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EQUITY IN SIGHT:

Addressing Disparities with Advanced Treatment Approaches

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Content Source

This continuing medical education (CME) activity captures content from a live-virtual symposium.

Activity Description

This supplement summarizes a discussion on health equity in retinal care.

Target Audience

This certified CME activity is designed for retina specialists.

Learning Objectives

Upon completion of this activity, the participant should be able to:

- **Examine** the influence of social determinants of health (SDOH) on access to retinal disease care
- **Assess** the impact of social determinants of health on patient adherence to treatment
- **Develop** strategies to reduce disparities in the management of retinal diseases by improving access and adherence to treatments in historically marginalized populations
- **Compare** the efficacy and outcomes of treatment across different racial and socioeconomic populations with age-related macular degeneration
- **Compare** the efficacy and outcomes of treatment across different racial and socioeconomic populations with diabetic macular edema

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PRETEST QUESTIONS

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1. Please rate your confidence in your ability assess the impact of social determinants of health on patients with retinal diseases (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. A 54-year-old Hispanic immigrant with type II diabetes presents for follow-up after his third bevacizumab injection 1 month prior. His VA remains 20/50 OD and 20/60 OS, but OCT shows persistent diabetic macular edema (DME) OU. He is unsure about his blood sugar and blood pressure (BP) control, and he has not been checking his sugars regularly. In-office BP is 161/92. Which of the following is the most important next step in managing this patient?

a. Coordinate referral to local PCP for management of diabetes and hypertension
b. Switch to aflibercept 2 mg injections every 4 weeks, as bevacizumab has been ineffective
c. Switch to faricimab injections every 4 weeks, as bevacizumab has been ineffective
d. Provide the patient with reading materials to educate him on his disease state

3. A 45-year-old African American man with moderate nonproliferative diabetic retinopathy and DME OD presents for delayed follow-up. He is phakic with normal IOPs OU. His VA declined from 20/30 to 20/80 OD since his last visit 5 months prior, when he had minimal macular edema and received aflibercept 2 mg for maintenance. OCT now shows worsening intraretinal cysts. He has a history of missed appointments and reschedules only when his vision worsens. He works 10-hour shifts Monday-Friday and must request time off 2 months in advance. You plan to inject aflibercept 2 mg today. What is the next best step in treating this patient?

a. Educate the patient about importance of regular follow-up in the treatment of diabetic retinopathy to improve treatment adherence
b. Switch to intravitreal triamcinolone injections for future injections to increase treatment durability
c. Switch to aflibercept 8 mg for future injections to extend the patient's treatment interval
d. Schedule future visits at least 2 months in advance to accommodate his work schedule

4. A 49-year-old Hispanic woman, with poorly controlled type II diabetes since immigrating 8 months ago, presents with blurry vision OU. Her teenage daughter assists with communication. She has no history of ocular surgery. VA is 20/60 OD and 20/25 OS. Fundus exam reveals dot-blot hemorrhages in all quadrants with intraretinal microvascular abnormalities OU, but no neovascularization. OCT reveals central intraretinal cysts OD and no central edema OS. You proceed with a bevacizumab injection OD. Which of the following is the LEAST APPROPRIATE action to aid patient adherence to care?

a. Provide Spanish-language materials explaining diabetic retinopathy and treatment options
b. Use a trained interpreter during visits to improve communication and explain treatment plans
c. Play an educational video on diabetic retinopathy during numbing to reinforce treatment importance
d. Give a Spanish-language after-visit summary with the next appointment to encourage follow-up

5. In a meta-analysis of the RIDE and RISE trials, which patient population was found to have significantly lower visual acuity gains compared to the White patient population?

a. Asian
b. Black
c. Hispanic
d. No difference between racial groups

Equity in Sight: Addressing Disparities with Advanced Treatment Approaches

Patient Presentation to Clinic and Access to Care

Which demographic fault lines become apparent when we explore the data related to retinal disease?

BY JENNIFER I. LIM, MD, FASRS, FARVO

Health equity is achieved when all individuals, irrespective of race, sex, sexual orientation, disability status, socioeconomic standing, geographic location, or other societal factors, possess fair and just access, opportunity, and resources needed to attain their highest potential for health. While this ideal is fundamental, the reality in the United States, particularly within eye care, falls short. Persistent disparities exist in access to care, treatment adherence, and outcomes for significant retinal diseases such as diabetic retinopathy (DR), diabetic macular edema (DME), and neovascular age-related macular degeneration (AMD), disproportionately affecting minority and underserved populations. These inequities often lead to delayed diagnoses, more severe disease levels at presentation, and ultimately, worse vision outcomes. Addressing the complex interplay of social determinants of health (SDOH) is crucial to leveling the playing field in retinal care.

DISPARITIES IN DISEASE PREVALENCE AND PRESENTATION

Evidence clearly demonstrates that the burden of diabetic eye disease is not evenly distributed across populations. An analysis of data from the American Academy of Ophthalmology IRIS Registry (Intelligent Research in Sight) revealed that the prevalence of DR and DME is greater among Black and Hispanic patients in the United States compared to White patients.[1] Furthermore, the risk of experiencing sustained vision loss from these conditions is higher not only for Black patients but also for Asian and female patients when compared to their White and male counterparts.[1]

The Hispanic population, the largest minority group in the United States, faces particularly high rates of diabetes—80% higher in adults and five times higher in children compared to non-Hispanic White individuals.[2] This minority group also bears a 66% greater risk of developing type 2 diabetes and often experiences worse health outcomes following diagnosis compared to non-Hispanic Whites.[3] Data from the IRIS Registry further corroborates this, indicating that Black and Hispanic patients often present with worse baseline visual acuity and greater DR severity compared to White or non-Hispanic patients.[4] Socioeconomic factors compound these racial and ethnic disparities. Studies have shown higher rates of DR among individuals lacking a high school education or those within lower income brackets.[5] Patients utilizing Medicaid tend to have lower baseline visual acuity than those with Medicare or private insurance.[5] Lower socioeconomic status is also associated with presenting at a more advanced stage of AMD, particularly in the first affected eye, suggesting delayed entry into the health care system for initial diagnosis.[6]

BARRIERS TO SCREENING AND ACCESS

Effective management of retinal diseases hinges on timely screening and access to care, yet significant barriers exist, especially for marginalized groups. Diabetic retinopathy screening rates remain low overall in the United States, and certain demographics are less likely to receive necessary eye care.[7]

A cohort study focusing on youths with diabetes eligible for DR screening found that those who had never received a diabetic eye exam were more likely to be non-White, have type 2 diabetes, be covered by Medicaid or public insurance, belong to households with lower annual incomes (≤$25,000), and have parents with a high school education or less.[8] Critically, even after statistical adjustments for insurance status, household income, and parental education level, minority youths remained less likely to have undergone a previous diabetic eye exam and were more likely to have DR (OR 0.29).[8] This persistence suggests that factors beyond simple economics or insurance coverage, possibly related to cultural or community-specific access issues, contribute to these screening gaps. The trend continues into adulthood, with data indicating that minority populations aged 18 years to 64 years are less likely to receive eye exams compared to their White counterparts (adjusted OR 0.61-0.75).[9] These low screening rates among minority patients are often associated with insufficient education regarding diabetes-related complications, highlighting a crucial area for intervention.[10]

GEOGRAPHIC AND SYSTEMIC INFLUENCES

Access challenges are further exacerbated by geographic and systemic factors. Secondary analyses of the US National

Ambulatory Medical Care Surveys (2012-2014) indicated that Black patients generally had poorer diabetes control compared to White patients. This racial gap was notably larger in rural areas compared to urban settings.[11] Patients residing in rural areas often face a confluence of barriers, including longer travel times to appointments, a lower density of available practitioners and health care facilities, and limited access to healthy food options. These populations are also more likely to have less than a high school education and lower household incomes.[11] Compounding these issues, health care practitioners in rural settings may be less likely than their urban counterparts to engage in discussions about diabetes prevention and risk reduction strategies, such as dietary counseling and physical activity recommendations.

MEDICAID AND UNDERINSURED PATIENTS

Health insurance status plays a significant role in how and whether patients access ongoing retinal care, particularly for conditions requiring intensive treatment like DME. The 2021 study by Malhotra et al found that a higher proportion of Black and Hispanic patients receiving anti-VEGF treatment for DME were covered by Medicaid compared to their White and non-Hispanic counterparts.[5] Importantly, patients covered by Medicaid presented with worse DR severity and worse baseline visual acuity at the time treatment was initiated.[5] Interestingly, the study also revealed a complex interaction: when stratified by both race/ethnicity and insurance, Hispanic patients holding private insurance had worse baseline and 5-year visual acuity outcomes than non-Hispanic patients covered by Medicaid, suggesting other unmeasured factors may be at play.[5]

Cost-sharing itself presents a barrier; a retrospective cohort study by VanderBeek et al published in 2020 utilized medical claims data from 6,220 DME patients and determined that having any type of copay significantly lowered the odds of a patient receiving treatment and reduced the likelihood of follow-up visits.[12] However, this study did not find an association between having a high-deductible plan nor association between the specific type of insurance plan and the initiation of treatment.

Roundtable Discussion: Strategies for Equitable Access

Dr. Lim: We've discussed the significant impact of SDOH and disparities on access to retinal care and patient presentation. Beyond identifying these complex issues, what practical steps can clinics implement to start bridging these gaps for patients facing SDOH barriers?

Jeremiah Brown Jr, MD, MS, FASRS: A crucial first step is fostering a welcoming and positive clinical environment. Many patients, especially those with chronic conditions like diabetes, may have had negative experiences elsewhere or feel judged. Using positive, constructive language, focusing on partnership in monitoring their vision, and avoiding labels like "noncompliant" or "poorly controlled" can make a significant difference. Language is incredibly important. Education is also key, right from the first visit. It's surprising how many patients aren't aware that diabetes can affect their eyes. Ensuring that initial conversation happens in an encouraging way sets a better tone for future engagement.

Rahul N. Khurana, MD, FASRS: As retina specialists, we often see these patients more frequently than their primary care physicians due to the nature of treatments like anti-VEGF injections. This gives us a unique opportunity to build rapport and impact their overall health, not just their eyes. We need to proactively inquire about potential barriers (eg, transportation, work schedules, cost) rather than assuming access is straightforward. Acknowledging these challenges is the first step toward finding solutions. Being aware of the SDOH affecting our specific patient population allows us to tailor our approach.

Dr. Lim: We all agree that poor health literacy is a major—perhaps the primary—hurdle. Given the time constraints in busy clinics, how can we effectively improve patient understanding and empower them about their condition and the importance of adherence?

Dr. Khurana: It's a challenge, but empowering patients is vital. When patients truly understand the gravity of their condition and why treatment is necessary, the perceived "treatment burden" often diminishes. They become motivated to attend frequent appointments because they grasp the stakes. We can leverage those frequent visits for brief, repeated educational moments, reinforcing key messages. Using clear, simple language, perhaps visual aids, and checking for understanding is important. It's about making education an ongoing dialogue, not just a one-time event. The goal is to shift them from passive recipients to active partners in their care.

Dr. Brown: Shared decision-making is key. When patients feel like allies in their care rather than being lectured, they are more engaged. Even if time is short, taking a moment to ask about their understanding or concerns reinforces that partnership. Health literacy isn't just about knowledge; it's about enabling patients to use that knowledge to make informed decisions and navigate the health system. If they don't understand why the follow-up is critical, even if they have insurance and transport, they may still miss appointments.

Dr. Lim: Finally, considering practical challenges like transportation, childcare, or needing to take time off work—factors that disproportionately affect patients with lower socioeconomic status. How can practices adapt structurally or better leverage resources like social workers to mitigate these barriers?

Dr. Brown: Integrating social workers or navigators into the clinic workflow can be incredibly valuable. They can connect

patients with resources for transportation assistance, help navigate insurance complexities or identify community support programs. Clinics might also need to evaluate their own accessibility. Are evening or weekend hours feasible? Even small adjustments can make a difference for patients struggling to balance work and health care needs.

Dr. Khurana: Exactly. Having dedicated personnel, like a social worker, who can address these not-medical-yet-critical barriers frees up clinical staff and physicians to focus on medical care. It requires investment and a systems-level approach within the practice or health system. Awareness is the starting point but actively implementing strategies like involving social support and potentially adjusting clinic operations are necessary steps to truly improve access for everyone.

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Treatment Adherence

What do the data tell us about how well (or how poorly) patients comply with treatment recommendations?

BY RAHUL N. KHURANA, MD, FASRS

Retina specialists encounter insurance-related barriers to health equity on a routine basis. These factors include step therapy mandates, too few insurance coverage options with low out-of-pocket expenses, and increased enrollment in Medicare Advantage (ie, Medicare Part C) plans.[1] The 2024 Preferences & Trends (PAT) Survey from the American Society of Retina Specialists found that a majority of US retina specialists reported that step therapy protocols have led to a lack of anatomic improvement, anatomic worsening, a lack of vision improvement, and worsening vision.[1]

Step therapy requirements present a number of barriers. Treatment decisions that providers are best equipped to handle are instead overridden by insurance carriers. When providers have the choice made for them, the relationship between patient and provider deteriorates. Delays in administering appropriate care for patients may lead to, as the above PAT survey data suggests, worse visual and anatomic outcomes in some patients.

A 2022 study from the DRCR Retina Network that randomly assigned patients with diabetic macular edema (DME) to bevacizumab or aflibercept 2 mg allowed patients in the bevacizumab group to move to aflibercept therapy if they met protocol-defined criteria for switching.[2] After 2 years, 70% of patients in the bevacizumab-first group switched to aflibercept therapy. Of course, within this study protocol, no prior authorization filings were required and barriers to switching were limited only by patient-centric factors rather than insurance-related factors, which means that real-world switching rates may be lower than the 70% found in this study. Still, this rate testifies to the frequency with which retina specialists switch patients off of mandated therapies.

Step therapy programs require patients to "fail" a less expensive therapy before a more expensive therapy can be administered. Frustratingly, different carriers have various definitions of failure; others have no clear definition at all. Parameters defining treatment failure often ignore patient-centered metrics with real-world consequences in favor of extreme limits. Medicare Advantage plans in Idaho, Montana, and Oregon, for example, require either a loss of at least 15 letters or proven failure after three doses of the agent mandated by step therapy requirements before a medication switch.[3]

As enrollment in Medicare Advantage programs increases at the expense of Medicare fee-for-service programs, retina specialists can expect to encounter more frequent roadblocks to administering the care they believe best suits a given patient. Medicare Advantage plans often appear initially attractive to patients, particularly those on fixed incomes, because of their low premium costs. However, patients often do not realize that the limitations associated with Medicare Advantage plans, such as limited doctor networks and restrictive formulary plans (including step therapy protocols), may frustrate their efforts to access care.

LOSING PATIENTS TO FOLLOW-UP IN DIABETIC EYE DISEASE

It is difficult for providers in busy clinics to keep track of patient compliance. To explore the rate at which patients with proliferative diabetic retinopathy (PDR) are lost to follow-up (LTFU), my colleagues and I turned to the American Academy of Ophthalmology (AAO) IRIS (Intelligent Research in Sight) Registry, which comprises

data from approximately 3,000 ophthalmic practices, nearly 16,000 ophthalmologists, and more than 79 million patients.[4]

This analysis included 73,595 eyes in 56,590 patients with PDR diagnosed from 2013 to 2015 and treated between 2013 to 2018. Patients were considered LTFU if they were not seen within 1 year of their most recent injection or panretinal photocoagulation (PRP) treatment. Specific factors linked to increased or decreased LTFU status are identified in the Table.

TABLE. FACTORS FOR HIGHER OR LOWER LTFU RATES AMONG PATIENTS WITH PDR IN AN IRIS REGISTRY STUDY

Factors Linked to Increased LTFU Rates		Odds Ratio
Race/Ethnicity	Black/African American	1.28
	Hispanic	1.28
	Native American/ Alaska Native or Native Hawaiian/Other Pacific Islander	2.69
Baseline VA (vs 20/40 or Better)	Baseline VA 20/50 to 20/200	1.25
	Baseline VA worse than 20/200	1.22
Factors Linked to Decreased LTFU Rates		**Odds Ratio**
Insurance Type (vs Private Insurance)	Medicare Fee-for-Service	0.71
	Medicare Managed	0.66
Geographic Location (vs. South)	Midwest	0.72
	West	0.83

Source: Khurana RN, Wang JC, Zhang S, et al. *Ophthalmol Retina.* 2024;8(10):953-961.

Black patients, Hispanic patients, and patients who were Native American or Pacific Islander were more likely to be LTFU, as were patients whose baseline VA was 20/50 or worse. Patients with Medicare fee-for-service plans and Medicare Managed plans had lower rates of LTFU compared with private insurance plans. Geography mattered, too: patients in the South were more likely to be LTFU than patients in the Midwest and West.

These findings complement findings from Obeid et al in 2018.[5] In that study of 2,302 patients with PDR, 584 patients (25.4%) were LTFU over approximately 4 years. Patients who underwent PRP were more likely to be LTFU than those undergoing anti-VEGF therapy (28.0% LTFU rate vs 22.1% LTFU rate, $P < .01$). Younger age was determined to be a risk factor for LTFU status, with patients 55 and younger achieving LTFU status in 28.1% of cases, patients between 56 and 65 years achieving LTFU status in 27.0% of cases, and patients older than 65 achieving LTFU status in 20.9% of cases ($P < .01$). LTFU status was lowest among White patients (19.4%) compared with 38.0% for Hispanic/Native American/Pacific Islander patients, 30.2% of Black patients, 19.7% for Asian patients, and 34.9% for patients of unreported race ($P < .01$).[5]

Interestingly, economic indicators also predicted LTFU status.[5] Lower regional adjusted gross income (AGI) levels were linked with higher LTFU rates. Patients with AGI $40,000 or less had LTFU rates of 24.0%, while those with AGI $41,000 to $80,000 and those with AGI above $80,000 had LTFU rates of 24.0% and 19.7%, respectively ($P < .01$).

A third study exploring LTFU rates in PDR patients helps flesh out the dynamics around potential LTFU risk factors.[6] That study followed 418 patients with PDR from 2014 to 2018 at a single center community hospital. In all, 61% were LTFU. Among risk factors identified for LTFU status were patients for whom English was not their primary language ($P < .01$), age 56 to 65 years ($P = .01$), and age older than 65 years ($P = .03$). Distance from the care setting was also a factor, with patients who lived within 20 miles of the institution having higher LTFU rates ($P < .01$).[6]

FOCUSING ON ANTI-VEGF THERAPY

If we widen the aperture of this discussion beyond a demographics-based framework, we see that compliance with recommended treatment schedules is a problem for all patients in general. A 2021 systemic review in *Ophthalmology* found that 50% of patients with wet age-related macular degeneration (AMD) who were treated with anti-VEGF agents had stopped presenting to the clinic after 24 months.[7] Further, the rate of nonadherence to a recommended dosing schedule was, depending on how nonadherence was defined, 32% to 95%.

LTFU rate among patients with wet AMD (N = 201) in a single-center French study was 57% at 5 years.[8] Significant factors for being LTFU in that study included older age at baseline (88.2 years vs 76.5 years, $P < .01$), worse BCVA at baseline (42.5 letters vs 51.0 letters, $P = .02$), and longer distance from the care setting (132 km vs 17.1 km, $P < .01$).[8]

Results from a 2023 IRIS Registry study were more encouraging than the two studies above, at least for LTFU rates in the general population.[9] That study examined 156,327 patients with wet AMD who were first dosed from 2013 through 2015 and were followed through 2019. Researchers examined both LTFU rates (defined as no follow-up within 12 months from the most recent anti-VEGF injection) and nonpersistence rates (defined as no follow-up within 6 months from the most recent anti-VEGF injection).[9]

Researchers found that 11.6% of patients were LTFU.[9] Age was found to be a risk factor, with those aged 81 to 84 years being LTFU more than 2.5 times than those aged 70 and younger. Odds of being LTFU were 1.3 times higher for Black patients than White patients. Patients with Medicaid were likelier to be LTFU compared with those with private insurance; those with Medicare fee-for-service insurance were less likely to be LTFU than those with private insurance. Disease status and male sex were closely linked with LTFU.[9]

Nonpersistence data showed that 14.3% of patients did not undergo follow-up with 6 months of their most recent injection.[9]

Again, patients who were 81 to 84 years older were more likely (odds ratio, 2.13) than patients 70 or younger to be categorized as nonpersistent. Black patients 1.38 times more likely than White patients to be nonpersistent, and Hispanic patients were 1.13 times more likely.

SOCIOECONOMIC FACTORS

Costs are a common barrier to treatment access. Even something as small as a copay may prevent patients from seeking care they require, which may account for higher LTFU rates among patients with private insurance compared with Medicare.[10] In the case of retinal drugs, copays may be so high that they represent a major barrier to care. Patients who struggle to fund copays could enroll in copay assistance programs, but that, too, represents a barrier. When we consider the monetary costs of care, we might better understand why patients fail to live up to the high bar set for them regarding treatment compliance.

Getting time away from work, especially for working-age patients with diabetes, may also be a barrier to care for many patients.[10] Such patients may be willing to put off appointments for weeks or months so they do not have to use vacation time or skip work shifts.

Transportation to and from clinics is a high barrier for some patients.[10] Patients who are unable to transport themselves to the clinic due to visual disruption or some other reason may choose to pay for transportation themselves (which comes with out-of-pocket costs) or may ask a caregiver to provide transportation (which requires a caregiver to make themselves available for such services).

If retina specialists learn about barriers to care, they should do their best to find solutions around those issues. If a patient is visiting a clinic with multiple locations, for example, can the office recommend visiting a clinic closer to their house? If the patient has difficulty paying for a copay, can the clinic facilitate enrollment in a copay assistance program? Finding solutions for patients is part of providing care.

Panel Discussion: Treatment Adherence

Dr. Khurana: Some patients are skeptical to engage the health care system at all. How do we lower barriers for these patients?

Jeremiah Brown Jr, MD, MS, FASRS: Part of the solution is to develop a relationship with patients, so that they stop thinking of the health care system as a faceless entity and start thinking of their relationship with specific providers. When patients with DR or DME visit my clinic repeatedly, I congratulate them on showing up and caring for themselves. It's a small gesture that goes a long way. I also underscore that their improvement (if it's occurring) is linked with their persistence and remind them that skipping appointments because they feel their vision is okay threatens to derail the progress they've built.

Jennifer I. Lim, MD, FASRS, FARVO: I, too, encourage patients to keep returning for follow-up and also mention their positive results. Patients intuitively understand imaging results. I show patients a side-to-side comparison of their current OCT image and their baseline OCT image as well as their most recent visit. I point out how consistent therapy has resulted in anatomic stability. We do not always see significant differences month to month, which is why I prefer comparing their most recent visit to the baseline visit, where the differences are more pronounced. If the patient has a caregiver, I try to make sure that person is in the room so they can understand how important their support is to the patient's success.

Dr. Khurana: What do you do for patients facing barriers to care who don't have a care network to support them?

Dr. Lim: This is where introduction to a social worker can be key. If I'm able to, I will connect the patient with a social worker via my EHR so the patient gets into the system as quickly as possible. If monetary cost is the only barrier, then I will use sample doses, while my clinic staff helps with enrollment in a copay assistance program.

If a patient misses an appointment, my staff reaches out to the patient to find out what happened. Perhaps the patient got acutely sick or has a chronic condition that required attention at the time. It's especially worth finding out why a patient missed an appointment if they have a history of compliance.

Dr. Brown: Keeping hours that are later in the afternoon may help some patients get to the clinic. I think of those patients whose caregivers need to take time off work to get them to the office. If they can get an appointment at 4 pm, then maybe they'll only need to take a few hours off work rather than an entire day.

Dr. Khurana: It's easy to think that metrics about LTFU rates apply to the field in general but not our clinics in particular—no one wants to think that their patients are the ones who follow national trends. Plus, we often think that our clinics are so busy, how could someone possibly fail to show? I would encourage my colleagues to review LTFU rates at their offices to understand their patients' compliance rates. If indeed patients are less compliant than you assumed, it may be time to reassess your strategies and tactics.

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Treatment Outcomes

Zooming in on demographic breakdowns in clinical trial data.

BY JEREMIAH BROWN JR, MD, MS, FASRS

We are all familiar with the recurring, frustrating reality that outcomes seen in large clinical trials are rarely seen in real-world clinical settings. Reasons abound for this disconnect—the sample of patients in a study may not reflect the population to be treated at a future date, life events interfering with treatment that would eliminate a patient from a clinical trial don't make a patient ineligible for real-world treatment—but it nevertheless persists, and these disconnects sometimes manifest in demographic terms.

A post hoc analysis of the DRCR Retina Network Protocol T study (which assessed the effects of aflibercept 2 mg, bevacizumab, and ranibizumab for the treatment of diabetic macular edema [DME]) found that African American patients with DME demonstrated the largest reductions in central retinal thickness (CRT) among any racial/ethnic demographic group at 2 years. However, this same group experienced smaller visual acuity benefits (reduction of 2.4 letters) compared with White (reduction of 1.5 letters) and other-race patients (reference group; $P = .02$).[1]

Similarly, a 2021 retrospective cohort study found that Black patients with DME experienced lower odds of visual acuity improvement compared with White and Hispanic patients when dosed with one dose of bevacizumab (OR 0.48, $P < .01$) and three doses of bevacizumab (OR 0.34, $P < .01$).[2]

WHAT DO RETINA SPECIALISTS THINK?

When asked in the 2024 ASRS PAT Survey if there were racial or ethnic differences (irrespective of socioeconomic differences) in response to treatment of diabetic retinal disease, and if so, if treatments were tailored to racial or ethnic status, a majority (51%) of US respondents said they did not believe there was a difference.[3] A smaller group of respondents (29%) believed that differences existed but did not tailor treatments, while an even smaller group of respondents (17%) said they believed that differences existed and tailored treatments accordingly.

UNDERREPRESENTED MINORITY POPULATIONS IN CLINICAL TRIALS ASSESSING NEXT-GENERATION ANTI-VEGF AGENTS

A 2021 study that sought to describe the racial/ethnic composition of ophthalmology clinical trials from 2000 to 2020 found that Black and Hispanic patients were significantly underrepresented compared with White patients.[4] As such, researchers have sought to better understand outcomes of underrepresented minority populations enrolled in various studies.

The PHOTON study, which enrolled patients with wet age-related macular degeneration (AMD) and assessed aflibercept 8 mg every 12 (8q12) or 16 weeks (8q16) after three monthly doses versus aflibercept 2 mg every 8 weeks (2q8) after five monthly doses, assessed BCVA changes at week 96 among various demographic subgroups.[5] White patients in the 2q8, 8q12, and 8q16 groups gained 7.9, 9.3, and 8.2 letters, respectively. Meanwhile, Asian patients in the 2q8, 8q12, and 8q16 groups gained 8.1, 7.7, and 3.9 letters, respectively, suggesting that while Asian patients on aflibercept 2 mg showed similar results to White patients, those who were on aflibercept 8 mg showed less robust letter gains.

A comparison of Hispanic/Latino patients to non-Hispanic/Latino patients in PHOTON was more mixed: Hispanic/Latino patients gained 10.4 and 5.8 letters in the 8q12 and 8q16 groups, respectively, and non-Hispanic/Latino patients gained 8.6 and 7.8 letters, respectively.[5] Tellingly, African American patients in the study could not be evaluated as a group due to the small sample size, as fewer than 15 patients were enrolled in two of the cohort groups.

A subgroup analysis of Asian patients was performed in the PULSAR study, which compared aflibercept 2 mg and aflibercept 8 mg in 2q8, 8q12, and 8q16 groups for the treatment of wet AMD. Researchers found that Asian patients gained 9.3 and 8.8 letters from baseline at week 48 in the 8q12 and 8q16 groups compared to gains of 6.1 and 5.9 letters in the 8q12 and 8q16 groups in the overall population. By week 96, Asian patients in the 8q12 and 8q16 arms gained 8.9 and 7.2 letters, respectively, compared with 5.5 and 5.4 letters, respectively, in the overall population.[6]

The ELEVATUM trial was designed to improve understanding of the use of faricimab for the treatment of DME in underrepresented patients. The study aimed to enroll approximately 45% Black patients, 45% Hispanic patients, and 10% Native American/Alaska Native/Native Hawaiian or other Pacific Islander patients. Patients needed an HbA1c ≤10%, but to improve recruitment, 20% of enrolled patients were permitted to have an HbA1c of up to 12%. All patients had DME and were treatment naïve at baseline.[7] The study reduced treatment burden by extending treatment intervals, scheduling late-day appointments, offering transportation, and reimbursing patients for childcare expenses if assistance was used to cover parenting duties during an appointment.

Importantly, no new safety signals were observed in ELEVATUM, and faricimab was shown to be effective at treating all demographic groups in the study.[7] Hispanic patients gained 14 letters at 1 year, compared with 11 letters in Black patients. This may be because Hispanic patients presented with more severe disease at baseline, with mean 490 µm central subfield thickness

(CST) in Hispanic patients compared with mean 467 µm CST in Black patients.[7]

As clinical trials more closely consider the demographic composition of their enrollment population, we may gain deeper insights into the treatment responses of various populations. The trials above explored racial and ethnic breakdowns, and future studies may consider socioeconomic factors such as household income. Expect deeper conversations about the roles of these extra-clinical factors in the years to come.

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Case 1: A Compliant Patient Feels "Cured" and is Lost to Follow-Up

Dr. Khurana: A 43-year-old woman with diabetes was referred for a dilated exam in 2019. Her HbA1c was 6.9, and her VA was 20/20. She works full time and has private insurance. Dilated fundoscopic exam revealed scattered hemorrhages in all four quadrants, though not initially impressive (Figure 1). However, fluorescein angiography (FA) showed early and late-phase leakage indicating neovascularization elsewhere (NVE) in approximately four or five areas in the right eye (Figure 2). The left eye also showed areas of NVE superiorly and inferiorly, which dilated more in the late phases (Figure 2).

Initially, the patient chose observation but decided to start treatment a few months later. My colleagues treated her aggressively with combination therapy involving ranibizumab and panretinal photocoagulation (PRP). Over 21 months, the right eye received 13 injections plus PRP, and the left eye received 11 injections plus PRP. She was very compliant, attending appointments almost monthly.

After the 21 months of treatment, her VA remained 20/20 in both eyes. Color fundus photography (CFP) showed resolution of most hemorrhages and peripheral PRP scars, perhaps lighter than ideal (Figure 3). FA showed significant regression of NVE in the right eye. The left eye showed marked improvement, although some small areas of leakage persisted (Figure 4). The plan was observation with follow-up scheduled in a couple of months. Unfortunately, the patient did not return for 3.5 years, having seen no eye care professional during that time. She presented again reporting floaters in her left eye for a few weeks.

On examination upon return, her VA was 20/20 in the right eye but had dropped to 20/400 in the left eye. The right eye showed apparent fibrosis and NVE infratemporally, with other areas superotemporally and superonasally (Figure 5). The left eye showed marked progression with vitreous hemorrhage, preretinal hemorrhage, and a large area of NVE with fibrosis inferiorly, plus other areas superotemporally (Figure 5). FA confirmed active, worsened NVE in the right eye. The left eye showed leaking neovascularization and blockage from the preretinal hemorrhage.

Dr. Lim: What was the motivation to initiate PRP? Was it because the anti-VEGF wasn't effective initially, or was there concurrent diabetic macular edema (DME) being treated?

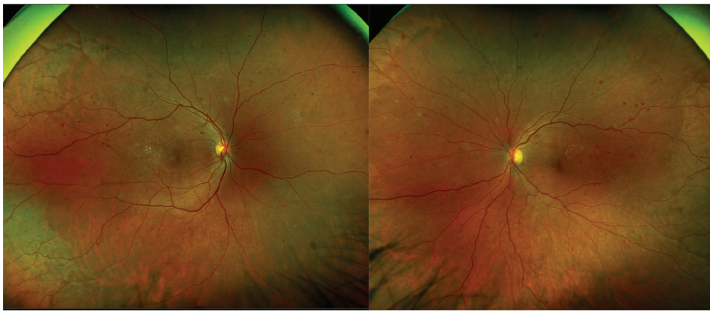

Figure 1. A 43-year-old woman with diabetes was referred for a retinal examination.

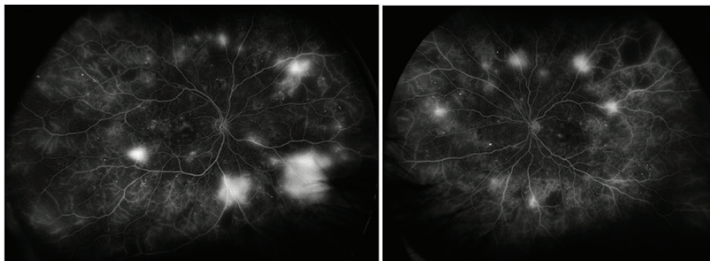

Figure 2. FA imaging revealed NVE in several areas in both eyes.

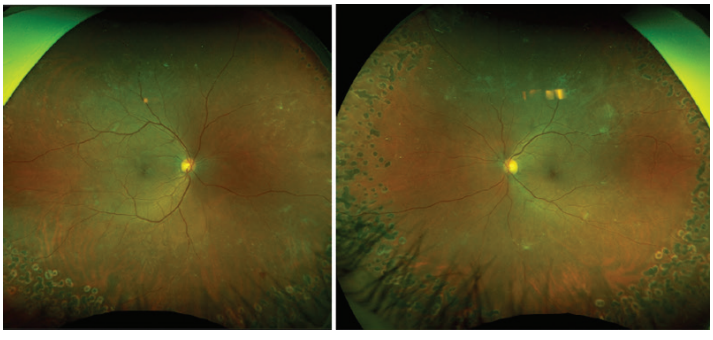

Figure 3. CFP after 21 months of treatment revealed peripheral PRP scars and hemorrhage resolution.

Dr. Brown: Also, I am surprised by the number of injections. This would make me think the patient has DME.

Dr. Khurana: There was no DME. I believe the treating physician's plan was always combination therapy, but the exact history of treatment was unclear. The patient started with anti-VEGF

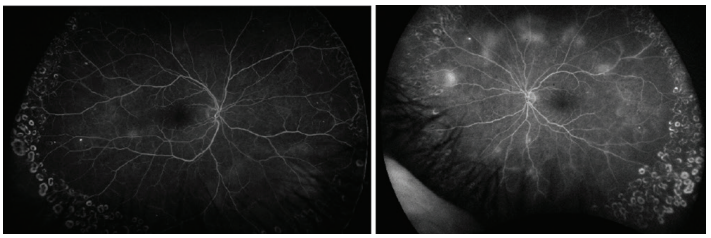

Figure 4. NVE in the patient's right eye, as depicted on FA, regressed after 21 months of treatment. Some leakage persisted in the left eye, but the patient's anatomy was nevertheless significantly improved.

injections, followed by PRP; the provider likely performed a few injections, followed with laser, perhaps reassessed with FA, and, upon observing persistent leakage, continued injections until the neovascularization stabilized.

Dr. Lim: Dr. Brown, do you use combination therapy, even though there's limited research proving its efficacy?

Dr. Brown: I do use combination therapy, although perhaps not with this many injections unless necessary, as this case seems to indicate it was.

Dr. Lim: I use combination therapy if both DME and severe proliferative diabetic retinopathy (PDR; florid neovascularization) are present. Otherwise, I use anti-VEGF alone. In a case like this with several areas of NVE, I would consider combination therapy. After achieving a response of PDR to anti-VEGF treatment, I might add PRP and would consider factors such as risk for nonadherence, comorbidities, travel distance, or inability to attend frequent appointments.

Dr. Khurana: Interestingly, this patient was at first extremely compliant, attending monthly visits for injections. The high number of injections likely resulted from interim FAs showing persistent leakage.

Dr. Lim: I don't typically repeat FA when treating PDR. When would you consider repeating FA?

Dr. Khurana: I perform repeated FA to confirm resolution. Otherwise, how do you decide when to stop treatment for PDR?

Dr. Lim: I assess clinically. Even after laser, lesions which are fibrotic and not active can show leakage on FA. So, I typically don't repeat FA unless I am evaluating ischemia.

Dr. Brown: I also assess clinically after about three or four injections and completion of PRP, which I might divide into two sessions. If the clinical appearance is good, I monitor. I'd only repeat FA if another event occurs.

Dr. Khurana: My experience is that clinically, things often look

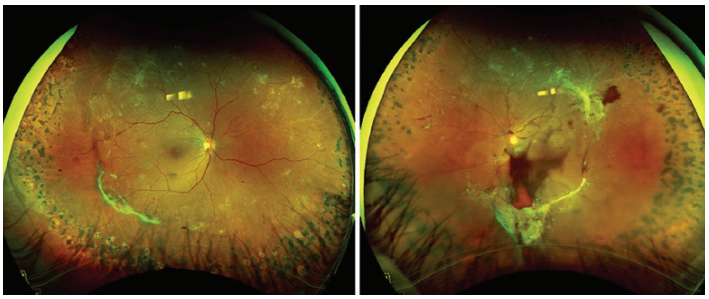

Figure 5. CFP showing fibrosis and infratemporal NVE in the right eye, and vitreous hemorrhage, preretinal hemorrhage, and inferior and superotemporal fibrotic NVE in the left eye.

improved after injections, with hemorrhages resolving. CFP might suggest severe nonproliferative disease, but FA often reveals persistent leakage. I'd argue for interim FA because you might see more activity. Whether to treat that leakage is debatable, but my concern is that untreated NVE can lead to poor outcomes. I also use ultra-widefield imaging, even nonangiographic photos, to monitor the periphery.

Despite initially presenting as a highly compliant patient, this case highlights what can happen when a seemingly well-managed, compliant patient is lost to follow-up (LTFU) for an extended period.

Dr. Lim: It shows that even compliant patients without typical high-risk factors can be LTFU, perhaps becoming complacent when doing well. The PRP wasn't fully extensive, but it underscores the ongoing risk in diabetic patients. Did she have an intervening illness?

Dr. Khurana: No, I asked her. She reported feeling she was doing well, seeing 20/20 throughout treatment, and felt "cured," so she didn't follow-up. While she faced some challenges being a working individual, these didn't prevent her intensive 21-month treatment. It's sobering because registry data often show patients receive treatment for 1 to 2 years and then get lost, even those doing well. Her left eye outcome is now poor, and the right eye, though 20/20, is at high risk for progression.

Dr. Brown: Regarding the PRP treatment as shown in the images, I typically pattern into the arcades, maybe less densely now with anti-VEGF availability, but I still bring it quite far in.

Dr. Khurana: I agree the PRP appears light. I try to spare some peripheral vision by not going all the way to the arcades. A challenge with anti-VEGF is that it makes things look good, but if treatment stops without a long-term solution like adequate PRP, I worry about recurrence, as seen here. She looked excellent immediately posttreatment, then deteriorated significantly without follow-up.

Dr. Lim: The take-home message should be emphasizing the need for continued follow-up, even when patients are doing well. We need to remind patients consistently about the importance of follow-up visits and ideally have systems for tracing patient follow-up and contacting them if they miss a visit.

Case 2: DME Treatment Extension from 4- to 12-Week Interval

Dr. Brown: A 46-year-old African American woman presented initially with 20/50 VA and a central subfield thickness (CST) of 446 µm due to diabetic macular edema. She has diabetes mellitus but no hypertension. At her first visit, fluorescein angiography (FA) showed significant leakage temporal to the fovea, but fortunately no significant neovascularization or capillary dropout (Figure 1). Optical coherence tomography (OCT) revealed foveal cysts and some subretinal fluid directly beneath the fovea. Her baseline VA was 20/50 (Figure 2). She was started on faricimab.

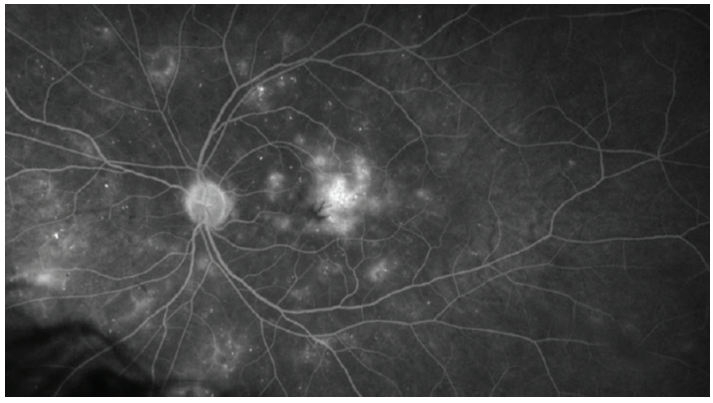

Figure 1. FA imaging showed leakage temporal to the fovea.

Four weeks later, her VA improved to 20/40, and her CST decreased by 165 µm (Figure 3). By week 16, her VA remained 20/40, with further improvement of intraretinal edema seen on OCT. Some hyperreflective foci were still present but improving. Tracking the progression out to week 16 shows a steady reduction in edema (Figure 3). At week 20, we extended her treatment interval to every 8 weeks. Her foveal contour was nearly normal on OCT (Figure 4). The FA at this point showed remarkable improvement compared to baseline.

This is a case where patient adherence leads to positive reinforcement. At the Q8 week interval, her VA improved to 20/25, and the hyperreflective foci resolved. At the 1-year mark, we extended her interval to every 12 weeks. Her VA remains 20/25. There might be a small amount of leakage starting to reappear temporally on FA, but clinically she is doing very well.

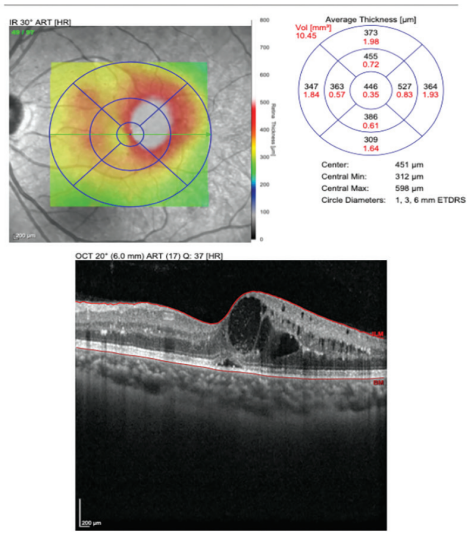

Figure 2. OCT imaging showed foveal cysts and an area of subretinal fluid directly beneath the fovea. CST was measured at 446 µm CST.

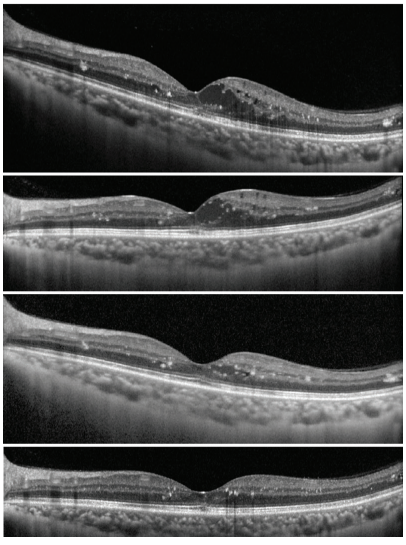

Figure 3. OCT images at weeks 4, 8, 12, and 16 (top to bottom).

Dr. Khurana: This case highlights important points. There's sometimes a misconception that only a few initial injections are needed. However, in many cases, intensive treatment in the first year leads to sustained improvement and a reduced treatment burden in subsequent years. It requires commitment through that first year. It's easy to feel a treatment is failing if fluid persists after three injections, but the reality is often that continued, committed treatment is necessary. As Dr. Brown showed, this commitment can lead to excellent outcomes.

Dr. Lim: Exactly. It's vital to manage patient expectations and prevent injection fatigue by emphasizing the long-term benefits, or the "light at the end of the tunnel." Also, while this patient achieved a Q12 interval, not everyone will reach that point. We need to be clear with patients that while a certain percentage might achieve extended intervals, their individual course is not known. We must let the patient know that we must monitor her/his progress and adjust the plan accordingly.

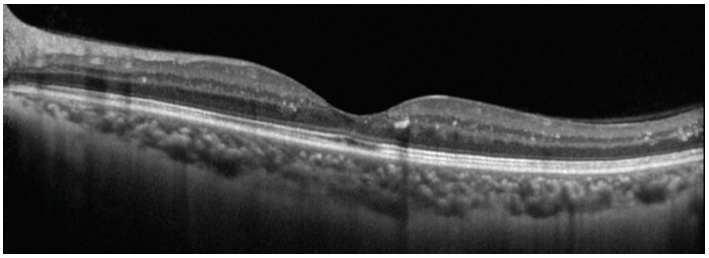

Figure 4. At week 20, foveal contouring had returned to healthy levels. The patient's CST was 220 µm and her VA was 20/25.

Dr. Brown: This case demonstrates why maintaining follow-up and encouraging patients is crucial, as excellent results are achievable within a year. To Dr. Khurana's point, keeping this patient on track through the first 12 months may lay a foundation for long-term success.

Equity in Sight: Addressing Disparities with Advanced Treatment Approaches

Release Date: May 2025
Expiration Date: June 2026

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DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ >20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week (with the disease targeted in this educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
____ >50

Region
___ Midwest
___ Northeast
___ Northwest
___ Southeast
___ Southwest

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	**Agree**	**Neutral**	**Disagree**
Examine the influence of social determinants of health (SDOH) on access to retinal disease care	_____	_____	_____
Assess the impact of social determinants of health on patient adherence to treatment	_____	_____	_____
Develop strategies to reduce disparities in the management of retinal diseases by improving access and adherence to treatments in historically marginalized populations	_____	_____	_____
Compare the efficacy and outcomes of treatment across different racial and socioeconomic populations with age-related macular degeneration	_____	_____	_____
Compare the efficacy and outcomes of treatment across different racial and socioeconomic populations with diabetic macular edema	_____	_____	_____

POSTTEST QUESTIONS

Please complete at the conclusion of the activity.

1. Based on this activity, please rate your confidence in your ability assess the impact of social determinants of health on patients with retinal diseases (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. A 54-year-old Hispanic immigrant with type II diabetes presents for follow-up after his third bevacizumab injection 1 month prior. His VA remains 20/50 OD and 20/60 OS, but OCT shows persistent diabetic macular edema (DME) OU. He is unsure about his blood sugar and blood pressure (BP) control, and he has not been checking his sugars regularly. In-office BP is 161/92. Which of the following is the most important next step in managing this patient?

a. Coordinate referral to local PCP for management of diabetes and hypertension
b. Switch to aflibercept 2 mg injections every 4 weeks, as bevacizumab has been ineffective
c. Switch to faricimab injections every 4 weeks, as bevacizumab has been ineffective
d. Provide the patient with reading materials to educate him on his disease state

3. A 45-year-old African American man with moderate nonproliferative diabetic retinopathy and DME OD presents for delayed follow-up. He is phakic with normal IOPs OU. His VA declined from 20/30 to 20/80 OD since his last visit 5 months prior, when he had minimal macular edema and received aflibercept 2 mg for maintenance. OCT now shows worsening intraretinal cysts. He has a history of missed appointments and reschedules only when his vision worsens. He works 10-hour shifts Monday-Friday and must request time off 2 months in advance. You plan to inject aflibercept 2 mg today. What is the next best step in treating this patient?

a. Educate the patient about importance of regular follow-up in the treatment of diabetic retinopathy to improve treatment adherence
b. Switch to intravitreal triamcinolone injections for future injections to increase treatment durability
c. Switch to aflibercept 8 mg for future injections to extend the patient's treatment interval
d. Schedule future visits at least 2 months in advance to accommodate his work schedule

4. A 49-year-old Hispanic woman, with poorly controlled type II diabetes since immigrating 8 months ago, presents with blurry vision OU. Her teenage daughter assists with communication. She has no history of ocular surgery. VA is 20/60 OD and 20/25 OS. Fundus exam reveals dot-blot hemorrhages in all quadrants with intraretinal microvascular abnormalities OU, but no neovascularization. OCT reveals central intraretinal cysts OD and no central edema OS. You proceed with a bevacizumab injection OD. Which of the following is the LEAST APPROPRIATE action to aid patient adherence to care?

a. Provide Spanish-language materials explaining diabetic retinopathy and treatment options
b. Use a trained interpreter during visits to improve communication and explain treatment plans
c. Play an educational video on diabetic retinopathy during numbing to reinforce treatment importance
d. Give a Spanish-language after-visit summary with the next appointment to encourage follow-up

5. In a meta-analysis of the RIDE and RISE trials, which patient population was found to have significantly lower visual acuity gains compared to the White patient population?

a. Asian
b. Black
c. Hispanic
d. No difference between racial groups

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low____

This activity improved my competence in managing patients with this disease/condition/symptom. _____ Yes _____No

Probability of changing practice behavior based on this activity: _____High _____ Low _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

Change in pharmaceutical therapy _____
Change in nonpharmaceutical therapy _____
Change in diagnostic testing _____
Choice of treatment/management approach _____
Change in current practice for referral _____
Change in differential diagnosis _____
My practice has been reinforced _____
I do not plan to implement any new changes in practice _____

Please identify any barriers to change (check all that apply):

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
_____ Other. Please specify: _____

The design of the program was effective for the content conveyed	___ Yes	___ No
The content supported the identified learning objectives	___ Yes	___ No
The content was free of commercial bias	___ Yes	___ No
The content was relative to your practice	___ Yes	___ No
The faculty was effective	___ Yes	___ No
You were satisfied overall with the activity	___ Yes	___ No
You would recommend this program to your colleagues	___ Yes	___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____

This information will help evaluate this activity; may we contact you by email in 3 months to inquire if you have made changes to your practice based on this activity? If so, please provide your email address below.

_____

_____