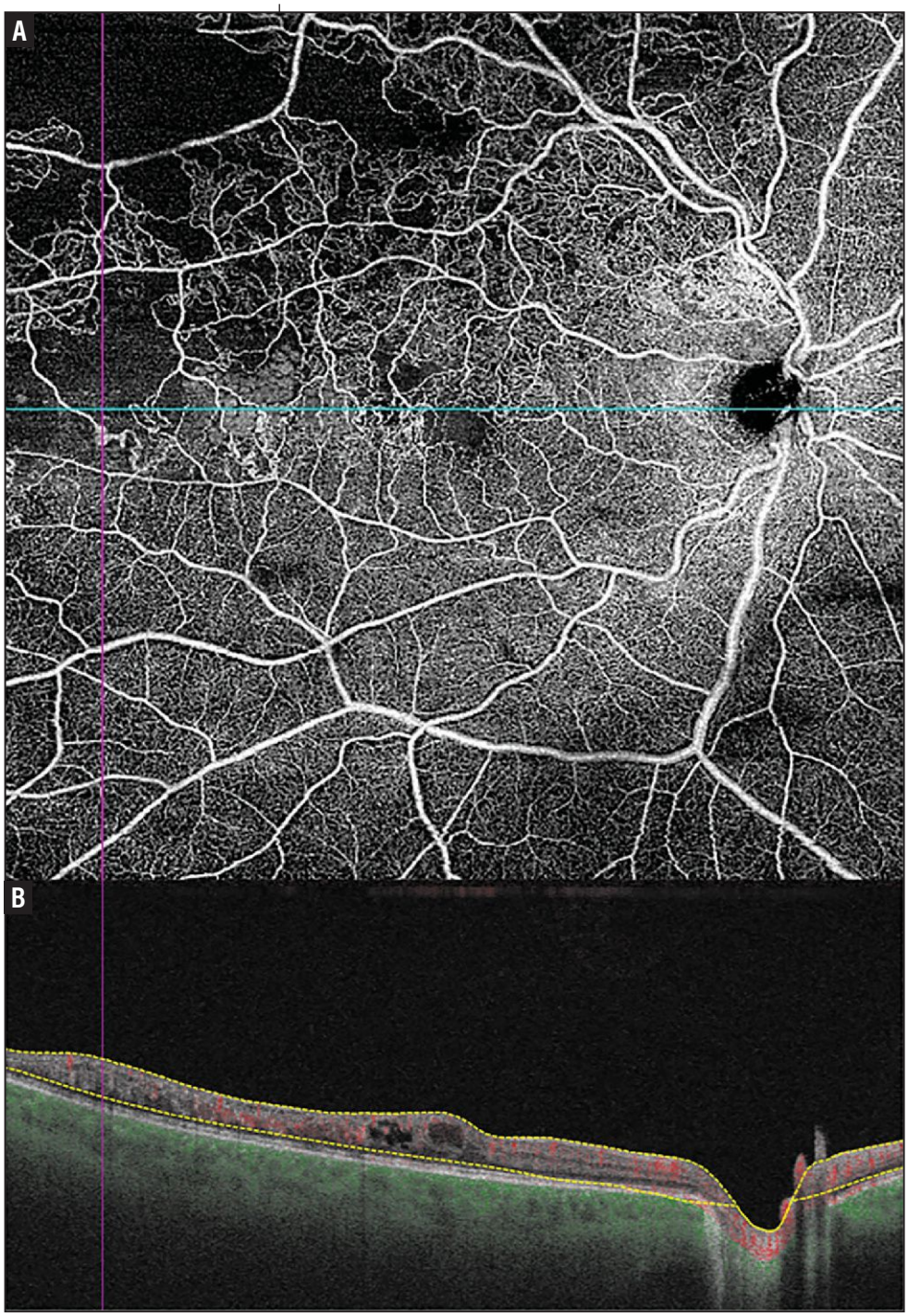

Figure 1. Right eye with branch retinal vein occlusion, imaged using expanded-field SS-OCTA (Zeiss PLEX Elite 9000) during routine follow-up. (A) 12 × 12 mm SS-OCTA image acquired at 100 kHz, demonstrating areas of non-perfusion (pink and blue lines indicate the location of the corresponding B-scan). (B) Corresponding B-scan with vascular overlay; yellow dashed lines represent segmentation boundaries.

over earlier SS-OCTA devices that typically operated between 10 to 50 kHz.[3] Ultrahigh-speed SS-OCTA also maintains the longer wavelength of earlier SS-OCTA models (~1050-nm) that contributed to deeper light penetration compared to SD-OCTA (~840-nm).[3,5]

Visualization of the retinal microvasculature

SS-OCTA can efficiently characterize many retinal microvascular metrics including retinal area and length densities, foveal avascular zone area, various flow areas and signal voids in microvascular networks.[4] The combination of faster scan speed and increased wavelength offers improved sensitivity roll-off and reduced potential for scattering from the retinal pigment epithelium. Taken together, these factors all contribute to improvements in accuracy. Such improvements are particularly important in evaluating densely vascularized areas such as the optic nerve head, where high precision is necessary to discern structures.[4] This higher speed is also helpful in visualizing deeper layers such as the deep capillary plexus and choroid, which are particularly susceptible to sensitivity roll-off.[5,6] Furthermore, faster scan speeds lead to reductions in artifacts that may

interfere with evaluation.[7] These characteristics may afford more accurate grading and characterization of retinal pathology.

Clinical implications

Differentiation in signals based on motion to distinguish blood flow from tissue and generate "decorrelation signals" underpins SS-OCTA. This non-invasive evaluation offers an advantage over dye-based modalities such as FA or indocyanine green angiography.[1,8] Subsequent development of scan speeds provided a marked advancement over earlier generations of SS-OCTA. These faster acquisition speeds have allowed grading and characterization of a wide array of retinal diseases at depths that were previously difficult to effectively discern with earlier SS-OCTA technologies. For example, SS-OCTA has shown improved depth resolution of the choriocapillaris layer compared to ICGA, and this effect is amplified at faster image acquisition speeds.[9] At these speeds, SS-OCTA even offers better assessment of choroidal vessels of greater size compared to SD-OCTA.[10]

These improvements in image acquisition have led to a number of novel applications, especially in clinical settings. This technology has been applied to detecting changes in CC perfusion among eyes with varying levels of AMD, and there is substantial potential for further evaluation of this relationship.[2,11] SS-OCTA has also demonstrated utility in both the early diagnosis and management of diabetic retinopathy. Compared to SD-OCT, SS-OCTA has superior visualization of the vitreoretinal interface, utility in convenient evaluation of non-perfusion area[12] and improved early detection of retinal microvasculature alterations and CC abnormalities.[10] Other applications of SS-OCTA have included characterizing areas of nonperfusion in eyes with ischemic retinal vein occlusion[10] and evaluating vessel density alterations associated with visual function changes in eyes with retinal artery occlusion.[13]

The ease of use, noninvasiveness and improved resolution of microvasculature may theoretically reduce the threshold to obtain imaging with SS-OCTA—whether it be initial scans to evaluate based on clinical suspicion or subsequent scans for longitudinal follow-up of retinal disease. As more cohorts are followed longitudinally, the findings in SS-OCTA that correspond to disease progression may be further characterized. Such understanding will compound the value of longitudinal retinal microvascular metrics for patients in a clinical setting by offering clues into potential for disease progression.

Challenges in SS-OCTA

Despite the advantages of SS-OCTA, there are still several challenges accompanying efforts to increase the scope of its use. First, though this technology offers improvements in artifact over earlier models with slower scan rates, artifacts still exist. Improvements in tracking can help limit motion artifacts, but manual correction is often required. The time-consuming nature of manual segmentation, which requires repeated adjustment of layer boundaries in areas of distortion, hinders efforts to efficiently analyze images for larger cohorts.[14] Semi-automated algorithms are increasingly being applied to streamline image analysis,[15] alongside current efforts to automate segmentation and correct errors in SS-OCTA images. Such advances would likely increase efficiency of research evaluation of disease complications and progression. Furthermore, automatic segmentation could ease the clinical implementation of SS-OCTA with improved efficiency of image analysis. Such improvements would allow for increased point-of-care utility without the need for manual correction of errors that would be impractical in fast-paced clinical settings.

With various SS-OCTA devices in use spanning different clinics and manufacturers–oftentimes with high inter-device variability in measurements such as vessel

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Despite the advantages of SS-OCTA, there are still several challenges accompanying efforts to increase the scope of its use.

From microphones to microlearning

How the digital classroom continues to transform ophthalmic education.

By Jayanth Sridhar, MD

When I first began recording a retina-focused podcast nearly a decade ago, digital education felt like an experiment. In 2016, podcasting was a curiosity—an emerging format somewhere between radio and lecture hall. Few journals had video archives, webinars were clunky and the idea that a retina surgeon might one day teach through a smartphone seemed improbable. Yet, less than 10 years later, the world of ophthalmic education looks almost unrecognizable.

What changed was not just technology—it was the culture of how we share, learn and connect as physicians.

The beginnings

In the mid-2010s, online medical education was still slow and centralized. Conference talks and society webinars dominated, and interactivity was limited to an occasional email follow-up. Podcasts and early YouTube channels were informal side projects—a way to share case discussions and journal insights with a wider audience. There was a sense of intimacy to it: a conversation between colleagues that happened to be broadcast.

Early listeners were residents on commutes, fellows between cases and attendings curious about new surgical approaches. Each episode or video felt handcrafted, more like a case report than a formal show. But as bandwidth expanded and social media matured, the scale of engagement changed dramatically.

The platform explosion

By the early 2020s, the educational landscape had fragmented and multiplied. The same conference that once depended on a few in-person sessions now spawned simultaneous streams, highlight clips and analysis posts across multiple platforms. Educational voices emerged on YouTube, TikTok, Instagram and LinkedIn, bringing surgical tips and study summaries to global audiences.

A one-minute reel demonstrating internal limiting membrane peeling might rack up 50,000 viewers overnight. A TikTok explaining diabetic macular edema could reach more people than a traditional CME lecture. Residents began sharing their own micro-lessons, while societies and journals hired media teams to produce podcasts, animated abstracts and cross-platform discussions.

For ophthalmology—and retina in particular—this explosion has been both thrilling and humbling. Knowledge that once required journal access and travel funding is now free and immediate. The boundaries between student, teacher and audience have blurred beyond recognition.

The price of accessibility

Democratization has a cost. The same accessibility that fuels innovation also invites misinformation and oversimplification. Algorithms reward emotion over nuance; a carefully designed study summary can be buried beneath a flashy but inaccurate claim about "miracle injections."

Even within professional circles, the pressure to stay visible online can distort priorities. Educational intent can drift toward self-promotion, and the line between influence and information grows faint. Yet, physicians shouldn't retreat from the digital

BIO

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DISCLOSURES: Dr. Sridhar is a consultant to Alcon, DORC, Genentech/Roche and Regeneron Pharmaceuticals.

space—it's precisely why credible clinicians must participate. Our presence ensures that accurate, ethical perspectives remain accessible amid the noise.

The modern classroom

Today, podcasting and short-form video have become default learning environments. CME courses and fellowship curricula now routinely include digital content, and many programs encourage residents to create educational media as part of training.

The most striking development isn't the technology itself but rather the community built around it. Podcasts create ongoing conversations that evolve with the field. Social platforms host journal clubs that span continents. Surgeons trade pearls via comments and DMs. The new classroom mirrors what medicine has always valued: mentorship; curiosity; and shared problem-solving—now transposed into pixels and audio waves.

Looking ahead

As we enter the second half of the decade, artificial intelligence and adaptive learning will likely define the next frontier. Algorithms already shape what learners see; soon, they may build personalized curricula. AI voice translation could make every podcast multilingual, and augmented reality could turn a surgical video into a virtual wet lab.

The question isn't whether these tools will arrive—they already have—but whether we can guide their use responsibly. How do we preserve clinical judgment in a world of instant answers and balance accessibility with accuracy?

Perhaps the answer lies in recognizing that the medium has never been the real message—the relationships are.

The continuity of connection

After nearly a decade of watching digital education evolve, one lesson stands out: Technology changes, but curiosity doesn't. Online education isn't replacing traditional teaching—it's extending it. The reach is broader, the cadence faster and the medium more visual, but the essence remains mentorship through conversation. Whether through a microphone, a one-minute reel or a virtual panel spanning time zones, we're continuing the oldest tradition in medicine—sharing what we've learned so someone else can do it better.

That, perhaps, is the truest measure of progress: not the format, but the fidelity of connection it sustains. RS

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density—establishing a consensus of measurement will be critical.[16] Similarly, limiting the variability of inter-device metrics will be critical. Such standardization will likely allow for more accurate longitudinal multicenter evaluation of patient cohorts. Lastly, cost remains a substantial limiting factor in the implementation of ultrahigh-speed SS-OCTA compared to SD-OCTA. This difference in price point is commonly attributed to the need for expensive laser components.[10] Efforts to reduce the cost of this component would likely help improve the accessibility of this device.

Bottom line

Ultrahigh-speed SS-OCTA offers substantial potential for non-invasively quantifying perfusion and vessel areas within retinal microvasculature. This technology has demonstrated utility in determining differences in retinal microvasculature between various stages of disease, such as for AMD and DR. Longitudinal research is ongoing to determine the most predictive metrics of visual function, progression or complications of specific retinal diseases. Challenges involve addressing artifactual errors and increasing consensus regarding accepted measurements. However, with continued work in this area, there is much promise regarding broad clinical implementation of this technology. RS

REFERENCES

1. Zheng F, Deng X, Zhang Q, et al. Advances in swept-source optical coherence tomography and optical coherence tomography angiography. Advances in Ophthalmology Practice and Research 2022;3:2:67.
2 .Moult E, Choi W, Waheed NK, et al. Ultrahigh-speed swept-source OCT angiography in exudative AMD. Ophthalmic Surg Lasers Imaging Retina 2014;456:496.
3. Potsaid B, Baumann B, Huang D, et al. Ultrahigh speed 1050nm swept source / Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second. Opt Express 2010;18:19:20029.
4. Baumann B, Potsaid B, Kraus MF, et al. Total retinal blood flow measurement with ultrahigh speed swept source/Fourier domain OCT. Biomed Opt Express 2011;2:6:1539.
5. Miller AR, Roisman L, Zhang Q, et al. Comparison between spectral-domain and swept-source optical coherence tomography angiographic imaging of choroidal neovascularization. Invest Ophthalmol Vis Sci 2017;58:3:1499-1505.
6. de Carlo TE, Romano A, Waheed NK, Duker JS. A review of optical coherence tomography angiography (OCTA). Int J Retina Vitreous 2015;1:1.
7. Bazvand F, Ghassemi F. Artifacts in macular optical coherence tomography. J Curr Ophthalmol 2020;32:2:123.
8. Li P, Cheng Y, Li P, et al. Hybrid averaging offers high-flow contrast by cost apportionment among imaging time, axial, and lateral resolution in optical coherence tomography angiography. Opt Lett 2016;41:17:3944.
9. Borrelli E, Sarraf D, Freund KB, Sadda SR. OCT angiography and evaluation of the choroid and choroidal vascular disorders. Prog Retin Eye Res 2018;67:30-55.
10. Laíns I, Wang JC, Cui Y, et al. Retinal applications of swept source optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). Prog Retin Eye Res 2021;84.
11. Choi W, Moult EM, Waheed NK, et al. Ultrahigh-speed, swept-source optical coherence tomography angiography in nonexudative age-related macular degeneration with geographic atrophy. Ophthalmology 2015;122:12:2532-2544.
12. Garg I, Uwakwe C, Le R, et al. Nonperfusion area and other vascular metrics by wider field swept-source oct angiography as biomarkers of diabetic retinopathy severity. Ophthalmology Science 2022;2:2.
13. Lu Y, Cui Y, Zhu Y, et al. Quantitative wide-field swept-source optical coherence tomography angiography and visual outcomes in RAO. Clinical Ophthalmology 2023;17:2505-2513.
14. Sampson DM, Dubis AM, Chen FK, Zawadzki RJ, Sampson DD. Towards standardizing retinal optical coherence tomography angiography: A review. Light Sci Appl 2022;11:1.
15. Garg I, Miller JB. Semi-automated algorithm using directional filter for the precise quantification of non-perfusion area on widefield swept-source optical coherence tomography angiograms. Quant Imaging Med Surg 2023;13:6:3688-3702.
16. Lu Y, Cwang J, Zeng R, et al. Quantitative comparison of microvascular metrics on three optical coherence tomography angiography devices in chorioretinal disease. Clinical Ophthalmology 2019;13:2063-2069.

Strategies to boost **profitability and efficiency** in your practice

Eye care practices are navigating a complex landscape of rising patient volumes, persistent staffing shortages and increasing operational demands. At the same time, the financial strain from managing high-cost medications, frequent reimbursement denials and supply chain disruptions continues to mount, directly impacting your ability to deliver consistent, high-quality patient care.

Amy Valley, Vice President of Strategic Roadmap & Execution at Cardinal Health, works with hundreds of practices nationwide, and sees these challenges firsthand.

"Without the right systems in place, it's harder than ever to deliver the level of care patients deserve," said Valley. "Managing these dynamics while maintaining day-to-day operations requires more than just resilience — it demands smarter systems and integrated support."

By adopting the following strategies, fueled by advanced solutions and support from Cardinal Health, your practice can optimize drug and medical supply management, streamline workflows, maximize reimbursement and stay ahead of change, so you can focus on what matters most: patient care.

Use a single source for pharmaceuticals and medical supplies, and harness the aggregated purchasing power of a specialty GPO

Cardinal Health can serve as a streamlined, reliable, single solution for specialty medications and medical supplies, eliminating the need to juggle multiple vendors.

"By using Cardinal Health as your single-source distributor and joining one of our affiliated specialty group purchasing organizations (GPOs), practices can benefit from unmatched, aggregated purchasing power," said Helen Mannhalter, Group Product Manager, Commercial Technologies at Cardinal Health. "Our Acuity™ GPO negotiates competitive contracts, discounts, and rebates on ophthalmology medications that individual practices would be hard-pressed to secure on their own."

Utilizing our integrated model, where Acuity™ GPO and distributor operate within the same organization, ensures seamless data flow and a single source of truth. This reduces discrepancies, enhances operational efficiency and simplifies inventory and financial management, which is especially important for high-cost therapies.

To help practices fully leverage their Acuity™ GPO contracts, Cardinal Health offers the GPO Contract Dashboard — a self-service tool that provides real-time visibility into contract performance and rebate opportunities. Since the dashboard is updated daily and integrated with Cardinal Health's distribution systems, it delivers accurate, actionable insights from a single source of truth.

Team of experts:

Amy Valley
Vice President of Strategic Roadmap & Execution

Helen Mannhalter
Group Product Manager, Commercial Technologies

Jeff Weaver
Group Product Manager, Commercial Technologies

Streamline specialty medication inventory management

"For many specialty practices, inventory represents one of the largest capital investments after payroll," said Jeff Weaver, Group Product Manager, Commercial Technologies at Cardinal Health. With shrinking margins and rising drug costs, there's no room for error. That's why managing high-cost medications is one of the most common pain points experienced by specialty physician practices."

Weaver says that technology-driven inventory management solutions help practices streamline operations and reduce administrative burden.

Cardinal Health™ RxID Select™ Platform provides full visibility into medication status across locations. Practices can reduce waste and spoilage by knowing exactly what's available and when it expires.

> "Inventory management isn't just about stock levels — it's about visibility, traceability and value. Our RxID Select™ Platform delivers all three, agnostic of your distributor," said Weaver.

RxID Select™ Platform enables practices to:

- Manage high-cost medications for fluctuating patient volumes
- Scan medications at receipt and dispense for full chain-of-custody tracking
- Access real-time inventory data across multiple locations
- Auto-adjust par levels based on dispense velocity, to match demand
- Prevent the dispensing of expired or recalled products
- Integrate with EHR (Electronic Health Record) or PMS (Practice Management System) systems for patient-level reporting and reduced manual errors

This automation helps reconcile discrepancies faster, reduces waste, and improves financial performance. "Inventory management isn't just about stock levels — it's about visibility, traceability, and value. Our RxID Select™ Platform delivers all three, agnostic of your distributor," said Weaver.

Leverage Advanced Practice Analytics to improve the financial and operational health of your practice

Understanding cost drivers and performance metrics has become increasingly vital — not only for internal operations, but also to empower you to drive better negotiations with payers.

"Inventory data is just one part of your practice's much larger operational picture. You can only benefit from the true value of analytics when inventory and dispense records are integrated with financial data, like reimbursement trends, purchasing history and GPO contract terms," said Mannhalter. "This comprehensive view is where platforms like Advanced Practice Analytics deliver transformative impact for specialty physician practices."

By connecting key data streams, Advanced Practice Analytics provides you with a 360-degree view of practice operations, including inventory dispense activity, purchasing and reimbursement records, GPO contract pricing, claims and billing data.

Beyond billing, Advanced Practice Analytics can empower your practice to:

- Monitor clean claim rates, by payer
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- Denial management
- Accounts receivable (AR) follow-up
- Provider enrollment and credentialing
- Benefits verification and prior authorization
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- Payer contracting support

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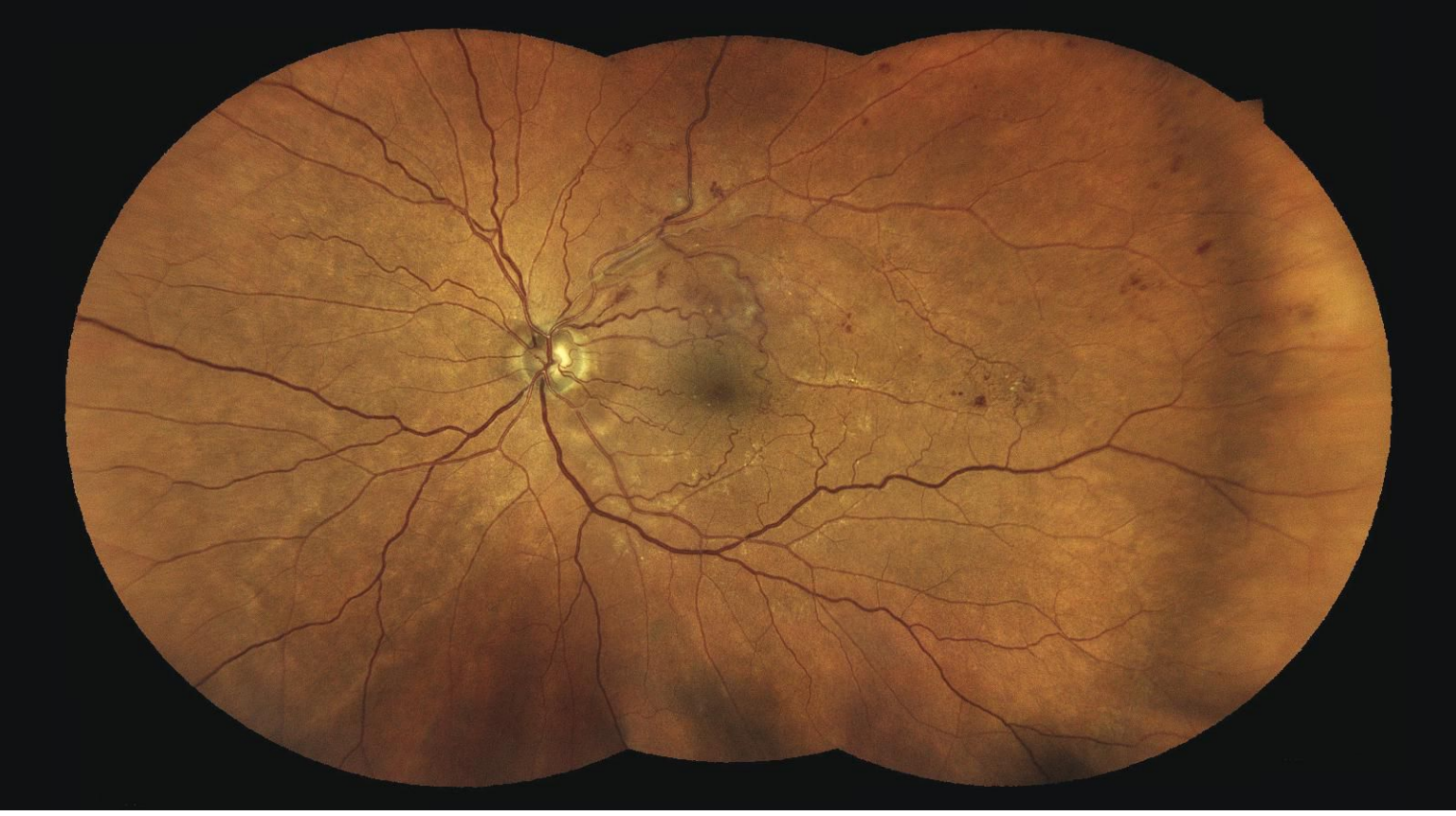

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