

Division of Diabetes Treatment and Prevention

Advancements in Diabetes Seminar Clinical Advancements in Diabetes Eye Care

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Mark Horton:

Well, as you've already heard, I'm an optometrist and ophthalmologist in the Indian Health Service and I've done a number of things for the Agency over the years, but the reason we're here today is my role in this telemedicine program that we have for remote diagnosis and management of diabetic retinopathy in Indian Country.

Everyone is entirely familiar with the information that's why this is a race that we're winning in the Indian Country where we've got more diabetes than most anybody else. The prevalence of diabetes doubles about every 10 years. With this epidemic in diabetes there is a parallel epidemic in diabetic retinopathy. Diabetic retinopathy touches every cell in the body as you already know and of course that includes every cell in the eye, and so you can see that there is a number of conditions in the eye that can result from diabetes, but the one that we'll pay most attention to is that which causes our biggest problem, which is the retinal vascular issues, and among these although all of those, none of those are good, but among these, the one that really whips us is retinopathy and maculopathy resulting from the diabetes. This is the main source of vision loss from diabetes among our patients.

Virtually, all diabetics get diabetic retinopathy and it is the leading cause of new blindness among adults in our patients and among all patients with diabetes in this Country. But the good news is diabetes can essentially -- or rather, blindness due to diabetes can essentially be eliminated by timely diagnosis and treatment, so you would ask how in the world is it that it can remain the leading cause of new blindness if it's entirely treatable. This is a dichotomy that came to cause the creation of this telemedicine program that we'll mention during this presentation. The reason is because since 50% of population do not get standard of care for diabetic retinopathy examinations and without that, you cannot get timely diagnosis and treatment that's necessary in order to prevent vision loss due to diabetes.

About 40% of all diabetics have some degree of clinically evident diabetic retinopathy. About 10-20% have diabetic retinopathy at time of diagnosis. The single strongest predictor for onset or progression of diabetic retinopathy is duration of diabetes, and you can see the statistics there for type 1 and type 2 diabetes. Type 2 of course is the one that this is most prevalent in our population. After 20 years, about 60% of the population has diabetic retinopathy. About third have diabetic macular edema, and we'll talk about that a little bit more. After 25 years, fully a quarter of all our patients have a form of diabetic retinopathy, proliferative diabetic retinopathy that is a high-risk element that is the final common pathway to blindness in diabetes.

As I mentioned, it is the leading cause of blindness. It's also the leading cause of moderate vision loss, most severe vision loss and moderate vision loss in our population. The most common cause in the working age group is diabetes and diabetic retinopathy. In any one moment, it is somewhere between four and five percent of our patients with diabetes have high risk features that need to be treated.

Severe vision loss and moderate vision loss is very preventable by adhering to acceptable standards, and that's what we're going to be talking about is the best practices that will help protect our patients from avoidable vision loss due to diabetic retinopathy. First, we have to identify all patients with diabetes. We have to control compounding factors in comorbidities. We have to diagnose the level of diabetic retinopathy at least yearly, maybe more frequently than that, depending upon the level of diabetic retinopathy that may be discovered and we have to apply timely treatment. And we'll talk about the treatment modalities that are available for us.

Standard of care: annual eye exam. Now, you can read a good science that says, "Well, maybe we don't have to do it annually." But the reality is the systems, these algorithms that allow us to extend the examination time past a year are complex. It can be confused by patients and by provider alike and so when you get right down to it, this is a horrible disease that makes our patients go blind. So, the safest thing is to keep it simple, annual eye exam for everybody with diabetic retinopathy, may be more frequently depending on the level of diabetic retinopathy they have.

Clinical management is delivered by a team. The primary care team is listed first for a very good reason. That is the single most important spot to begin treatment, diagnosis and treatment of diabetic retinopathy. The other element of the team is the eye care provider and what we're trying to do here, the best practice involved systemic controls, timely or maybe early diagnosis as we'll talk about, and timely and maybe early treatment. The team working on these interventions is our only opportunity to prevent avoidable vision loss among our diabetic patients.

Now, there's an enormous amount of very good science for this. We're not going to go through this science step by step. We will touch on some of these clinical trials, but basically there is little question about what diabetic retinopathy looks like, what its natural history is, how to treat it, when to treat it, what to expect when we do treat it. If I start to wander away from hard science, I'll let you know during this presentation. The first thing I want to do is very briefly mention this because everyone on this call knows this information, but just for completeness, we'll mention that the Diabetes Control and Complications Trial showed us that there are opportunities to mitigate microvascular complications in the retina with intensive control of blood sugar. They looked standard versus intensive control and showed that among patients with no baseline diabetic retinopathy, intensive control produced a very dramatic fall in the onset and progression of diabetic retinopathy as shown in this graph. There was a 76% reduction of developing progressive retinopathy if intensive control was implemented.

Now, intensive control and DCCT is now what we call intensive control now, that is directly related to how well we get the blood sugar. This holds also for mild to moderate retinopathy. There was significant decrease in the retinopathy onset and progression. Basically, it shows that about half of the patients had a reduction in progression of diabetic retinopathy and in development of severe or proliferative diabetic retinopathy, and 60% reduction in need for laser surgery. Now, these microvascular changes that are prevented by intensive control is mirrored by other end organs as well. As you could see here, it's not just retinopathy, it's also seen in peripheral neuropathy and nephropathy as well.

Now, the DCCT cohort was studied for another 10 years in the EDIC study, looking at long-term effects of conventional versus intensive diabetes control and looking at the same complications, and it showed that there were long-term benefits of improved control, and the effects were sustained even after some slippage in the degree of control. So, once the process leading to microvasculopathy has begun as a complication of diabetes, it tends to be self-perpetuated so it's important to get those controlled early.

Now, UKDPS is a similar study that was done in type 2 diabetics, looking at standard versus intensive glucose control, and also with blood pressure control. A similar source of protection was seen, both in the progression and for laser surgery, and blood pressure was shown to be as important as glucose control for mitigating the risk of diabetic retinopathy. Once again, there was a legacy effect with glucose control. So, the intensive treatment group continued to experience significant reductions in

microvascular disease as compared to conventional treatment, but there was no legacy effect for intensive blood pressure control.

So, the compounding factors for diabetic retinopathy, blood pressure, glucose and lipids, these are the things we have to control. The absolute number has changed over time. This is the party-line here, 130 over 85 for blood pressure, 6.5 to 7.0 for the A1C. Now, there has been some adjustment in this based upon the age of the patient and other issues. We have to watch out for risk of complications and blood lipids. So, when we exercise control of these compounding factors, there's a decreased risk of diabetic retinopathy, development of progression and a decreased need for laser surgery.

Now, I asked a little earlier -- Jan, can you show me the -- can we look at those results real quick? Okay. Looking at the FIELD study, 81% have not heard of the FIELD study. I've got to let you know that that's actually higher than the score I get when I use a poll for this. Obviously, if you haven't heard about the FIELD study, then you're not going to be familiar with the results and that's consistent with previous polls I've taken. The ACCORD study, a much larger fraction of you know about the ACCORD study and the comment about the fenofibrate offering us any microvascular protection is also consistent. So, please know that the way you've responded is entirely consistent with previous polls that I've taken.

Let's go back to the slides now and let's talk about this a little bit, because this is a very important data. Not all of it is new, but some of it is relatively new. The interpretation of it, I think, is critical since it does offer us some new opportunities for mitigating the risk of diabetes and diabetic retinopathy.

The FIELD study was about 10,000 folks, five-year study. A thousand patients were involved in a sub-study for diabetic retinopathy. In this group, there was a 78% reduction in progression among patients with preexisting retinopathy and about a third of the patients had a reduction in the need for treatment. This is an incredible data, incredible data. This is right up there with laser treatment impact, so very important information we got from the FIELD study. Based on this FIELD study data, in some countries, fenofibrate now has an indication for treatment of diabetic retinopathy.

In the ACCORD study, there was a subsection that the 10,000 patients that were studied for diabetic retinopathy, even though the primary end point was the cardiovascular one, retinopathy was taken as the secondary endpoint in about 3,500 patients. As was reported in the poll we just took, there was no appreciable benefit of fenofibrate, but only for the cardiovascular events.

Now, what's happened is that everybody remembers and they're aware of the cardiovascular event, but what's failed to get recognized in the medical community is that fenofibrate offered a terrific advantage in diabetic retinopathy and maybe other microvasculopathic end organs. Overall, there was about a 38% reduction of diabetic retinopathy onset and progression looking at all the patients, but those with only mild diabetic retinopathy at onset, there was a 78% reduction. So once again, this is huge and it's something that we probably should pay attention to.

Now, it's very important to recognize that the mechanism of action of the microvasculopathic protection of fenofibrate has nothing to do with the lipids. So it's totally irrelevant as to whether or not the patient needs lipid control. All of these patients were being treated with a statin already. Fenofibrate or a placebo was added to that, and the data showed that the outcome for diabetic retinopathy had zero to do with lipid mechanism, but there are other non-lipid mechanisms with this drug. The drug also has an influence on endothelial function. It has an impact on apoptosis. It also has antioxidant effects. It protects the blood retinal barrier and that has to do with the macular edema. There's neuroprotective effect and that is very important. It has an anti-angiogenic effects and that is a common pathway to blindness in diabetic retinopathy is blood vessels proliferating. So this is very important information.

Now, many of us worry about fenofibrate having some patient safety issues, but both in the FIELD trial and in the ACCORD trial, it proved to be a very safe drug. In contrast, gemfibrozil which does have a

very high complication rate when used with a statin, but it was very well tolerated in both FIELD and in the ACCORD study, so this is not something we really need to be particularly concerned about.

Now, the NIDDK and the IHS has worked together with a proposed study to look at this because there are some gaps in the evidence. We don't know exactly when is the best time to treat, except it doesn't afford any protection that the patient does not have any manifest diabetic retinopathy, but there are some questions about when is the best time to treat and some other gaps in evidence. The study has been proposed and I would like to say out of the clever fellow that has brought up this title FARSIGHTED, but we have considered a study and we're looking for funding right now to look at that in Indian Country to see if it can provide any protection for our patients in order to decrease the onset and progression of diabetic retinopathy and need for surgery.

This is how it would be combined with telemedicine in the schema that I'm showing you here. On the left side, it's a conventional approach for diabetic retinopathy management. It is specialty clinic-centered and it's failing 50% of the patients. They are lost in follow-up as I mentioned earlier. The other 50% make it to the eye doctor, about 45% of that 50% have no need for treatment and so they go back into the system, which includes a 50% loss to follow-up rate.

Alternatively, moving to a primary care diabetic retinopathy management program that is patient-centered, all the patients could conceivably be examined by telemedicine. Any patients with advanced disease could be referred directly to a specialty environment and hopefully bypass the part of the large fraction that was lost to follow-up, and then the remainder could be treated with fenofibrate to enjoy the benefits that we've just discussed.

So in this scheme of primary care treatment with fenofibrate becomes the first and early approach to diabetic retinopathy, to treat early in the course of the disease instead of late, treat by a primary care provider without a referral until the patient is discovered to have high-risk disease by the telemedicine. There's no need for difficult and costly travel to subspecialty eye care. Many of you are familiar with what's involved with getting your patients to a subspecialist for diabetic retinopathy evaluation and treatment. And it could be naturally incorporated into a primary care based teleophthalmology program such as the JVN program that we have deployed in the Agency for the combined benefits of patient recruitment and treatment.

There's the possible other collateral benefits. The FIELD and the ACCORD show that there is some microvasculopathy end organ protection. Prominent among them are renal and peripheral neuropathy and it is far less costly, far less costly to the patient and health care system to avoid the complications than to treat the complications.

Moving now to the details of the JVN program, let me make sure that everyone is familiar with the basic concept of diabetic retinopathy. Diabetic retinopathy exists in two basic forms. The non-proliferative form with hemorrhages and microaneurysms primarily, and that passes seamlessly to the proliferative form with new blood vessel formation, hemorrhages in the vitreous with superficial contracture and retinal detachment. This is how patients go blind from diabetic retinopathy.

In both of these categories, both non-proliferative and proliferative, the macula, that portion of the retina that's tasked to see 20/20 can become edematous, fluid can accumulate and that causes moderate vision loss. The non-proliferative form of the disease and the proliferative form of the disease before there is hemorrhage is totally asymptomatic, patient sees 20/20 here. That's why it's so important to examine the patient on an annual basis because patient can see 20/20 and have dangerous levels of diabetic retinopathy, and diabetic macular edema is associated with moderate vision loss, not blindness.

Now, the culprit here as everyone knows is hyperglycemia. It is the mechanism that leads to vision loss, both moderate and severe vision loss. The hyperglycemia does this by damaging the

endothelium of capillaries by changing the way the blood vessel actually -- the red blood cell is actually slow in the vessels. There is oxidative stress on the retina as a result of this hyperglycemia and also there is inflammation. This has a pathway that leads to leaky blood vessels, retinal edema and moderate vision loss. However, at the same time, there is from the hyperglycemia, we have capillary occlusion and that capillary occlusion results in an angiogenic cascade that leads to new blood vessel formation. Does that make sense? The capillaries occlude, the retina gets relatively anoxic. Normal mediators are liberated and says, "Give me some more blood vessels. I need a little air." The difficulty is that these are incompetent blood vessels. They lead to hemorrhage, scarring, retinal detachment and blindness.

This is basically what it looks like. Here is a pre-retinal hemorrhage in an eye, this is vitreous hemorrhage. If this is not managed, it leads to retinal scarring, retinal detachment then blindness, and then these blood vessels are leaky, they're causing retinal edema and moderate vision loss.

Now, the treatment that we have for this works at various points in this cascade. We can use laser or steroids and special injection -- medications can be injected in the eye to stop the vascular permeability in the moderate vision loss. We could do laser to address the capillary occlusion issue, and basically, the way this works is simply by removing or killing the retina in a strategic fashion that's not very noticeable to the patients, so if there's less metabolically active retina to use the little bit of oxygen that's available. In addition, we can inject a drug in the eye that blocks the angiogenic cascade directly; and if we don't do any of that, the patient starts to get retinal detachment. We can go inside the eye and remove the components.

Now, the clinical division of diabetic retinopathy, this existed -- in this international scale, and this is not how we do research, but the way we do this clinically is we divide this between no diabetic retinopathy, mild non-proliferative, moderate non-proliferative, severe non-proliferative and proliferative. Remember, proliferative is what we treat. So what we do is we watch carefully if the patient progresses through this continuum and then finally treat at this level before the patient loses vision.

Macular edema is divided just into two categories, one that you need to watch, but not treat and one you need to treat and we call that macular edema non clinically significant and then clinically significant. We follow these patients annually unless they have more severe levels of diabetic retinopathy and then we may follow them more frequently.

Once again, the idea is to withhold this treatment. Laser treatment is invasive; sticking needles inside the eye is invasive. It all comes with a risk. So, we don't treat any sooner than we have to in order to balance the risk and the benefit. Here is some evidence of laser placed in the eye. I said we destroy retina in order to decrease the metabolic load on the little bit of oxygen is available for the diabetic retina. We place these laser treatments though a laser delivery device that you see here.

The idea and the evidence is to reduce the risk of blindness or severe vision loss due to diabetic retinopathy, proliferative diabetic retinopathy or other forms, high-risk forms. This tracing you see here is the event rate, that percentage of the patient population with high-risk disease that loses vision due to untreated diabetic retinopathy. You see that after three years, it's enormous. A third of the population is blind. However, if you instead, you treat this patient instead of observing them, as what happened if you didn't exam them and didn't know about the disease, then they move to this tracing down here which has only 2% of the population suffering disease. So, you can see that it's very nearly preventable. Blindness is very nearly preventable with simply timely diagnosis and treatment.

Macular edema, the treatment is less effective. It's only about 50% effective, but nonetheless, it prevents ongoing vision loss in about half the population if diagnosed in a timely fashion. Now, one of the newer treatments we have, the laser treatment that we've been talking about, our understanding of that developed in the late '60s, '70s and early '80s. This treatment you're seeing here is less than 10 years old and we inject directly inside the eye a substance that acts on the pathological mechanism that

causes macular edema. I don't expect you to be able to read this, but those gaps and holes you see here, this thickening the retina is the pathology, and after treatment you can see a normal contour to the retina here.

Here is the problem with that. With these injections, that you see here, the first layer of intravitreal anti-VEGF injections, they cost about from \$1,000 to \$2,000 a dose and you've got to get three hits of this and then over the next two years, you get about 2.7 injections per year. There is an off-label use of a similar drug called Avastin that's only \$60 a dose. It doesn't work quite as good as the other two and there are two additional drugs, that are steroids that you can see, they vary between about \$1,300 a dose and almost \$9,000 a dose. The \$9,000 version lasts 36 months. These drugs come with potential complications of glaucoma and cataract. Obviously, we prefer not to have to treat with these intravitreal injections but they do work very well.

If we miss our opportunities to stop this pathological process that leads to vitreous hemorrhage and retinal detachment, there is still an opportunity. We can go inside the eye. We can remove the vitreous hemorrhage. This allows us to then do a laser treatment once that hemorrhage is out and/or repair the retinal detachment that exists. This is how that looks. You can see that instruments are placed in the eye and using a mechanical process where we're able to remove the hemorrhage and fix the retinal detachment in most cases. But the reason why we have this problem of serious vision loss despite these various mechanisms to prevent it or correct it, is that 40% to 60% of the patients fail to find their way to timely treatment.

Now, here is some evidence in the Indian Health Service that is our special basis for that. What you see in this tracing is about 50% of the American Indian/Alaska Native population fails to get an annual eye exam. You'll notice, however, and we'll talk about this a little bit later, starting about 2008, you can see that there has been a consistent uptick, and I'll tell you with great pride why that is a little bit later. Here, you can see that the annual examination rate for the various Areas, there are highs and lows, but basically across, about half the folks fail to get an eye exam, and the reason why is not because we want it to be that way, it's just because our system is designed to achieve that. We didn't design it to fail, but the system we're currently using does fail, and it doesn't fail just in Indian Country. This is everywhere. Now, the data I'm showing you here, for example, the red tracing is we are tracing is Medicare patients. If you're over age 65, so the annual examination rate is in the 60s, you can see that it used to be lower than that. If instead, they were looking at the commercial providers and also Medicaid, you can see that it's down in the 50s, about a 50% annual examination rate. In Indian Country, we're in the low 60s. So, we're actually doing much better than most patients that are less than 65 years of age.

Now, this is not a problem with eye doctors, and I know that's the intuitive thing to consider is that we'll get more eye doctors or make our eye doctors work harder. This is not a problem with eye doctors. About half of all patients with diabetes choose not to get an annual exam by an appointment to the eye clinic. That's been proven time and time again, this is not just Indian Country, this is downtown metropolitan USA, folks choose for whatever reason and we can speculate on that, they choose not to get an eye exam consistently. Now, we recognize this as a horrible problem. There is some regulatory oversight for this in the Indian Country through GPRA. In 2016, we had a target of 61.6%. I have not seen the 2016 data yet. My guess is we met that. Next year, in 2017, the target of 63%. It's very difficult to get numbers like this using the conventional approach of an eye clinic based exam by appointment. So, the JVN program, our telemedicine program that we have in the Agency has helped us with that, as we'll discuss.

Now, in order to get a GPRA tally, there are only three ways by which that can be achieved. A dilated eye exam by an optometrist or ophthalmologist and that is the conventional clinical method. It's our entry level approach. This is the way that we commonly achieve the standard of care. However, it is not the gold standard. The most accurate way to diagnose diabetic retinopathy and the method that we achieve this in research studies is by something called the seven-standard field studies using the Early

Treatment Diabetic Retinopathy Study methodology. This is seven 30 degree stereoscopic fields using slide or digital imaging. This is a research methodology; it is not practical for community-based surveillance. So we have one other photographic method that can be used and tallies for GPRA, and that is any other photographic method that has been formally validated to the early treatment of diabetic retinopathy. It's not just any photograph that's interpreted in any fashion, but if it has been formally studied with scientific methodology to be equivalent to this then they can be used instead of the seven standard fields Early Treatment Diabetic Retinopathy Study. Now, if it has been validated, as has been done with the methods that we use in the IHS, then we can count it as a qualifying examination for GPRA and for meeting the standard of care for diabetic retinopathy surveillance.

The JVN program has been validated and it was created about 2000 and put into clinical operation about 2001 for the remote diagnosis and management of diabetic retinopathy. It is centrally funded. Over the 16-year course of the JVN in Indian Country, we've come to appreciate the benefit that it provides us. It's quick and painless because it uses very low levels of illumination and no pupil dilation, and because of this, because of its very non-invasive fashion, it can be easily interlinked with other patient encounters. So, a patient that comes in to the primary care environment for whatever reason, if that patient can be identified as failing a standard of care, then the JVN encounter can be conducted and a standard of care for diabetic retinopathy diagnosis can be satisfied. Importantly, it has been validated so it can be tallied for GPRA.

Now, we have two imaging devices. Our legacy device is this instrument here, and over the past 18 months we've been upgrading certain of our deployments with this device here. In both instances, the images are acquired by a certified imager. Demographics are harvested from RPMS. The imager supplements the history, provides some patient education, using the patient's own images for that purpose, which would provide additional value, and then the data, both the images and the clinical data for that patient are transmitted to the reading center. At the reading center, there's a very structured and standardized process for interpreting the images. Computer-assisted decision support is utilized with special reading software that produces an automated diagnosis that's validated by our eye doctor readers, and then the documentation is created automatically and sent to the hosting site.

Now, I showed you where we use -- we have two different cameras. Our legacy device took images that's consistent with the industry standard and that is this area here, the early treatment of diabetic retinopathy seven-standard fields that we talked about. It's this piece of the retina. Although the retina is much larger than that, this is where the science was created and this is standard of care for determining the level of diabetic retinopathy. The new camera we have actually is able to look at this more expansive area. Notice, in this demonstration photograph of an actual patient, most of the diabetic retinopathy is located outside the seven-standard fields. Now, we've come to appreciate the significance of that by careful studies using this more expansive imaging technique.

What you're seeing here is our first year of experience of using Ultrawide field Imaging in the Indian Health Service. We looked at 8,000 patients that were imaged using Ultrawide field and compared them to over 17,000 patients that were used for the standard photographic method during the same period of time, and there were some very remarkable data that's revealed from this study. There was a profound reduction in that fraction of the studies that were ungradable. If we do not get a technically, a high quality, a high technical quality image, then we cannot interpret or grade it in a fashion that's consistent with the original validation data and so we have to say it's ungradable and recommend that patient for a dilated retinal examination. With the Ultrawide field imaging, we cut this remarkably. It was a profound decrease from about in the 20s to low single digit. In addition, there was a two X increase in the rate of diagnosing diabetic retinopathy. This new technique, detected twice as much diabetic retinopathy. Now, obviously, the photographs aren't creating disease, it's just detecting disease that would otherwise have gone undetected.

Importantly, this additional data, the peripheral data raised the severity level by 9%. So that means that the imaging -- the studies that we were doing and validated to be equal or better than live eye exam in

the standard methodology was missing 9% of the disease. This is a very important finding. The combination was that we reduced the unnecessary referral rate in about 4,000 patients per year. Very exciting data in the first year, and we'll continue to collect this data.

Now, here's a paper published by the Joslin Diabetes Center looking additionally at the importance of these peripheral lesions. This is not Indian data here. This was done in Boston. And what they've discovered is that these peripheral lesions, when they take on a certain pattern, they're able to risk stratify the patients in a much more refined fashion. If these peripheral lesions are found and these peripheral lesions can only be found by imaging, we can't do it with a live eye exam, there's a 3.2 risk, a 320% increased risk for progression of diabetic retinopathy and a 4.7 times risk for proliferative disease. So once again, not only did we lower the ungradable rate, but we're getting data that helps us manage the patient better and do it in a fashion they cannot be duplicated by a live exam.

Now, of course, we talked about why diabetic retinopathy is the leading cause of new blindness. If the treatment works so well, well it's because they're not getting examined. Here's a study that we conducted for four years at the Phoenix Indian Medical Center and it showed that the examination rate could be increased 50% by implementing a primary care based telemedicine program for diabetic retinopathy examination and that was associated with about the same percentage, 51% increase in laser treatment. Very important finding.

I won't go over the details of this, but we did a very careful study looking at Indian Country specific financials and epidemiology and showed that this technique is also very cost-effective. It's less costly and more effective for detecting diabetic retinopathy, identifying patients that require laser treatment and very importantly, preventing severe vision loss.

Here is a map and a listing of the sites I don't expect you to read the small type showing where we're positioned in 25 states. We have 96 telemedicine sites and 13 portable sites. The portable sites are the hottest products these days and we continue to expand that. What I'm showing here is the way that we have ramped up our examinations and we're well over a 120,000 studies. Cumulatively, we examined 20,000 patients last year. What I'm trying to show here is the impact that it's had on us as a national group. What I've shown in this data is that since 2008, we have stopped the consistent decline in the diabetic examination rate in Indian Country and there had been a consistent decline, as you can see in the linear regression analysis of the examination rate before 2008. As compared to after 2008 there's been a consistent increase and since that time the examination rate had increased 23.6%. A remarkable impact that can only be due to this change in the way that we're examining diabetics in Indian Country. Now, when we enjoy -- when we enjoy these sorts of improvements, we're able to re-task the recovered resources. If we examine the patients with the Joslin, we can take the staff that are liberated from those exams and task them on other unmet needs and we can also re-task the dollars and assign those to other targets of opportunities. Of course, there's an enormous advantage in the person-years of sight that are preserved by timely diagnosis and the treatment, and of course, the secondary impact on the family, society, and the healthcare system.

Other folks are using telemedicine, the VA. They have a higher prevalence rate of diabetes and they have a much different population that they serve. They did 500,000 annual exams last year, actually more than that now. In the United Kingdom who uses telemedicine as a default method for diabetic retinopathy diagnosis. If you lived in the UK, the default method for getting the diabetic retinopathy examination is telemedicine. In 2014, for the first time in 50 years, diabetic retinopathy is no longer the leading cause of severe vision loss in the UK and it's thought to be through the improved examination rates afforded by the telemedicine.

So, the best practice is patient education. Try your best to get the patients in, to get their eyes examined and also to manage their diabetes better, control the compounding factors of glucose, lipids, blood pressure and smoking, maybe fenofibrate. There's been some discussion that perhaps using fenofibrate on a limited basis, as a best practice in Indian Country. As I mentioned, we're still trying to

get funding for the study so we can accumulate the additional science that would help us in that effort. Of course, the annual diabetic retinopathy examinations for timely diagnosis and treatment. Now, I know I went quick or quickly. The slides are available for the more masochistic to review at your leisure, and I stand available by email and also by phone if anyone wants to discuss this in more details.

But if there are some questions. Jan, did we get some questions?

Jan Frederick:

We did and we have gathered those up for you. Lots of good questions and interaction, it seems like mostly around JVN. Do you see those there Dr. Horton?

Mark Horton:

Is that over on the right or -- there are some at the bottom?

Jan Frederick:

We've gathered them up for you on the right. They're the same.

Mark Horton:

Okay, on the right. "Does any diabetes department uses JVN outside the optometry visit?" Okay, and I apologize for not making this clear. Please understand, this is not an eye care tool, this is a primary care tool. If you put it in the -- if it's in the eye clinic, then all it's going to do is QA, it's going to do quality assurance on the optometrist or ophthalmologist. It's virtually never used in or during the optometry visit.

"Do you ever take the patient to the JVN after the primary care clinic?" It's in the primary setting. That's where this device -- if it's anywhere other than in the primary care clinic, then I'm not -- people are doing that outside my awareness because it's a tool to be used in the primary care environment. All the patients come to the primary care clinic, only half of them go to the eye clinic. So the idea is to fish in the pond with the best chances of catching what you want. If we make it available in the primary care clinic, our patient comes in, we can identify them as failing standard of care, we don't give them an appointment, we just march them through to the camera, no dilation drops, no fuss, no muss, quick and easy, take their pictures, they're done.

"Are you guys using it in place of a dilated fundus exam?" Absolutely positively without hesitation or equivocation, yes. It's been validated equal, or better than a live exam. If the patient is asymptomatic, the dog hasn't eaten their contact lenses, they're not seeing double, they don't have glaucoma, they're not otherwise interested in their eye exam, then this absolutely qualifies. It is not a step down in quality. The science actually shows it's a step up. So, there's no reason to avoid this as a second best method for obtaining standard of care. It's equivalent or better than the live eye exam particularly in the case of the new technology, the Ultrawide field actually gives us data that cannot be obtained by a live eye exam.

All right. "Does this system of testing only work with RPMS? We use NextGen".

Okay, it will work completely disconnected from RPMS. So the answer is yes, it will work with NextGen, it will work with -- I don't know what MACT is. That's at MACT. Yeah, it will work with NextGen. We have used it with NextGen. What you lose is when you don't use RPMS is that we have -- we have created interoperability between this telemedicine modality and RPMS EHR. So, it can be used in a manual method with NextGen, EPIC, Centricity, any other form of technology, you just won't

get the automated interoperability. It still works, it still provides the same public health benefit, it's just they had -- instead of doing something in an automated fashion with respect to data flow, you have to do manual. Take manual effort on that.

"The turnaround rate for the JVN report, does it take long to get a report?" Well, that's a really good question. A normal time, it depends on the time of year. Normally, a report is returned to the hosting site within three to five days. But remember, we're dealing with a disease that the periodicity is measured in months, 12 of them. It doesn't really matter if much of it takes one week, two weeks, three weeks, or more to get that back because you're measuring this in a yearly basis anyway. Now, if a patient -- if the imager thinks that the patient has unusual disease when they capture the images and they're trained to do that, then they call us up and say, "Don't wait to do this in line. We want to move it front of line." We do a stat read. When I say it's three to five days, that's not for everyone.

Now, I said it varies from time of year. Unfortunately, many of our sites are not as attentive to imaging patients early in the GPRA year, and they will frequently get to the end of the GPRA year and say, "Holy molly, look at our GPRA rate. Somebody do something quick with that JVN." So we can really accumulate a backlog in the last half of May and June. We didn't so much this year. We were anticipating it, but that can be a problem.

"So, the JVN is really supplementary?" Absolutely, positively not! It is a method that's equivalent to a dilated fundus exam. So it is not supplementary in that context. Now, if patients all went to the eye doctor and got their dilated fundus exam, then there wouldn't be much of a reason to do this except to enjoy the improvement in quality and economics.

But as I mentioned, it is cheaper and works better than a live eye exam, so there's a reason to do it independent of the fact that patients -- 50% of the patients do not go and keep their appointment or even make one. It's hard to say it's supplementary, but it is something that's used in concert with a live eye exam. If patients get a live eye exam, then they do not necessarily need to get the JVN. But together, working together, we've managed to increase the surveillance rate at 23.6% as of 2008.

It works in portable sites by essentially making it movable, and I'm running out of time but we have made the JVN portable. It's a desktop JVN. It's removed two ways, it has a special case that we've designed and tested in very adverse conditions and it works great. Call me for more information.

"What is a CR2?" I don't know. There is a camera, I think, that has a CR2 designation. Please send me that question in more detail and I'll see if I can address it for you. "Just to be clear, this would take the place of an eye exam, if the JVN comes back." It takes the place of a diabetic retinopathy examination. It doesn't give you glasses. If you're seeing double, it doesn't fix that. It doesn't mow your yard, babysit your kids, or change your oil. It satisfies standard of care for an annual diabetic retinopathy examination, the failing of which occurs in 50% of our patients and it's the proximate cause of the single, most prevalent reasons for serious vision loss among our patients. It does not replace a live eye exam, it just takes the place of a standard of care that can eliminate the number one cause of blindness among our patients.