Testing for Diabetic Retinopathy in Primary Care

DIGITAL DIAGNOSTICS
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Strengths and Limitations of Telemedicine and AI Solutions

Introduction

Up to 24,000 Americans go blind annually due to diabetic retinopathy. However, **early detection and treatment can prevent or delay blindness** caused by this disease that occurs in more than 85 percent of people with diabetes.

Diabetic retinopathy (DR) causes damage to blood vessels in the back of the eye, and represents the leading cause of blindness in working age adults, according to the U.S. Centers for Disease Control (CDC).[1]

To avoid complications associated with DR, the American Academy of Ophthalmology (AAO) recommends that people with diabetes undergo an eye examination every year[2] - but on average just half of people with type 2 diabetes receive this important annual eye exam, according to the CDC.[3]

To a large extent, low rates of DR testing are associated with lack of access to eye care specialists.[4] DR exams are typically performed by eye care specialists such as ophthalmologists and optometrists – after the patient is referred by a primary care provider (PCP). Care access issues will continue to grow worse as more people are diagnosed with diabetes.

Fortunately, telemedicine and recent advancements in artificial intelligence (AI) diagnostic technologies make it possible for PCPs to assess for DR in their offices.

These are convenient options for individuals with diabetes who are already visiting with their primary care providers for regular diabetes monitoring and do not have a history or symptoms of vision loss.

In addition to increasing patient access to care, testing for DR in primary care offices may also have the potential to reduce costs for patients and payers.

This paper examines the strengths and limitations of two options for assessing DR in primary care – telemedicine and AI-based diagnostic systems.

>85%

Over 85% of individuals with diabetes will develop diabetic retinopathy within 20 years

~24,000

Americans go blind annually due to diabetic retinopathy

~50%

DR exam compliance rate

Advantages and disadvantages of using telemedicine to assess for DR

Here's how the use of telemedicine to assess DR typically works:

A person with diabetes visits their PCP's office to monitor their diabetes. If the patient is due for an annual eye exam, a staff member at the physician's office uses a fundus camera to capture images of the patient's eyes.

The images are then sent to a reading center or individual specialist who review them for signs of DR.

The major advantage of this approach is patient convenience associated with visiting their PCP - the medical professional the patient is likely most comfortable with and already visits for their diabetes care.

By undergoing the exam at the primary care office, the patient is freed from the time, expense and complication associated with a separate visit to a specialist's office.

Using telemedicine to detect DR does come with some drawbacks. For example, because primary care physicians have to wait for a human to interpret the images, there can be a significant delay in receiving the results - from hours to as long as a week.

Test results are rarely delivered while the patient is still in the PCP's office, requiring staff time to follow up with the patient on the results.

Even more problematic is that most telemedicine solutions lack meaningful image quality feedback, which may result in the physician receiving insufficient or borderline images.

This may require the patient to return to the physician's office to have another image captured, or the specialist may make a diagnosis based on a borderline image. If image quality is insufficient, signs of disease may go undetected, resulting in vision loss.

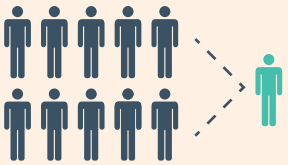
Finally, telemedicine is not a scalable solution to test for DR. Because telemedicine requires a human to review each image, if there are not enough experts available to read images, it can create a bottleneck when there are a large number of patients who need to be screened.

Strengths of Telemedicine

- Convenient for the patient
- Less costly than seeing a specalist

Limitations of Telemedicine

- Results arrive after patient has left the office
- Poor image quality may affect diagnosis quality
- Need human overread limits to scale



If there are not enough experts available to read images, it can create a bottleneck when there are a large number of patients who need to be screened.

Advantages and disadvantages of using an AI diagnostic system

With the FDA's clearance of LumineticsCore™ (formerly IDx-DR),

the first autonomous AI system for the detection of diabetic retinopathy, providers now have the option to test for diabetic retinopathy in their office without needing a specialist to interpret images – a distinct contrast from telemedicine.

The potential benefits of using AI-based systems to detect DR in the primary care setting are significant, potentially lowering costs, enhancing quality of care, increasing patient convenience, and creating greater consistency across diagnoses.

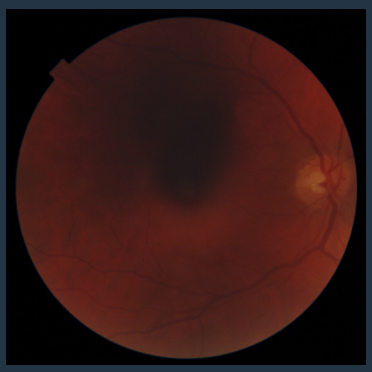
Perhaps the greatest advantage of AI-based systems is the immediacy of the results, which enables providers to include the DR results when discussing diabetes care and management with their patients.

This also means no additional follow up is necessary to communicate test results, saving staff and patients' time.

Another advantage of an AI diagnostic is that it provides FDA-cleared, real-time, interactive image quality feedback to the operators.

Imporant questions to ask when assessing telemedicine

- Who will be interpreting the images?
- What is the imaging protocol for the system? (e.g., how many images needed and requirements?)
- How often do operators need to retake images?
- How easy is the imaging system to use by novice operators?
- How is continuous quality and improvement measured and monitored?
- What is the typical time interval for return of results? (Average, minimum, maximum)
- How many exams is the telemedicine system processing on a periodic basis?
- What is the capacity of the current system for scale?



Insufficient images quality may obscure signs of disease

Presentation of DR results may occur immediately after imaging

If an initial image isn't of sufficient quality to definitively make a diagnosis, the AI system can quickly alert the operator of the problem, and then instruct the operator to capture another image.

This stands in stark contrast to the telemedicine options that lack image quality feedback, which may result in insufficient quality images not being identified until a human has the opportunity to review it – in many cases hours after the patient has left the physician's office.

In addition, there are studies that suggest AI systems may deliver more consistent and reliable output than human experts.[5]

In a pivotal clinical trial for LumineticsCore, the system achieved 87% sensitivity and 90% specificity.[6]

While LumineticsCore was not directly compared to clinicians, there are a number of studies that report sensitivities as low as 33% in a representative sample of board-certified ophthalmologists when using the same reference standard.[5]

Cost, of course, is always a concern as many healthcare systems transition to value-based care. Because AI diagnostic systems do not require a human to be involved in the assessment, they can reduce costs for virtually all care-delivery participants. This is a significant consideration given that DR exams typically cost about $200, according to a 2017 study in the New England Journal of Medicine.[7]

It is important to note that LumineticsCore is intended for use to automatically detect more than mild diabetic retinopathy (mtmDR) and macular edema in adults ages 22 years of age or older diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy.

Patients should be advised to immediately report to an eye care provider if he/she experiences vision loss, blurred vision, floaters or any other symptom as these symptoms require the immediate attention of an eye care provider.

Unfortunately, we know that 50% or more of people with diabetes are not seeing an eye care specialist regularly, and many are not currently experiencing symptoms of vision loss. For these individuals, using an AI system to catch early signs of diabetic retinopathy could prevent vision loss.

Strengths of AI diagnostic system

- Immediate results while patient in office
- No physician needed to interpret images
- Immediate image quality feedback
- Consistently high accuracy
- Convenient for the patient
- Less costly than seeing a specialist

Limitations of AI diagnostic system

- Indications for use to detect more than mild diabetic retinopathy only
- Not indicated for use for individuals previously diagnosed with diabetic retinopathy (recommended to be under the care of an eye care professional)

AI-Based Systems: Separating What's Real From the Hype

There are a number of recently published research papers on high-performing algorithms that detect disease in retinal images.

However, there are several factors to consider when assessing algorithm performance. First, look at the reference standard used for reading retinal images. If the study contrasts the AI system's performance with human experts, does it account for inter-observer variability? Even highly qualified specialists have been shown to vary in their assessments. A study that establishes a specified protocol for performing the reading can limit this diagnostic drift.

A formal reading center that has published inter- and intra-observer (and preferably was involved in studies that helped establish current disease management guidelines) allows for a more objective assessment of AI system performance.

Second, look for a rigorously-designed study that is prospective rather than retrospective. A prospective study pays close attention to subject demographics to ensure the most diverse enrollment population that is reflective of the population for which the system will be used.

Retrospective studies, on the other hand, do not collect the validation sample at random.

For example, it is typically easier to collect data in high-income areas compared to low-income areas, which may result in selection bias that leads to wrong assumptions about safety in all people with diabetes.

Similarly, spectrum bias, where only the patients with the least or most disease are collected, can lead to wrong assumptions of safety in intermediate severity of disease.

Prospective studies typically are associated with fewer potential sources of bias than retrospective studies.

Additionally, it is important that the study's setting is aligned with the technology's intended use. For a study to adequately assess the effectiveness of a certain technology system's ability to improve detection of a disease in a primary care setting, the study must be performed in that same setting – not a specialist's office, for example.

To further ensure patient safety, the AI should be "locked down" and tested in a preregistered clinical trial and held by an algorithm integrity provider. In a preregistered trial, researchers work with regulators to establish a hypothesis and required endpoints to prove an AI system's safety and efficacy. This prevents researchers from analyzing data and fishing for favorable results.

The most important factor, however, is whether the AI-based system has been cleared for use by the U.S. Food and Drug Administration, which possesses a long track record of effectively evaluating novel technologies before their transition into healthcare.

Important questions to ask when assessing AI diagnostic systems

- What are the indications for use for the AI system?
- What is the performance of the system? Has it been tested in a real world setting?
- What is the "truth" or reference standard by which the AI system was validated?
- What are the outputs of the device? Are follow up recommendations included with the result?
- How is the device monitored for continuous efficacy?
- How is the AI system designed? Can the manufacturer explain how the AI makes its decision?

Summary

Telemedicine and AI-based systems represent two of the most promising routes to expand DR testing in the primary care setting, which is critical given the soaring rates of diabetes across the U.S. and the globe.

By the year 2050, diabetes prevalence is projected to increase to 21% of the U.S. adult population.[8]

Every person with diabetes is at risk of developing DR. About 33 percent of people with diabetes have some degree of DR and about 10 percent will develop a vision-threatening form of the disease, according to the International Agency for the Prevention of Blindness.[9]

Thus, something has to change in our approach to assessing patients for DR. Shifting the setting of diabetic retinopathy exams to primary care offers a roadmap to increasing quality of care, reducing costs, enhancing convenience for patients and introducing a more consistent, standardized approach to testing.

About Digital Diagnostics

Digital Diagnostics Inc. is a pioneering AI diagnostics company on a mission to transform the quality, accessibility, equity, and affordability of global health care through the application of technology in the medical diagnosis and treatment process.

The company, originally founded by Michael Abramoff, MD, PhD, a neuroscientist, practicing fellowship-trained retina specialist, and computer engineer, is led by him and co-founders John Bertrand and Seth Rainford. Digital Diagnostics is paving the way for autonomous and assistive AI technology that is free of bias to become a new standard of care, contributing to democratizing health care and closing care gaps. The company works closely with patient advocacy groups, provider organizations, regulators, and other quality of care and ethics-focused stakeholders to enable the adoption of health care AI. For more information and the latest news follow: digitaldiagnostics.com

References

1. "Vision Health Initiative | Economic Studies." U.S. Centers for Disease Control, 11 Apr. 2017, www.cdc.gov/visionhealth/proj- ects/economic_studies.htm
2. "Diabetic Retinopathy Preferred Practice Pattern Guidelines." American Academy of Ophthalmology, Dec. 2017, www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017
3. "Keep an Eye on Your Vision Health." U.S. Centers for Disease Control, July 2018, www.cdc.gov/features/healthyvision/index.html
4. Lee, David J et al. "Dilated eye examination screening guideline compliance among patients with diabetes without a diabetic retinopathy diagnosis: the role of geographic access" BMJ open diabetes research & care vol. 2,1 e000031. 23 Aug. 2014, doi:10.1136/bmjdrc-2014-000031
5. Pugh JA, et al. Screening for diabetic retinopathy. The wide-angle retinal camera. Diabetes Care 16:889–895. June 1993.
6. Abràmof, MD, et al. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. npj Digital Medicine 39. 28 Aug. 2018, doi:10.1038/s41746-018-0040-6
7. The DCCT/EDIC Research Group. Frequency of Evidence-Based Screening for Retinopathy in Type 1 Diabetes. N Engl J Med 376:1507-1516. 20 Apr. 2017, doi: 10.1056/NEJMoa1612836
8. Boyle, James P et al. "Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence" Population health metrics vol. 8 29. 22 Oct. 2010, doi:10.1186/1478-7954-8-29
9. "Diabetic Retinopathy." International Agency for the Prevention of Blindness, www.iapb.org/knowledge/what-is-avoidable-blindness/diabetic-retinopathy/