Abstract
The significant increase in newly-diagnosed cases of diabetes promises a subsequent rise in the number of people with diabetic retinopathy—a complication that is already the leading cause of blindness among working-age adults in the United States. In spite of physician recommendations that people with diabetes obtain annual dilated retinal examinations to detect sight-threatening lesions, only about half of all known diabetics receive this standard of care. For many in underserved areas of the country, and for many more who do not recognize the risks or who do not have the financial ability to pay for care, diabetic retinopathy threatens to deprive them of their vision and a productive and fulfilling existence.

Digital detection of diabetic retinopathy uses high-resolution retinal imaging as a technological means of bridging the gap between recommendations and real access to healthcare. It is able to reach patients who would not obtain dilated retinal examinations any other way, and offers a streamlined and efficient method of shepherding those patients with treatable retinopathy toward the ophthalmic specialist care they need to preserve their sight.

Introduction
As healthcare providers (and consumers), we live in dangerous times—caused by a unique confluence of socioeconomic stress, healthcare system breakdown, rising costs, lack of insurance, ethnic and racial disparities, increasingly sedentary lifestyle, poor nutrition, increasing obesity1 and skyrocketing new cases of chronic illnesses like diabetes.2,3 Taken singly, each of these issues represents a severe public health problem. In concert, they form a "perfect storm" that threatens millions of people with permanent disability and poses a great danger to the physical and economic well-being of society.4,5

In the case of diabetes, the following maxims are uncontroversial:
1. The longer a patient has diabetes and the more severe the disease, the greater the chance of developing diabetic retinopathy.
2. Diabetic retinopathy has a well-understood natural history with a prolonged asymptomatic early stage.
3. Early treatment results in improved visual outcomes.

Strategies to detect and treat diabetic retinopathy have been validated by the results of numerous multicenter clinical trials and have been translated into evidence-based patient care. When applied rigorously, annual dilated retinal examinations and laser photocoagulation reduce the risk of vision loss and can preserve useful vision. However, the recommended care standards are not obtained universally by known diabetics. Highly educated and affluent patients who live in major metropolitan areas are most likely to be examined and treated regularly. Patients who are indigent,6 elderly,7 poorly schooled, members of an ethnic or racial minority,8,9 or who live in a rural area are less likely to obtain annual eye examinations and thus are more likely to suffer the consequences of untreated disease.

Remote detection of diabetic retinopathy, using digital imaging and telemedicine, is a useful addition to conventional physician-provided screening.10 It overcomes time, money and logistical constraints, improves access, reduces disparities, provides equity of care and improves outcomes—even in the case of today's unprecedented increases in newly diagnosed cases of diabetes.

Materials and Methods
In countries with a centralized healthcare authority, programs to extend screening opportunities to most known diabetic patients have already been established. Both England11 and Scotland12 have developed extensive back-
ground documentation, program descriptions, protocols and quality assurance schemes, making these documents readily available on the World Wide Web.

Several approaches to diabetic retinopathy screening are evolving in the United States, a country that lacks centralized healthcare management and has a long history of ad hoc, market-driven healthcare delivery approaches. These vary in certain technical details, such as angle of view, stereo or monoscopic imaging, selected wavelength or full color, image resolution, use of dilating agents and the number of recorded fields. The one important similarity is that these programs offer screening opportunities in non-traditional (e.g. non-ophthalmological) settings, most often a general healthcare or primary care clinic.

This approach breaks with the historical model of eye care providers delivering specialty eye care services to patients who visit them in their own clinics. The new method consists of eye care providers delivering care remotely to patients in primary care clinics, with technology serving as a surrogate for the usual face-to-face physician-provided examination.

The following sections describe the approach used by the Vanderbilt Ophthalmic Imaging Center (VOIC) screening program.

**VENUE**

At present, the VOIC network is comprised of five screening sites. Four of these provide screening as a component of direct patient care; the fifth site acquires data for a research grant funded by an outside agency.

Two of the patient care sites are community health centers, staffed by primary care physicians, nurse practitioners, residents and allied health personnel. The other two screening sites are located within Veterans Administration medical centers where they are situated close to primary care clinics.

The full-time availability of the camera and screening personnel facilitates patient screening. Some of the sites make appointments for patients to return for screening at a later date, while others offer on-demand screening.

**SCREENING STAFF**

Each of our participating clinics provides screening staff to the program. These individuals do not have ophthalmic photography backgrounds, but rather are trained to perform screening according to the VOIC protocol. Our current screeners include licensed practical nurses, medical assistants and research assistants.

Training consists of an initial didactic presentation and practical demonstration, followed by continual monitoring of technical quality.

**ON-SITE HARDWARE AND SOFTWARE**

The screening encounter begins with visual acuity measurement. In the often-cramped and always busy internal medicine spaces of a community health center, we believed that the use of a wall-mounted self-illuminated test chart and 20 feet of unobstructed viewing space could not be reliably obtained. Instead, we elected to use a desktop visual acuity measurement device equipped with an ETDRS test target (Optec 800, Stereo Optical Company, Chicago, IL) (Figure 1). This unit has a built-in illumination system and is equipped with a pinhole attachment to help overcome refractive errors. The results of this measurement are entered into the patient’s database and thus become part of the electronic record.

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Figure 1: Optec visual acuity measuring device. This self-contained desktop unit incorporates its own illumination and optics. We use a log-mar test target based on the ETDRS target, providing measurements from 20/200 to 20/12. To overcome possible refractive errors, a pinhole attachment is inserted when the patient cannot read better than 20/50.

Figure 2: Retinal screening camera in use. The screener (R) is able to compose and focus the image by observing the built-in monochrome screen (IR image) attached to the camera. Our network uses the Canon CR6-45NM camera with pharmacologic dilation.
We use screening-type retinal fundus cameras, designed to produce a moderately wide angle view of the retina through a physiologically dilated pupil. These instruments are meant to be used in a darkened room, where the patient’s pupils are expected to dilate sufficiently to admit the illuminating rays from the camera and to produce an artifact-free image. Screening cameras typically utilize an infrared focusing light and a small video monitor. The screener adjusts composition and focus by watching the monitor, but the infrared illumination is virtually invisible to the patient and does not interfere with the dilating process. We use Canon CR6-45NM cameras (Canon Medical Products, Irvine, CA) in each of our screening clinics (Figure 2), although we pharmacologically dilate all patients.

The retinal images are captured on digital cameras which are attached to the fundus cameras. The first two camera sites were equipped with 3-megapixel cameras (the highest quality cameras then available in the so-called ‘prosumer’ class.) Since then, 6-megapixel cameras have become affordable and the more recent sites are equipped with them.

Images are held temporarily in a laptop computer attached to the camera stand. The Dell Latitude C-600 series (Dell Computer Corporation, Round Rock, TX) is used throughout our network.

The resolution, bit-depth and playback characteristics of the digital images are associated with the ability of the process to identify pathological conditions. As currently configured, our equipment records images that are 8.5MB in size. These large files are saved as .PNG (Portable Network Graphic) files, a lossless compression algorithm that preserves image detail but reduces slightly the overall size.

The software for image acquisition and database entry is designed exclusively for retinal screening programs. The EyeQ Superlite program (Digital Healthcare, Cambridge, UK, available in the US from Canon Medical Products, Irvine, CA) is used at each capture station and interfaces with its counterpart “review” software in the VOIC Reading Center.

**Telecommunications and Server**

We use “store and forward” technology to transmit the digital images from the screening sites to our Reading Center. Because we do not need live motion or real-time interaction, we store the images and patient identifiers in the laptop computer temporarily, and then upload them at the end of the day’s clinical activities. Each patient’s file is at least 35MB in size and takes about 3.5 minutes to upload over our T-1 broadband connection. This configuration is point-to-point (camera site to computer) and is considered secure because it does not traverse the Internet.

T-1 lines are affordable only within fairly short distances. Alternatives include frame relay, the various DSL (digital subscriber line) iterations and the use of VPN (Virtual Private Network) software and hardware solutions. We established a strategic partnership with our local telecommunications service provider (BellSouth Corporation, Atlanta, GA) to facilitate the correct design and implementation of this crucial component of our program. We urge new programs to establish a close working relationship with their local telecommunications provider, and believe that such a relationship is mandatory to ensure that data is handled safely and efficiently. These vendors should also be fully aware of Federal regulations mandated by HIPAA.

We use a Dell PowerEdge server configured in a RAID array, which offers the safety associated with multiple disc drives. The server is configured so that incoming images are held in a working directory. After review and grading, the images are archived in the same machine. We use digital data tape to back up the server every day. As storage capacity nears, we plan to consider off-site automatic data backup using a SAN (storage-area network).

**Analysis and Grading**

Our review stations are equipped with Mitsubishi Diamond Pro 2060U 22” CRT monitors (NEC-Mitsubishi Electric Visual Systems, Tokyo, Japan), configured to display 2,048 x 1,536 pixels (Figure 3). We are thus able to display each image in its entirety on the screen. Use of the review software permits additional magnification of either the entire image or selected portions as needed.

The software also permits a variety of image processing tools, including red-free viewing and adjustments of contrast and brightness. These tools help elucidate ambiguous lesions and enhance the viewing of retinal pathology when the patient has media changes. None of these enhancements permanently alter the original file, however. They are used only to improve our understand-

**Figure 3:** Image grading. Drs. Cynthia Recchia (L) and Kamel Guentri (R) use Mitsubishi CRT 22” monitors, set at 2,048 x 1,536 pixels, to review screening images.
ing of findings that may require referral for more thorough analysis by an ophthalmologist.

We use a customized grading form that uses checkboxes to denote the presence of a wide variety of lesions customarily associated with diabetic retinopathy. The form also includes boxes for optic nerve cupping, hypertensive changes and text boxes for the entry of comments. It features suggestions for referral exhibited as three options: rescreen in one year, non-urgent referral and urgent referral, all based on the severity of diabetic (Figure 4) and other retinal lesions detected upon review.

This paper’s authors serve as the core grading team for the program. The first level grader (K.G.) is a physician trained as a dermato-venereologist. This background gives him the ability to identify significant lesions based on such morphologic factors as color, shape and size. The intermediate grader (L.M.) has photographed patients with retinopathy for 30 years, including participation as study photographer in several multicenter clinical research trials. The senior grader (C.R.) is a fellowship-trained vitreoretinal specialist with experience interpreting high resolution digital images.

In concert, the three graders achieve excellent inter- and intra-grader agreement. The VOIC workflow requires at least two graders to independently grade each patient, with a third expert grader used to adjudicate disagreements and/or to provide consultation for unusual findings. To track which graders participated in the review, the report form has space for the graders’ initials.

Since the original design of our grading form, we have incorporated a new grading scheme into our program. The recently proposed international classification system for diabetic retinopathy, derived from the various levels of severity described in the Early Treatment of Diabetic Retinopathy Study (ETDRS), is a streamlined method of description that facilitates communication between ophthalmologists and primary care physicians. As such, it is a boon to a program like ours in which the managing physician or nurse practitioner prefers to receive a simple description of the patient’s current retinal status and direct clinical management suggestions to optimize patient care.

**REPORTING AND ARCHIVING**

Unlike conventional physician-provided examinations in which the patient is told about his or her condition directly, our program conveys clinical information to the supervising primary care physician. In effect, this process gives the primary physician another tool with which to take care of his patients. Responsibility for the screening encounter and the interpretation is delegated to the screening program, and the results are then conveyed back to the PCP. Referral for ophthalmic follow-up care is done by the PCP, using local providers. In the case of VA patients, the VA eye clinic manages patients who need further specialist care.

Some of our participating clinics still use paper charts, and for these we print out a copy of the grading sheet and mail, fax or hand-deliver the report. For clinics using electronic medical records, the grading form is used as a worksheet in order to enter the findings and recommendations as an electronic consultation report.

We do not include copies of the retinal images with the report, but if a clinician requests it, we can burn images to CD as JPEGs or TIFs.

Turnaround time is designed to be brief. Typically, all patient images arrive at our server during the evening and are fully graded by noon the next day. Thus, the final report is available within 24 hours of the screening visit.

After the report has been generated, we archive the image and data package in our server. Archiving makes the images permanent and no further changes can be applied to the grading sheet. At present, we use digital tape to create daily backup records of the archives; within the next year we plan on outsourcing this function to a company that provides an automatic data storage and disaster recovery product.

**ECONOMIC CONSIDERATIONS**

A key attribute of effective population-based screening initiatives is economic sustainability. The test must be affordable in order to be used. By using a technology-based solution and staffing the program with screeners, who function well but who lack in-depth ophthalmic
and/or imaging experience, we are able to deliver this model of care for a unit price far below that of conventional physician-provided face-to-face care. Funds thus saved may be re-allocated to help defray the costs of laser treatments that will be required by screen-positive cases.

**Results**

Our screening initiative has now been in operation for 24 months. It began with a single camera, and has now grown to five units in metropolitan Nashville and Middle Tennessee. Participating clinics include community health centers, primary care clinics and Veterans Administration medical centers.

To date, we have screened 3,100 patients. Of all patients screened, 58.7% were found to be within normal limits, or with mild background diabetic retinopathy below the threshold for referral. Each of these “normals” obtained the dilated retinal examination recommended for all people with diabetes, albeit through a technology-based solution.

Aggregate data from all participating sites shows that 30.8% were non-urgently referred for evaluation of findings that may lead to vision loss. Most of these were found to have vision of 20/50 or worse with pinhole correction. The next largest number of non-urgent cases were people whose optic nerves demonstrated a cup-to-disc ratio of .6 or greater.

Finally, 10.4% were referred urgently. Leading the list of referral reasons was presumed clinically significant macular edema, appearing in these non-stereo images as exudates within one disc diameter of the center of the fovea. Other reasons for urgent referral included optic nerve pallor or disc edema, proliferative diabetic retinopathy with or without high-risk characteristics, vitreous hemorrhage and inflammatory lesions such as toxoplasmosis. A small but significant subset of patients was found to have retinal thromboembolic lesions, and we immediately alerted their primary care physicians so that appropriate medical evaluation could be ordered without delay.

Although the primary reason for this screening initiative is the discovery of lesions associated with diabetes, we analyze every image for the presence of any pathology whatsoever, even if unrelated to hyperglycemia, and diligently report those findings so that the patient can obtain proper follow-up care (Figure 5).

**Discussion**

There are many barriers to conventional physician-provided dilated retinal examinations, including cost, geographic location, and the time required to travel back and forth as well as to wait for the provider once in the correct place. By placing the screening encounter within a familiar healthcare setting, retinal imaging can occur during a routine clinic visit. This simplifies the process for the elderly and infirm patients who may require public transportation. For the working poor who may not be given time off for multiple medical appointments, integrating the screening opportunity into an already-scheduled visit reduces the time away from work.

Screening-type retinal cameras are designed to be easy to operate and they incorporate various optical components that simplify alignment and focus. By observing the image on the attached monitor, these instruments

Figure 5: Samples of non-diabetic findings. In addition to lesions commonly associated with diabetic microangiopathy, we find many patients with increased optic nerve cupping (A), epiretinal membranes (B), hypertensive retinopathy (C) and intraretinal thromboemboli (Hollenhorst plaques) (D, E).
provide an indication of the real image, rather than forcing the screener to work through the challenge of aerial image focusing customarily encountered in clinical fundus cameras. This simple instrument allows the use of screeners with non-traditional backgrounds and thus the labor costs associated with this program are economically sustainable. In our model, the actual salary and fringe benefits are paid by the participating institution rather than by us. This enables screeners to perform other tasks in the clinic when there are no patients to be photographed. We usually train two people at each site to perform screenings, as this provides for lunch breaks, vacation and sick time without incapacitating patient flow.

The specific acquisition and playback parameters we use for digital imaging are based on the nature of diabetic lesions and the need for a robust, easily replaceable instrument. The resolution of the entire system (camera and review station) should be sufficiently high to resolve very small subject detail while simultaneously being compact enough to be transmitted in a reasonable interval over telecommunications links. To understand the morphology of an unknown lesion, we believe at least 4-6 pixels should contribute to the image, providing an indication of area and color variation. The minimum standards recommended by the UK’s National Health Service stipulate 1,300 x 1,000 pixels. The least sensitive camera in our system offers a resolution of 2,160 x 1,440, while the most sensitive digital back provides 3,072 x 2,048 pixels. This issue is essential to running an accurate screening program, because higher image quality translates into greater opportunities to correctly identify subtle lesions that are important indicators of the patient’s status. To understand whether a yellowish spot is a drusen body or an exudate, or whether a very faint reddish area on the optic nerve is a tiny tuft of proliferative tissue, we must use the highest level of technology.

Furthermore, we must ensure that the integrity of these large files is protected from the moment of exposure until they are archived. Lossless file compression is mandatory and the PNG algorithm provides us with a modest reduction in non-essential background information while simultaneously reducing total file size of each individual image to 8.5MB.

Our current telecom network uses T-1 lines, but even these high-bandwidth connections require lengthy uploads. For a typical patient set of four images along with a small packet of patient identifiers, the 35MB file takes 3.5 minutes to upload to our server. Other telecom variants will result in slower speeds (Table 1).

Table 1: Average Upload Times (in hours) for 25 Screening Studies @ 35MB. A set of four full resolution retinal images is 35MB in size. These files take some time to transmit. Although a simple DSL (Digital Subscriber Line) may be used, upload times are shortened significantly with broadband connections. We suggest that screening programs work closely with local telecommunications service providers to design a network that has adequate bandwidth and is cost-effective.

We dilate every patient with a short-acting mydriatic agent. Tropicamide 1%, used alone, is not associated with systemic side-effects or an increased risk of angle-closure glaucoma. However, it significantly improves the optical performance of the camera by permitting uniform retinal illumination even when the patient’s iris is no longer capable of adequate physiological dilation.

Perhaps the most controversial aspect of retinal screening concerns the issue of stereoscopic versus monoscopic imaging. For clinicians who are used to clinical trials with stereo imaging, the effectiveness of a non-stereo image in denoting macular thickening is problematic. However, we have found high sensitivity with single image recording, and rely on a combination of visual acuity measurement and the use of ‘surrogate markers’ (typically lipid exudates) within one disc diameter of the fovea to represent presumed retinal edema. It is also much easier to produce a single high quality image as compared to stereoscopic views, especially when the screener is not a professional ophthalmic photographer.

Our program uses a modified EuroDiab imaging protocol, in which the first image is created with the fovea in the center; the second image centers the optic nerve in the recorded field (Figure 6). While some believe that a single 45-degree fovea-centered image should be sufficient for screening, the large numbers of patients who may be at risk for glaucoma necessitated the addition of the second image. Because our software can very precisely calculate discrete anatomical areas and thus compute cup-to-disc ratios, we elect to acquire a centered, en-face view of the optic nerve for each eye, thus providing a geometrically true frontal image that does not exhibit any perspective distortion. We manually trace the on-screen outlines of the disc and use color and vessel configuration to approximate the edge of the cup, and then the program calculates areas and ratios.

Screening programs may change the demographics of the typical ophthalmic clinical practice. Using typical numbers, about half of the known diabetics in a service area obtain conventional physician-provided examinations. Of these (based on ethnicity, race, disease duration and A1C levels), most are normal, while about a third
require intervention for retinopathy. For practices associated with a digital screening program, normal diabetics may no longer attend the clinic for routine screening exams. However, many more patients will be screened in that geographic area and proportionately more patients will be referred to the practice for care. However, virtually all of these will require fundus photography, fluorescein angiography and laser photocoagulation, resulting in commensurately higher third-party reimbursement as well as the application of the physician’s expertise to many more patients who require it.

Digital screening is not intended to be a replacement for a comprehensive eye examination. Indeed, issues concerning any eye findings NOT including the retina (such as motility, lids, cornea, tear film, intraocular pressure, refraction, lens opacities and the like) cannot be addressed with fundus image-based retinopathy detection. What these programs do most effectively, however, is extend access to people who otherwise would never obtain any ophthalmic care at all.

**Summary**

For many, on-demand screening in the primary care clinic saves them weeks or months of waiting for an appointment at an eye care facility for a traditional physician-provided dilated eye examination. For some, digital imaging is their first experience in obtaining ophthalmic healthcare. For those patients found to have vision-threatening disease, digital screening brings them one step closer to obtaining the expert ophthalmic treatment they require to preserve their vision and to remain productive members of society.

We believe that every patient screening encounter represents an improvement in healthcare delivery. Each screening can overcome racial, ethnic and economic disparities. Each contributes to equity of care. Each is a victory over apathy, ignorance and lack of access to high quality healthcare—barriers that, far too often, lead to blindness for people with diabetes.

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**References**

At its winter 2004 meeting, the OPS Board of Directors voted to endorse the Retinopathy Prevention Act of 2003 (H.R.3458), recently introduced in the House of Representatives by Congressman Jim Cooper of Tennessee’s 5th District. The bill requires Federal reimbursement through Medicare and Medicaid for diabetic retinopathy screening using fundus photography, and also provides funding for pilot programs to bring mobile screening to underserved areas in the US.

Diabetic retinopathy not only continues to be the leading cause of new blindness among working age adults, but may create a public health catastrophe as the diabetes pandemic accelerates. Up to 90% of vision loss from diabetes is preventable, provided that patients obtain routine dilated eye examinations and follow through with treatment recommendations. However, only about half of known diabetics obtain these exams. In some urban and rural areas, few patients are ever seen by ophthalmologists until they become symptomatic—often too late to preserve vision.

“Ophthalmic photographers are certainly no strangers to the effect of retinopathy,” says Paul R. Montague, CRA, FOPS, OPS President. “We’ve all photographed patients who have suffered from macular edema and proliferative disease. Many of these people went years without being examined, and we’ve photographed them at the end of the line as far as their vision is concerned. The OPS endorsement puts our society front and center among organizations dedicated to preserving vision. After all, the OPS represents the art and science of imaging as applied to the preservation of vision. Of all groups fighting blindness, the OPS should be one of the strongest supporters of this bill.”

The bill is now in the House Ways and Means Committee and the Commerce Committee, and is accruing support and co-sponsors, but more are needed. “I invite all OPS members to get involved in this issue by contacting your congressional representatives and senators and asking them to strongly support HR 3458,” Montague says. “This piece of legislation deserves bipartisan support. It’s the right thing to do to help save sight. After all, if both a Democratic congressman and Newt Gingrich, a conservative Republican, can agree on this approach, it should become law.”

For more information about the bill, read “pending legislation” at www.retinopathyscreening.org. The website also features a wizard to facilitate sending a note to your own legislators. For an interesting summary of Gingrich’s position, go to www.healthtransformation.net.