

MODERNOPTOMETRY

THEN, NOW, AND TOMORROW:

Evolving the Management of
Diabetic Retinopathy and the
Role of the Optometrist

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A CE activity provided by Evolve Medical Education LLC

This activity is supported by an unrestricted educational grant from Regeneron and
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Then, Now, and Tomorrow: Evolving the Management of Diabetic Retinopathy and the Role of the Optometrist

Release Date: June 15, 2019
COPE Expiration Date: May 8, 2022

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CONTENT SOURCE

This continuing education (CE) activity captures content from a round table discussion that occurred on March 4, 2019.

ACTIVITY DESCRIPTION:

Diabetic retinopathy (DR) is the most common ocular complication of diabetes, responsible for more than 10,000 new cases of blindness yearly in the United States. This activity focuses on information for optometrists, as their role is crucial in educating patients with diabetes about the potential ocular complications of their systemic disorder and the benefits of diabetic eye exams and early treatment.

TARGET AUDIENCE

This certified CE activity is designed for optometrists involved in the management of patients with diabetes.

LEARNING OBJECTIVES

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

- **Discuss** the increasing prevalence of diabetes and diabetic retinopathy.
- **Identify** which patients need to be screened earlier based on their disease state.
- **Explain** to patients the need for early referral to retina specialists.

- **Summarize** how diabetic eye disease may affect patients with visually significant cataract and initiate appropriate treatment for these patients.
- **Discuss** how imaging devices may be able to provide earlier diagnosis of disease or disease progression.

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COPE Course ID: 62633-PS

COPE Event ID: 117503



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PRETEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation.

1. Rate your level of confidence in your ability to diagnose and screen patients with diabetic retinopathy and diabetic macular edema:

- Not at all confident
- Not very confident
- Neutral
- Confident
- Very confident

2. Rate your level of confidence in your ability to triage and refer patients with diabetic retinopathy and diabetic macular edema:

- Not at all confident
- Not very confident
- Neutral
- Confident
- Very confident

3. A 42-year-old female patient with an 8-year history of diabetes presents for her annual eye examination. She has been referred by her endocrinologist after complaining about her vision becoming blurry. What tests are you likely to perform at this first visit?

Add a check mark to the items below that are consistent with your current clinical practice.

Action	Consistent	Not Consistent
Take detailed history of present illness discussing visual complaints, signs, and associated symptoms		
Proceed with an ICG angiography		
Perform B scan ultrasonography		
Perform tonometry		
Complete dilated posterior segment examination		
Perform color vision testing		
Assess visual acuity		
Complete Amsler grid monitoring		
Implement anterior segment examination		
Recommend AREDS vitamins		
Perform fundus photography		
Take axial length measurements		

4. Which minority population is more likely to develop diabetic retinopathy in the United States than others?

- Non-Hispanic Whites
- Native Americans
- Hispanics
- African Americans

5. A 35-year-old woman with a history of type 2 diabetes presents for her annual evaluation. She has marked hemorrhages in 4 quadrants, exudates and thickening with the macula, plus some evidence of neovascularization elsewhere present in the left eye. All of the following are evidenced-based approaches to the patient EXCEPT?

- The patient may benefit from an ultra widefield angiogram to evaluate for proliferative diabetic retinopathy
- The patient likely has severe NPDR. Close observation is warranted
- The patient has proliferative diabetes and therefore anti-VEGF or panretinal photocoagulation (PRP) is indicated
- The patient should be investigated for signs of neuropathy and nephropathy

6. In the PANORAMA study, what percentage of patients in the two arms showed a 2-step or greater improvement in DRSS scores after treatment with aflibercept for one year?

- 60% in the q16 week arm and 35% in the q8 week arm
- 65% in the q16 week arm and 80% in the q8 week arm
- 80% in the q16 week arm and 65% in the q8 week arm
- 35% in the q16 week arm and 60% in the q8 week arm

7. According to the Centers for Disease Control and Prevention, approximately _____ of diabetic patients older than 40 also have diabetic retinopathy.

- 10%
- 20%
- 30%
- 40%

8. Diabetes is associated with serious comorbidities that include all but which of these?

- Heart disease
- Rosacea
- Stroke
- Nephropathy

9. What evidence exists linking A1C to the efficacy of intravitreal anti-VEGF treatments?

- The pivotal trials for aflibercept suggested people with higher A1C levels fare better with anti-VEGFs than they do if they undergo laser.
- The pivotal trials for ranibizumab suggested people with higher A1C levels fare better with anti-VEGFs than they do with steroid implants.
- The pivotal trials for ranibizumab suggested people with higher A1C levels fare better with ranibizumab than they do when treated with bevacizumab.
- There is no evidence to suggest A1C levels impact the efficacy of anti-VEGF treatment.

10. A 55-year old Native American male presents for a yearly eye exam for the first time. He is slightly overweight, with known hypertension and diabetes, and reports having had a stroke 5 months previously. He underwent LASIK 20 years ago, and is now complaining of blurry vision. Imaging on an Optomap shows intraretinal hemorrhages and exudates. Exam reveals macular thickening. What is an evidence-based approach for this patient?

- Refer to a retina specialist for a diabetic eye exam and potential treatment based on imaging.
- Send the patient to a refractive surgeon for LASIK enhancement.
- Educate the patient about the ocular risks of diabetes, but do not refer to a retina specialist.
- Evaluate the patient for prescription spectacles for his presbyopia.

11. Which of the following imaging tools is considered a "game changer" in diagnosing diabetic retinopathy?

- OCT angiography
- Color fundus imaging
- Fluorescein angiography
- Ultra widefield angiography

12. The FDA recently approved the IDx-DR software that provides one of two results: referral to an eye care professionals in cases of "more than mild DR detected," or _____.

- rescreen in 12 months if the images are deemed negative for mild DR.
- rescreen in 24 months if the images are deemed negative for mild DR.
- observe and rescreen every 6 months
- referral to an optometrist for monthly monitoring

13. The Diabetic Retinopathy Clinical Research Network's Protocol S compared ranibizumab to PRP and found less visual field loss, less hemorrhages, less progression of tractional detachment, and less DME with ranibizumab within the first 2 years of the study. The 5-year results found that peripheral ischemia continued to progress, and that patients who did not undergo PRP continued to lose visual field and that overall about 40% of patients were lost to follow up by year 5. In light of this evidence, what may be an appropriate treatment regimen for patients with PDR with DME?

- Treat only with anti-VEGF, preferably ranibizumab
- Treat only with PRP, as the progression to PDR shows patient noncompliance
- Treat with a combination of anti-VEGF and PRP
- Treat with a combination of anti-VEGF and PRP, starting immediately with laser and adding anti-VEGF only when the patient regresses or progresses

Then, Now, and Tomorrow: Evolving the Management of Diabetic Retinopathy and the Role of the Optometrist

Diabetic retinopathy (DR) is the most common ocular complication of diabetes, responsible for more than 10,000 new cases of blindness yearly in the United States.¹ Estimates suggest 33% of diabetic patients will develop DR, and 11% will develop diabetic macular edema (DME).^{2,3} Minority populations in the United States are more likely to develop DR than non-Hispanic whites, with Native Americans having one of the highest prevalence rates (45.3%).⁴

Medical therapies have reduced the severity of DME and DR and timely treatment can reduce severe vision loss by 90%.⁵ Some studies have shown that patients who respond to treatment may need chronic monthly treatments, while others suggest treatment may be successfully tapered.⁶⁻⁸ There is no evidence to suggest A1C levels impact the efficacy of intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatments, meaning treatment for diabetic eye disease can begin even if the systemic disease is not controlled.

Treating the diabetic eye disease regardless of systemic disease control is crucial. Both ranibizumab and aflibercept have shown in pivotal studies to provide substantial vision gains, that earlier treatment (meaning, treating patients with less severe disease at baseline) resulted in better vision gains, and that patients who have a delay in treatment do not fare as well.⁹⁻¹¹

Because optometrists are typically the first-line eye care provider, it is even more important that this group of eye care professionals recognizes the clinical signs of the disease to both educate their patients and to refer to a retina specialist when appropriate.

—Eric Nudleman, MD, PhD, Moderator

Q | ERIC NUDELMAN, MD, PHD: Prevent Blindness America has estimated more than 7.6 million people in the United States have DR as a result of their systemic diabetes.¹²

The prevalence of DR has been estimated at about 29% for those with diabetes and about 1.5% of adults with diabetes and proliferative DR (PDR).¹³ Dr. Rahimy, can you frame this problem for us in terms of the prevalence of diabetes and the impact as a public health issue?

EHSAN RAHIMY, MD: Diabetes is a worldwide epidemic problem^{14,15} that is affecting our entire health care system. The Centers for Disease Control and Prevention (CDC) estimate there are 30.4 million people in the United States with diabetes (9.4% of our population), and estimated 7.2 million people are undiagnosed.¹⁶ We know diabetes is associated with serious comorbidities that include heart disease, stroke, and nephropathy.¹⁷ Specifically within our niche as eye care providers, it's not just the retina specialists who are shouldering this burden—2.6% of blindness can be attributed to complications from diabetes¹⁸—it's every eye care provider.

We need to do a much better job as health care providers of getting our patients screened earlier—unfortunately, the number of these diabetes diagnoses is projected to increase.¹⁶ We need to work together and communicate better with other specialists and general practitioners to get people screened.

DR. NUDELMAN: Although diabetes affects every part of the country, some parts are more dramatically affected than others by

diabetes and its complications. For example, Dr. Pitcher covers a very large geographic area. What has been your experience with the level of diabetes that you typically see in your clinic?

JOHN D. PITCHER III, MD: As you mentioned, about 10% of the United States has diabetes. Per the CDC statistics, almost 30% of diabetic patients older than 40 also have DR.^{16,19} The National Eye Institute has projected upwards of 15 million people will have DR by 2050.^{20,21} In my practice region, we see a lot of people with DR who have vision-threatening complications, which is likely due to our seeing them first when they have a more advanced stage of disease, and most have not been getting annual eye exams.

We typically state about one-third of patients with DR may have vision-threatening complications or risk of severe vision loss.^{2,3,22} That statistic might be even higher among some populations, including those who don't have eye care providers in their community or those not receiving recommended screenings.

DR. NUDELMAN: Dr. Steinle, what kind of differences do you see in your practice in terms of the level of diabetes in areas that may not have the same access to care?

NATHAN STEINLE, MD: We cover coastal California and also inland California. Between the two regions, there are definitely socioeconomic differences. Our inland patients present with much higher A1C levels and much more advanced stages of DR. As a side note, I was in the Middle East last year to present on this topic, and I was

amazed to find their increasing rates of diabetes in areas where our Western fast food and chain restaurant diets have become much more popular.

DR. NUDLEMAN: This has been illustrated in maps of the United States, showing the prevalence of diabetes and how closely that correlates with the prevalence of obesity (Figure 1).

The prevalence of diabetes is increasing exponentially, with most states now harboring prevalence rates of more than 9%. The spread of the high calorie diet appears to have had a dramatic effect.

We've touched on both diet and access to care, what other issues are contributory?

DR. RAHIMY: Other factors may include variables such as noncompliance with physician recommendations, or a sedentary lifestyle, or lack of exercise. That goes to the point of eye care specialists being in the unique position to have the opportunity to impact, mold, and help reform the lives of our patients. Every one of us has had that one patient who only started to care about their health and treatment compliance when they realized they were about to permanently lose their vision. Those of us in eye care are in an incredibly unique and privileged position to make that type of impact on someone's life.

DR. STEINLE: That is really a good point. We're in a leadership position in health care in that we can really motivate patients. I continually find that when my patients hear their creatine is going up and their kidneys are not functioning properly, it doesn't really resonate with them. But when we tell them they are going to lose their vision, or be unable to drive a car, those very tangible deficits are great motivators. We should use that to our advantage to reinforce and motivate patients to make positive, proactive changes in their lives.

(CO)MANAGING THE PREDIABETIC PATIENT

Q | DR. NUDLEMAN: That also fits in nicely with the "prediabetic" patient. The American Diabetes Association (ADA) defines prediabetes as any adult who is overweight, with numerous additional risk factors that includes an A1C of at least 5.7% and hypertension, among others.²³ Does this panel see patients with prediabetes who are not yet on systemic therapy?

DR. PITCHER: We are seeing some of those patients come through. The ADA guidelines aren't very clear on how to treat them. To comment on Dr. Steinle's observations, as retina specialists we may not see these patients until they've developed DR. But primary eye care providers have an opportunity at an even earlier stage to provide education and hopefully have an impact at an earlier time point in the patient's disease.

Another reason this epidemic is exploding is because we're seeing more patients each day, so there's less time to spend talking about diet, exercise, etc. That's how the optometrist can intervene possibly better than we can to educate the patient and possibly help prevent some of these complications we see as retina specialists.

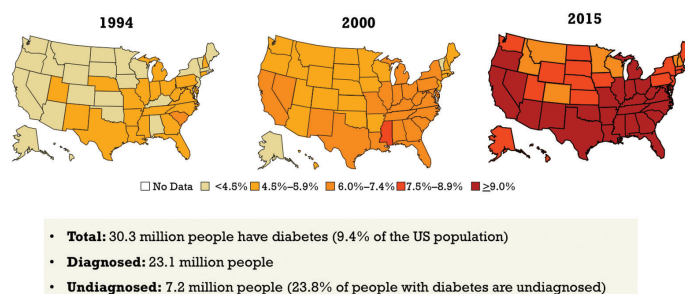


Figure 1. US prevalence of diabetes.¹⁶

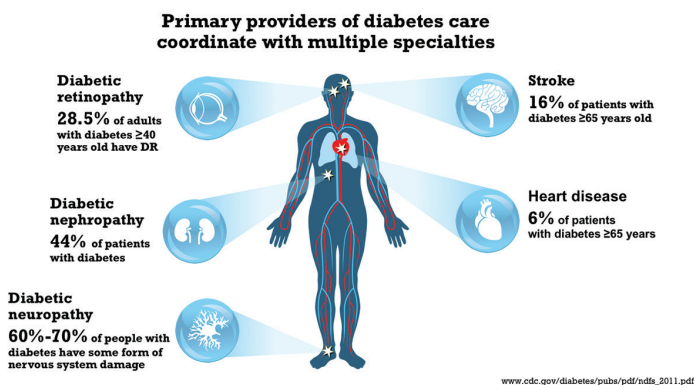


Figure 2. Diabetes is associated with serious comorbidities.¹⁶

DR. NUDLEMAN: Every time I see a diabetic patient that is referred to me for diabetic eye exams, even when they have no signs of DR, I take the opportunity to discuss the disease. I reemphasize that it's a systemic disease that affects every organ in the body (Figure 2).¹⁶ I talk about the damage to the microvasculature in their kidneys, brain, heart, fingertips and toes, in addition to their eyes. I think it is an excellent opportunity for us to provide some input on their general health care, which may influence their life, not just their vision.

DR. RAHIMY: I've seen quite a number of prediabetics in my practice, most of whom have been referred by their endocrinologist or primary physician to get a baseline screening. I have been surprised at the number of times I've ended up finding signs of early DR in these patients, sometimes with an overlying hypertensive component.

Because we're able to look at in vivo tissue, we can truly help our colleagues on the other side of the medicine clinic. Being able to detail the health of blood vessels can help our colleagues better manage the patient's disease or become more aggressive in treatment if we can show the patient has signs of intraocular involvement.

INCREASING IMPORTANCE OF IMAGING

Q | DR. NUDLEMAN: Even in patients with prediabetes, or those who have well-controlled hemoglobin A1C, with no obvious evidence of DR (meaning, no intraretinal hemorrhages, exudates, or obvious microaneurysms), some of our newer imaging modalities can pick up minor changes much earlier.

As retina specialists, how are you evaluating these patients? How does that compare to the screenings done in an optometrist's office?

DR. STEINLE: The “game changer” in the past few years for me has been ultra widefield angiography.²⁴⁻³⁰ Before widefield, we would use color fundus images, and then fluorescein angiography (FA), which did an “okay” job. We would montage the information together and have a grasp on the disease. But widefield imaging, especially for FA, has improved to the point that it changes my clinical management.

Our practice is involved in a large number of clinical trials, where we frequently send our images into centralized grading centers before enrolling patients in a potential diabetic trial. Thus, when I image a patient, I try to grade the FAs and then compare my results to the reading center results. Invariably, the reading center grades the image worse than I have. My take-home message is that even though we have patients with very little retinopathy on clinical exam, wide-field angiography always reveals much more damage.

For practices without widefield angiography, I recommend using infrared imaging because I've found it much easier to see the contrast of the microaneurysms, dot blot hemorrhages, hard exudates, and even neovascularization with black-and-white image versus with colored images.

Optical coherence tomography angiography (OCTA) has really been a game changer for me, too, because I've been able to find microstructural changes on OCTA that I can't pick up on traditional angiography, and certainly can't find on clinical examination.

DR. NUDLEMAN: I also can cite examples of looking at what I thought was a normal fundus (and the patient has good vision), but then using an OCTA have found microvascular damage, particularly around the fovea.

DR. STEINLE: Not only can you see the microaneurysms, but sometimes you can also find capillary drop out on OCTA.

DR. NUDLEMAN: OCTA also shows expansion of the foveal avascular zone (FAZ). The changes in the FAZ are really quite striking, and help to educate patients about the potential for progression of the disease.

DR. STEINLE: Seeing the damage to the FAZ sometimes gives me the explanation for the “unexplained” vision loss patients note when there is nothing else that's obvious. We've all likely had patients who look good on exam, but complain they're not happy with their vision. When we obtain an OCTA, we find macular ischemia that was already there, just “under the radar.”

DR. NUDLEMAN: We recently did a study about contrast sensitivity in patients who have no frank DR.³¹ If you test for contrast sensitivity formally, patients with diabetes do have reduced contrast sensitivity, even before there's any structural damage.

DR. STEINLE: That doesn't surprise me, but nice work in parsing that out. That's a very interesting finding.

USING GUIDELINES TO DICTATE TREATMENT

Q | DR. NUDLEMAN: Dr. Pitcher, do you routinely take wide-field angiography and OCTAs on all patients with diabetes whom you evaluate?

DR. PITCHER: We have widefield fluorescein capabilities as well as OCTA capabilities, but I find myself doing them rarely in diabetic patients in my practice. I don't see a huge change in my treatment patterns based on the angiography. I find that using the Diabetic Retinopathy Severity Score (DRSS)³²⁻³⁵ provides an accurate portrayal of where the patient is on the scale, and therefore, who should be treated and who should be observed. So far, the large trials showing improvement in DR with anti-VEGF have been based on DRSS. I think OCTA adds a lot of information on macular perfusion and widefield imaging could suggest if the patient may progress, but I don't think we have enough good evidence yet that using angiography should be guiding your actual management strategy.

DR. NUDLEMAN: That is an important point. We don't have evidence in terms of interventions when there are early changes. In my opinion, however, OCTA does help show patients exactly what their disease is affecting, and that may help to drive home the need for routine follow-up.

DR. STEINLE: OCTA can absolutely be a good motivator for patients.

THE CRUCIAL ROLE OF THE OPTOMETRIST

Q | DR. NUDLEMAN: That segues nicely into comparing what testing we do and what the patient typically has done in the optometrist's office. When patients are referred in by an optometrist, what kind of imaging has already occurred?

DR. RAHIMY: I think you'll find regional differences here, too. Most optometrists in my practice environment in Palo Alto, California, do have an Optomap (Optos). Additionally, I'd say close to 50% of optometrists' offices have OCT; however, most do not yet have OCTA. But in my practice setting, most patients referred into us have shown some degree of intraretinal hemorrhages, microaneurysms, or exudates on the Optomap. If the optometrist has access to an OCT, they may have noticed exudates during a prescription eye exam and wants the patient to be referred for possible treatment.

DR. NUDLEMAN: In your practice, the patients being referred already have at least moderate nonproliferative diabetic retinopathy (NPDR)?

DR. RAHIMY: That is correct. Usually patients with mild disease are not being referred. I do think that's an important point—we may be missing the milder cases of diabetic eye disease on routine examination. It's very easy to miss tiny microaneurysms, particularly when you're using an eagle-eye imaging modality like an Optomap or other widefield fundus photography. In such instances, it may not be until the patient is in moderate stages that they're being referred because the damage is easier to find on imaging.

DR. NUDLEMAN: Dr. Pitcher, do you think there is value in referring a patient with diabetes into our offices before they have noticeable changes on OCT or an Optomap?

DR. PITCHER: I do. We need to see these patients before there's PDR, and in my region, that's when the referrals usually occur. I want to see these patients earlier rather than later in their disease progression. Referring to your original point, about 20% of my optometry referrals have an Optomap available for imaging, and about the same percentage have an OCT.

We have many good optometrists in my state, and they rely heavily on their examination skills. But I'm hoping as we learn more about treatment options, we can get these patients referred to us at earlier stages, when we can make more of a positive impact.

DR. NUDLEMAN: Dr. Steinle, do your referral patients have any imaging beyond Optomap or an OCT?

DR. STEINLE: It's rare when patients have any imaging beyond those two. But in our practice, the referred patient may have no imaging, may just have an OCT, maybe just a color photograph. Once in a while, I'll see someone with both color imaging and an OCT, but that's not consistent.

DR. NUDLEMAN: I find the same in my area. Some patients have had both of those imaging modalities, while others have had none. Some have had only an exam, but are being referred because of frank DR on exam. To me, that drives home the point that imaging can find things you will not discern from a nondilated exam. The Optomap is incredible in showing the peripheral retina in a non-dilated patient.

Imaging provides the ability to show patients the extent of the disease and damage. That's when the conversation about follow-up gets patients' attention.

WHEN TO INITIATE TREATMENT OR REFERRALS

Q | DR. NUDLEMAN: Let's talk about the patient with early DR. This is certainly not a patient in whom we would consider starting anti-VEGF therapy. If they're in your offices, what do you do? You've had a conversation with them about the impact of the disease, you've shown them their images. What do you now do? How do you comanage this patient with the referring optometrist?

DR. RAHIMY: I'll reiterate that it is really important to see these patients earlier and earlier in the course of disease, even if there is no treatment warranted. Psychologically, there is nothing more valuable than that little bit of face-to-face time you're giving the patient. Not every one of our conversations needs to end with us telling the patient they need an injection in their eyes.

I believe there is great value and utility for both the patient and for us when we start to develop a relationship without having to jump immediately into treatment. When I see a patient with mild enough disease that treatment is not warranted, and I don't necessarily need

to see them in the near future, I may discharge them to the referring optometrist. I do want them to continue seeing their optometrist, particularly if I do not necessarily agree with the initial severity diagnosis, to continue with regular refraction exams.

Over time, we also develop relationships with our optometric colleagues, so you begin to notice which optometrists have exceptional imaging capabilities, who has access to better diagnostic tools, etc. When the relationship with other eye care specialists is there, we can resume a normal 9- to 12-month follow-up schedule with these patients. If the patient comes from a clinic without access to multimodal imaging, that's the patient I'm more likely to follow myself.

DR. NUDLEMAN: Would anyone handle that any differently?

DR. STEINLE: I wouldn't do anything different than what Dr. Rahimy described. I think those are all really good points. I try and offset my appointments so the optometrist sees the patient once a year, and we see the patient once a year, but I try to arrange it so that we're basically seeing the patient every 6 months between the two of us.

DR. NUDLEMAN: Dr. Pitcher, you see many patients who travel a long distance. How do you comanage?

DR. PITCHER: Some local optometry settings do not have much or any interest in medical care. They may refer a patient with mild DR. I'll still see the patient and counsel them on the potential for progression, and the need for good glycemic control. We know that once DR is present, glycemic control can forecast progression from one stage to the next.^{36,37} Then I would attempt to triage the patient to an optometrist who has an interest in monitoring medical eye diseases, including DR.

I do want to reiterate that we want to see the patients who are at high risk or who need treatment. Our practice does have patients who come from long distances, so we want to optimize and select those patients who are going to benefit most from our services.

DR. NUDLEMAN: I often have that scenario, and the addition of widefield angiography can confirm that the level of disease is worse than the referring physician thought when making that initial referral. If the patient is being seen yearly by their optometrist, I also follow what Dr. Steinle does and try to schedule their appointments with me 6 months after their optometrist. Another advantage to comanagement is that, as a retina specialist, I'm not looking carefully at the lens or determining when the patient needs a cataract surgery consult, or reviewing the optic nerve to check for glaucomatous damage. Much of the patient's comprehensive care is still being done by the referring specialist.

DR. STEINLE: That's a really good point. We know that glaucoma is a vascular disease,³⁸⁻⁴⁰ but I am not hyper vigilant about monitoring for early glaucoma changes in the setting of a busy retina clinic. It's probably good to have our colleagues watch and follow that.

DR. NUDLEMAN: I rarely image the nerve. I tell patients I'll be following the retina and monitoring their DR, and that if they progress to the point where treatment is needed, I'm responsible, but the rest of their eye care should continue to be with their optometrist or, if surgery is needed, by a comprehensive ophthalmologist, cornea, or glaucoma specialist.

The point Dr. Rahimy touched on earlier about patients traveling long distances is an important one. We all want to see patients earlier to ensure we're not missing disease. What role can telemedicine play?

DR. RAHIMY: The overarching goal of telemedicine is to increase access to care and give entry into the system for people who don't have one right now. In our group, we've been trying to install this type of system for the past few years, and it's moving along slowly but surely. Even the initial pilot programs have been in areas that are already reasonably served by our colleagues. But when you start thinking on a bigger scale, the people who would benefit most from teleretinal screen are going to be those who may not have routine access to get to an optometrist's or an ophthalmologist's office, never mind a retinal specialist.

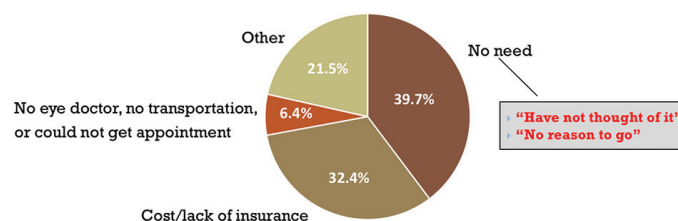
In my opinion, that's where we have to start thinking more creatively. Where should we place these types of camera systems? Is it better served being put into the primary care doctor's clinic? Is it better off in the endocrinologist's clinic? Maybe we could consider placing them in pharmacies at major organizations. Or perhaps in a lab where patients go for blood work. We know about 40% of people with diabetes are not getting annual eye exams (Figure 3),⁴¹ and that lack of transportation is a leading factor.⁴² But it's multifactorial; patients have other doctors they're seeing for their systemic disease. Telemedicine can minimize the number of unnecessary visits or extra steps the patient has to take just to get another screening. If we could tie in a retinal scan when the patient is at their endocrinologist or when they're at the lab getting blood work done, we would have a real potential and opportunity to improve screening adherence well into the 70% to 80% range, maybe even greater than that.

DR. NUDLEMAN: Telemedicine as a program is still evolving. What about the idea of getting photos from referring doctors? Does anyone ever have a referring doctor text an Optomap image or an OCT image?

DR. STEINLE: I'm really impressed with the imaging our referring colleagues do, and I get a lot of texts. I would say about three times a day I'm getting an image texted to me, and it's almost always an Optomap. I think it's really helpful because I can triage the situation. I can give advice on which patients I think are urgent and need immediate referral, versus which patients the primary eye care provider can hold onto themselves.

DR. NUDLEMAN: In my mind, that is a form of telemedicine. You are providing an evaluation remotely of a patient based on a photo.

DR. PITCHER: I also have that happen quite a bit. Oftentimes, it's



Chou CF, et al. *Diabetes Care*. 2014;37:180-188.

Figure 3. Patient-reported reasons why they do not receive annual eye examinations.⁴¹

from doctors who are in remote clinics, but I've also had that happen within the metro area. It's a great opportunity to manage in a way that allows the patient to maintain the relationship with their optometrist, and not necessarily have to come in for a formal consultation if it's not indicated.

NEWER DIAGNOSTIC TOOLS

Q | DR. NUDLEMAN: In 2018, the FDA approved the IDX-DR, a software program that uses an artificial intelligence (AI) algorithm to analyze images of the eye taken with the Topcon NW400 (Topcon Medical).⁴³ Does anyone have experience with that program yet?

DR. PITCHER: None of the providers in our area have fully implemented it yet, or have the cameras yet.

DR. RAHIMY: To the best of my knowledge, there aren't any in my state, either. We've had discussions with the manufacturer about evaluating some protocols as an investigator, however.

DR. NUDLEMAN: The software allows you to pick up hemorrhages and exudates. If the images are of sufficient quality, the software provides one of two results: referral to an eye care professional in cases of "more than mild DR detected," or rescreen in 12 months if the images are deemed negative for mild DR. The FDA evaluated data from a clinical study of retinal images obtained from 900 patients with diabetes at 10 primary care sites. The IDX-DR was able to correctly identify the presence of more than mild DR 87.4% of the time, and able to identify those patients who did not have more than mild DR 89.5% of the time.⁴³

Do you expect that something like that is going to be integrated into other commercially available imaging devices that we have?

DR. RAHIMY: Yes—it's not a matter of *if*, it's a matter of *when*. There are some clinicians who are concerned these technologies are going to replace us, but I disagree. These devices will augment what we do, not replace us. In the AI community, it's generally accepted that machine plus human always does better than either component alone.

Teleretinal screening is in its infancy. The infrastructure isn't fully implemented everywhere yet. When people talk about the AI machine-learning component, they're discussing the automation.

That will eventually come, because we're going to be drowning in the number of images and cases we'll need to review. Having that AI component is going to be helpful and I think it will improve the accuracy of diagnosis and having patients referred into our clinics faster. But it's going to require human oversight. The public at large isn't necessarily ready to trust the algorithm right off the bat.

DR. NUDLEMAN: My concern is that the software refers patients with moderate disease, but the referral is based on images of the posterior pole only—it's not a widefield image. As we've discussed at some length, we've all found the level of disease is much worse with widefield imaging with angiography than what we'd see with just a posterior pole exam.

One likely development in the future is that we're going to have AI imaging of the far periphery that will lead to many more referrals. We are going to be challenged with the task of determining when patients who have earlier disease should be treated.

ANTI-VEGFS, LASER, AND OTHER TREATMENTS

Q | DR. NUDLEMAN: There has been quite a lot of data recently that suggest earlier treatment has a benefit in regressing the stage of DR. What are your thoughts about treating proliferative disease with anti-VEGF therapy?

DR. STEINLE: There is room for debate on many different levels. When the Diabetic Retinopathy Clinical Research Network (DRCR.net) started Protocol S, which compared ranibizumab to panretinal photocoagulation (PRP), I was really impressed by the year-1 and 2 results with ranibizumab—less visual field loss, less hemorrhages, less progression of tractional detachment, and less DME with ranibizumab.⁴⁴

I was a little disheartened by the 5-year results, which showed about 40% of patients were lost to follow-up, the peripheral ischemia continued to progress, and that patients who did not undergo PRP lost a good deal of visual field just from progression of the peripheral ischemia, not necessarily from the PRP.⁴⁵

I've swung both ways on the pendulum. At first, I tried giving a lot of injections for proliferative disease, but now I'm back giving PRP because I know it's a safe and effective treatment, and it's very cost-effective for patients. If the patient has progressed to PDR, they've shown to me they're fairly noncompliant and fairly irresponsible. If I can take that responsibility from them and give one or two PRP laser treatments, I can really save that eye going forward.

Most of us can give an anecdote about a patient who does really well with injections for months or years, but then has a treatment interruption for a few months due to illness, insurance, travel, or transportation issues. And when they return, they've now developed neovascular glaucoma, or vitreous hemorrhage, or tractional retinal detachment.⁴⁶ That's a disheartening feeling, because I know that eye could have been saved with PRP.

DR. NUDLEMAN: Those are excellent points, and thank you for summarizing the data. Dr. Pitcher, if you have a patient who is referred for what looks like moderate disease on exam, and on

widefield angiogram there is some mid-peripheral neovascularization and leakage, but no edema, what is your first-line treatment?

DR. PITCHER: I'll treat them with both injections and laser, in a modified Protocol S or S-plus treatment. Dr. Steinle highlighted the problems with some of these patients (noncompliant, or lack of follow-up).

I had a patient years ago in whom I performed laser on the inferior retina and the patient was subsequently lost to follow-up. We were initially going to do laser in both eyes. Well, when the patient did return, there was tractional detachment in the eye that didn't have laser. The eye treated with laser actually looked pretty good. Because these patients are at high risk for DME, often I will still treat with intravitreal injections of anti-VEGFs initially and in between laser treatments.

DR. NUDLEMAN: What's your timing typically like? On that first visit when you're in clinic, do you recommend laser right away? Or do you start with a series of injections and do laser later?

DR. PITCHER: I will usually do an injection initially, in the eye we're treating and then 2 weeks later I'll start laser, and then 2 weeks after that another injection. I typically stagger treatments in 2-week intervals and alternate between injections and lasers. I try to start and finish with an injection.

DR. NUDLEMAN: Dr. Rahimy, how do you manage that scenario?

DR. RAHIMY: There are two big take-home points from Protocol S for me. First, I think believers on either side are going to see the benefit of their chosen treatment regimen. The reality is, Protocol S isn't about an either/or scenario. There is a need for both treatments. The second point is that we have an obligation to treat the patient first and then the disease. We can't ever forget that.

Over time, you start to learn (or at least get a good idea) which patients are going to be compliant with follow-up and who is more of a flight risk. I've worked in county hospitals and dealing with numerous really sick diabetic patients. We have such a unique, precious moment in time in a patient's life when they're in our care and we have this opportunity to prevent severe vision loss.

I don't have a set treatment plan; sometimes I'll use laser first, other times injections. If they're compliant with follow-up, I'll continue injections. But each patient is essentially individualized care. I was concerned that the 5-year results of Protocol S found almost half of the participants in each group developed vitreous hemorrhages.⁴⁵ To me, that reinforces that even laser is not a "one and done" treatment, and it's not always just "inject, inject, inject" either. There is a role for both of these treatments in our toolbox to fight DR.

It is important to reinforce that diabetes and its ocular component are chronic diseases that will often require the use of both the anti-VEGFs and laser in the long run. People who have undergone PRP and are lost to follow-up may fare better than patients who have undergone only injections and are lost to follow-up for an

extended length of time. I tend to not lose as much sleep at night over the PDR patient lost to follow-up at least with PRP on board, as I do the patient who has only gone through the dose-loading phase with anti-VEGFs and then is lost to follow-up.

DR. NUDLEMAN: There's no question that PRP reduces the risk of vision loss events. Anti-VEGFs, in my opinion, are effective at reducing neovascularization. When I see regression, that's when I'll start adding PRP. My preferred treatment regimen is a series of injections to allow the neovascularization to become fibrotic, and then add in the PRP. I do agree with Dr. Rahimy that these are not "one and done" treatments. Even after laser, I will continue to treat with injections when necessary, particularly for our one-eyed patients.

Let's talk about eyes with earlier disease. What about data that support intervention in eyes with NPDR? What has PANORAMA taught us and how does it influence your practice?

DR. PITCHER: PANORAMA was the study that looked at intravitreal aflibercept versus sham for patients with moderately severe or severe DR.^{47,48} There were about 400 patients enrolled, randomized to sham or intravitreal injections and after the 3-month loading doses were then switched to a treatment regimen of every 8 (q8) or 16 weeks (q16).⁴⁸ That translated to about six injections in the q16 arm and nine in the q8 arm during the first year. Wykoff et al found impressive results, similar to those from the pivotal trials like RIDE/RISE and VIVID/VISTA, which showed a significant amount of patients achieving a 2-step or greater improvement in the DRSS score.^{9,49} In PANORAMA, more than 65% in the q16 arm and 80% in the q8 arm had a 2-step or greater improvement in DRSS scores.⁴⁸ I was particularly interested in the severe DR group (level 53), in whom the numbers improved to 94% and 82% in each arm, respectively.

One of the most important aspects of this study is that while DRSS improvements are great, what we really care about is data on patients who had a reduction in vision-threatening complications or center-involved DME. Those numbers were quite high as well—overall, four of 10 patients had an event that compromised or threatened their vision if they were not receiving injections. That percentage increased to 53% in severe DR.⁴⁸

That's an opportunity for us, if we're intervening at any of those levels, to reduce the chances that they'll progress onto either vision-threatening complications or center-involved DME. In PANORAMA, aflibercept was an effective treatment and moderately severe and severe patients achieved a reduction in risk of vision loss.^{47,48}

DR. NUDLEMAN: We now have a number of studies that show anti-VEGFs improve the underlying disease (although those were retrospective observations and not study end points). We saw that in RIDE/RISE and VISTA/VIVID.^{9,49} That's what motivated the studies to use anti-VEGFs for PDR, as seen in CLARITY and Protocol S.^{44,45,50} Those data were so compelling that we moved forward to do the PANORAMA trial. For me the take-home point is worth reiterating—four of 10 patients in the sham group had a vision-threatening complication within the first 52 weeks.⁴⁸ That

point absolutely drives home the need for us to see patients earlier, to have them diagnosed earlier, and to potentially treat earlier so we can reduce vision threatening complications.

DR. STEINLE: I thought it was rather bold to have a 6-month primary outcome, too. But the point was made even with the short time frame. So not only can patients progress quickly without treatment, but they can also improve quickly with anti-VEGF therapy.

DR. NUDLEMAN: As we've discussed, more comprehensive imaging can improve our detection of the extent of disease and allow us to show the changes to our patients. Doing this, we are likely to detect many more patients with evidence of disease. What should we be doing, if anything, to improve the management of all of these new patients?

DR. RAHIMY: This is the conundrum we're all going to tackling during the next 5 to 10 years. One of the ways this can be offset is by learning more efficient means of treatment. Is every 4 weeks necessary? Probably not. I start patients off monthly, but I start extending out to 3- or 4-month intervals if their FA looks good. This is where a biomarker would be helpful. With age-related macular degeneration (AMD), we can follow the fluid. We haven't found the universal biomarker for DR and DME.

DR. NUDLEMAN: Anti-VEGF therapy at some regular interval is going to stabilize and perhaps regress the disease, and preserve vision for a vast majority of patients with diabetes. How are we going to sustain giving that level of therapy for such a huge population of patients?

DR. STEINLE: In AMD, Genentech is evaluating a port delivery system.⁵¹ Naturally, Genentech has started to investigate continuous delivery devices for DME/DR/PDR as well. The combination of a port delivery system and longer term anti-VEGF agents should reduce treatment burden.

DR. NUDLEMAN: The evidence from RIDE/RISE and VISTA/VIVID, particularly after the crossover to treatment from sham, showed patients never recovered the amount of vision compared with those patients who were in the treatment arm.^{9,49} That also speaks to the chronicity of the disease and the benefits of earlier intervention.

DR. PITCHER: There may be issues with access to care. With our primary eye care and optometry colleagues, we can try to select those patients who are really going to benefit from treatment. That may become even more important when we're talking about potential surgical interventions. I have an in-depth conversation with each patient when we're initiating anti-VEGF therapy for NPDR. It really comes down to whether this patient wants to stick to this plan or not. It's not just about the treatment but it's about the entire picture.

DR. NUDLEMAN: We may be treating patients who have good vision and no edema. We need to keep the lines of communication

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open so our optometry colleagues know we are going to continue to comanage them even if we're seeing them more frequently.

DR. PITCHER: One last thing is the issue of treatment completion. When are we going to stop injecting them, and when are they going to go back to annual exams? That still needs to be determined. We need to work with our optometry colleagues to communicate that data when it comes forward. There's still a lot to be figured out, so stay tuned.

DR. STEINLE: One last learning point for primary eye care providers: the nomenclature change. Unlike years past, we do not typically use "clinically significant macular edema" anymore. Now we use DME center-involved versus noncenter involved. The referring clinician can just write "central DME" versus "noncenter involved DME," depending on whether the central subfield OCT region demonstrates thickening.

DR. NUDLEMAN: Thank you to all the participants. This was a really great conversation, and I appreciate your time and expertise. ■

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Evolving the Management of Diabetic Retinopathy and the Role of the Optometrist

Release Date: June 15, 2019
COPE Expiration Date: May 8, 2022

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To receive credit, you must complete the attached Posttest/Activity Evaluation/Satisfaction Measures Form and mail or fax to Evolve Medical Education LLC; 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please visit click <http://evolvemeded.com/online-courses/1908Supplement1>. You will need to register if you do not already have an account. If you are experiencing problems with the online test, please email us at support@evolvemeded.com. Certificates are issued electronically; please be certain to provide your email address below.

Please type or print clearly, or we will be unable to issue your certificate.

Name _____ ☐ OD ☐ non-OD participant

Phone (required) _____ ☐ Email (required) _____

Address _____

City _____ State _____ Zip _____

License Number _____

OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession	Years in Practice	Patients Seen Per Week (with the disease targeted in this educational activity)	Region	Setting	Models of Care
___ OD	___ > 20	___ 0	___ Northeast	___ Solo Practice	___ Fee for Service
___ NP	___ 11-20	___ 1-5	___ Northwest	___ Community Hospital	___ ACO
___ Nurse/APN	___ 6-10	___ 6-10	___ Midwest	___ Government or VA	___ Patient-Centered Medical Home
___ PA	___ 1-5	___ 11-15	___ Southeast	___ Group Practice	___ Capitation
___ Other	___ <1	___ 16-20	___ Southwest	___ Other	___ Bundled Payments
				___ I do not actively practice	___ Other

LEARNING OBJECTIVES

DID THE PROGRAM MEET THE FOLLOWING EDUCATIONAL OBJECTIVES?

AGREE

NEUTRAL

DISAGREE

Discuss the increasing prevalence of diabetes and diabetic retinopathy.

Identify which patients need to be screened earlier based on their disease state.

Explain to patients the need for early referral to retina specialists.

Summarize how diabetic eye disease may affect patients with visually significant cataract and initiate appropriate treatment for these patients.

Discuss how imaging devices may be able to provide earlier diagnosis of disease or disease progression.

POSTTEST QUESTIONS

1. Rate your level of confidence in your ability to diagnose and screen patients with diabetic retinopathy and diabetic macular edema based on this activity:

- a. Not at all confident
- b. Not very confident
- c. Neutral
- d. Confident
- e. Very confident

2. Rate your level of confidence in your ability to triage and refer patients with diabetic retinopathy and diabetic macular edema based on this activity:

- a. Not at all confident
- b. Not very confident
- c. Neutral
- d. Confident
- e. Very confident

3. A 42-year-old female patient with an 8-year history of diabetes presents for her annual eye examination. She has been referred by her endocrinologist after complaining about her vision becoming blurry. What tests are you likely to perform at this first visit?

Add a check mark to the items below that are consistent with your current clinical practice.

Action	Consistent	Not Consistent
Take detailed history of present illness discussing visual complaints, signs, and associated symptoms		
Proceed with an ICG angiography		
Perform B scan ultrasonography		
Perform tonometry		
Complete dilated posterior segment examination		
Perform color vision testing		
Assess visual acuity		
Complete Amsler grid monitoring		
Implement anterior segment examination		
Recommend AREDS vitamins		
Perform fundus photography		
Take axial length measurements		

4. Which minority population is more likely to develop diabetic retinopathy in the United States than others?

- a. Non-Hispanic Whites
- b. Native Americans
- c. Hispanics
- d. African Americans

5. A 35-year-old woman with a history of type 2 diabetes presents for her annual evaluation. She has marked hemorrhages in 4 quadrants, exudates and thickening with the macula, plus some evidence of neovascularization elsewhere present in the left eye. All of the following are evidenced-based approaches to the patient EXCEPT?

- a. The patient may benefit from an ultra widefield angiogram to evaluate for proliferative diabetic retinopathy
- b. The patient likely has severe NPDR. Close observation is warranted
- c. The patient has proliferative diabetes and therefore anti-VEGF or panretinal photocoagulation (PRP) is indicated
- d. The patient should be investigated for signs of neuropathy and nephropathy

6. In the PANORAMA study, what percentage of patients in the two arms showed a 2-step or greater improvement in DRSS scores after treatment with aflibercept for one year?

- a. 60% in the q16 week arm and 35% in the q8 week arm
- b. 65% in the q16 week arm and 80% in the q8 week arm
- c. 80% in the q16 week arm and 65% in the q8 week arm
- d. 35% in the q16 week arm and 60% in the q8 week arm

7. According to the Centers for Disease Control and Prevention, approximately _____ of diabetic patients older than 40 also have diabetic retinopathy.

- a. 10%
- b. 20%
- c. 30%
- d. 40%

8. Diabetes is associated with serious comorbidities that include all but which of these?

- a. Heart disease
- b. Rosacea
- c. Stroke
- d. Nephropathy

9. What evidence exists linking A1C to the efficacy of intravitreal anti-VEGF treatments?

- a. The pivotal trials for aflibercept suggested people with higher A1C levels fare better with anti-VEGFs than they do if they undergo laser.
- b. The pivotal trials for ranibizumab suggested people with higher A1C levels fare better with anti-VEGFs than they do with steroid implants.
- c. The pivotal trials for ranibizumab suggested people with higher A1C levels fare better with ranibizumab than they do when treated with bevacizumab.
- d. There is no evidence to suggest A1C levels impact the efficacy of anti-VEGF treatment.

10. A 55-year old Native American male presents for a yearly eye exam for the first time. He is slightly overweight, with known hypertension and diabetes, and reports having had a stroke 5 months previously. He underwent LASIK 20 years ago, and is now complaining of blurry vision. Imaging on an Optomap shows intraretinal hemorrhages and exudates. Exam reveals macular thickening. What is an evidence-based approach for this patient?

- a. Refer to a retina specialist for a diabetic eye exam and potential treatment based on imaging.
- b. Send the patient to a refractive surgeon for LASIK enhancement.
- c. Educate the patient about the ocular risks of diabetes, but do not refer to a retina specialist.
- d. Evaluate the patient for prescription spectacles for his presbyopia.

11. Which of the following imaging tools is considered a "game changer" in diagnosing diabetic retinopathy?

- a. OCT angiography
- b. Color fundus imaging
- c. Fluorescein angiography
- d. Ultra widefield angiography

12. The FDA recently approved the IDx-DR software that provides one of two results: referral to an eye care professionals in cases of "more than mild DR detected," or _____.

- a. rescreen in 12 months if the images are deemed negative for mild DR.
- b. rescreen in 24 months if the images are deemed negative for mild DR.
- c. observe and rescreen every 6 months
- d. referral to an optometrist for monthly monitoring

13. The Diabetic Retinopathy Clinical Research Network's Protocol S compared ranibizumab to PRP and found less visual field loss, less hemorrhages, less progression of tractional detachment, and less DME with ranibizumab within the first 2 years of the study. The 5-year results found that peripheral ischemia continued to progress, and that patients who did not undergo PRP continued to lose visual field and that overall about 40% of patients were lost to follow up by year 5. In light of this evidence, what may be an appropriate treatment regimen for patients with PDR with DME?

- a. Treat only with anti-VEGF, preferably ranibizumab
- b. Treat only with PRP, as the progression to PDR shows patient noncompliance
- c. Treat with a combination of anti-VEGF and PRP
- d. Treat with a combination of anti-VEGF and PRP, starting immediately with laser and adding anti-VEGF only when the patient regresses or progresses

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this CE 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

I plan to make changes to my practice based on this activity. ____ Yes ____ No

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

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

The design of the program was effective for the content conveyed.	☐ Yes ☐ No	The content was relative to your practice.	☐ Yes ☐ No
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The content supported the identified learning objectives.	☐ Yes ☐ No	The faculty was effective.	☐ Yes ☐ No
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The content was free of commercial bias.	☐ Yes ☐ No	You were satisfied overall with the activity.	☐ Yes ☐ No
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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	☐ Medical Knowledge
☐ Practice-Based Learning and Improvement	☐ Interpersonal and Communication Skills
☐ Professionalism	☐ System-Based Practice

Additional comments:

☐ I certify that I have participated in this entire activity.

This information will help evaluate this CE activity; may we contact you by email in 3 months to see if you have made this change? If so, please provide your email address below.

MODERN OPTOMETRY

