Title

The Promise of Primary Care–Based Screening for Diabetic Retinopathy: The Devil Will Be in the Details Comment on “Telemedicine and Retinal Imaging for Improving Diabetic Retinopathy Evaluation”

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creased quality of life. As the prevalence of DM is projected to increase from 25 million Americans to 125 million Americans by the year 2050,[9] the number of patients requiring annual retinal evaluation will far exceed the capacity of ophthalmologists.

Primary care physicians are at the frontline of this epidemic and already play a critical role in primary prevention of retinopathy with the management of serum glucose and lipid levels and blood pressure. Telemedicine potentially allows primary care physicians to manage the screening and monitoring of this potentially blinding disease. Specifically, they can distinguish patients who only require surveillance with retinal photography from those who need urgent referral. Such a paradigm could lead to better use of physician and patient resources. In our group, for example, most patients (89%) did not have retinopathy and therefore did not need referral to an ophthalmologist for DR screening.

Telemedicine screening at the point of care of the primary care physician represents a potential paradigm shift in the management of DM, can improve screening, and may ultimately prevent vision-threatening DR.

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INVITED COMMENTARY

The Promise of Primary Care–Based Screening for Diabetic Retinopathy: The Devil Will Be in the Details

Diabetes, a major cause of morbidity and mortality in the United States and the leading cause of new cases of blindness in adults, affects more than 25 million people, or 8.3% of the population.[1] Currently, only 60% of persons with diabetes receive standard-of-care screening examinations for retinopathy, and the number is even lower in the safety net.[2,3] Given that the projected increase in the prevalence of diabetes will increase the demand for screening examinations, we must identify alternative ways to screen for diabetic retinopathy (DR).

Primary care practitioners (PCPs) are frontline providers of diabetes care and, with the advent of the patient-centered medical home, a logical choice for an extension of specialty care services. The Research Letter in this issue of the *Archives* provides important evidence that fundus cameras designed to photograph the retina through an undilated pupil can be used effectively in primary care settings to screen for DR.[4] As the authors note, most of the published data on primary care–based teleretinal DR screening in the United States have come from the robust program in the Veterans Health Administration.[5] However, other large regional studies both in and out of the safety net (those health care providers who disproportionately care for the uninsured and publicly insured) have shown similar results.[6,7] While these studies certainly indicate that we may have found a strategy to rapidly increase screening for retinopathy, there are important issues that we must resolve to successfully move DR screening into the primary care setting.

Most importantly, we must avoid creating an unregulated cottage industry. Instead, we should strive for national standardization in the protocol and workflow processes from the outset, including use of a validated grading scale, furnishing reading centers with certified readers and ophthalmic oversight, and enabling seamless bidirectional communication between primary care and specialist providers through the use of electronic health records (EHRs). This standardization would both ensure the accuracy and reliability critical to fully realizing the potential of this technology to prevent blindness and mitigate the risks associated with false-negative results.

We must insist on uniform reporting of results using an internationally accepted grading scale, such as the modified Airlie House classification established by the Early Treatment of Diabetic Retinopathy Study.[8] Uniform reporting would allow us to move this technology to the standard expected for most diagnostic screening tests. As a diagnostic test, risk-stratified DR results can be reported with simple action-oriented response items for a busy PCP, similar to reports currently provided for mammograms and bone density scans. For teleretinal DR screening, the crux of the action item is the flagging of persons with diabetes who are in need of specialty eye care. This not only expedites care for those truly in need, improving clinical outcomes, but it also provides better understanding of the number of patients for whom specialty eye care is needed.

However, for health systems to accurately estimate the true need for specialty eye care, linking to a shared EHR and/or diabetic registry is crucial. This linkage enables data collection regarding diagnosis, follow-up, and treatments received. Obtaining this information is the only way we can truly understand the resources needed for efficient, high-quality workflow, cost, and long-term vision outcomes. In the era of EHR "meaningful use" stipulations by the US government, a seamless, transparent connection between primary and specialty care EHRs is not only feasible, it is essential if we are to decrease preventable blindness attributable to diabetes.

These data could also be useful in helping to target populations that may benefit the most from comprehensive, primary care–based screening. As noted in the Research Letter by Garg et al,[4] racial and ethnic differences in prevalence and severity of DR exist. Importantly, however, previous research suggests that much of this difference is driven by associated risk factors such as socioeconomic status, education, and level of diabetic and/or hypertensive control. For these reasons, we might expect that patients in rural or urban resource-poor settings would have a higher prevalence and severity of DR identified at the time of initial screening than those in settings with greater resources. Latinos have been shown to have one of the highest rates of retinopathy among all safety-net groups,[9] a difference that remains significant even after controlling for the aforementioned risk factors.[10] Genetics has been posited as one reason for the difference in disease rates and severity, and studies are under way to investigate this. Whether it is socioeconomic status, health access, or genetics of the population served, there is a disproportionate burden of DR among those seen in the safety net. Many of these patients already have severe DR at their first screening eye examination; one safety-net study found that, on average, up to 12 years elapsed between diagnosis of diabetes and first retinopathy screening.[11]

In addition to increasing opportunities for screening, patient education should not be overlooked as a contributor to low rates of initial presentation to eye care providers. Inadequate understanding of the disease and its processes is a formidable barrier for patients, since DR can be asymptomatic until very far progressed. Without comprehension of the risk of impending blindness, common problems for patients in underserved areas such as transportation and inability to take time off from work can make keeping eye appointments difficult. Basing screening in primary care settings, where these patients are likely to present for a wide array of other medical concerns, will alleviate many of these logistical and cost barriers reported by patients.

Using teleretinal imaging to move screening for DR into the primary care arena has the potential to substantially reduce blindness among some of the most vulnerable persons in the US population. However, we must think before we act; we must recognize the fundamental necessity of standardization of these screening programs as we begin the implementation process, holding health care systems to the standard of care we have come to expect from diagnostic tests that guide primary care actions in other specialties. This standardization, combined with linkage to EHRs shared by primary care and specialty providers, holds promise for decreasing the large number of diabetic patients needlessly going blind from this treatable disease.

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RESEARCH LETTER

New Drugs and Safety: What Happened to New Active Substances Approved in Canada Between 1995 and 2010?

Monitoring the safety of drugs is increasingly recognized as a major issue in light of recent experience with products such as rofecoxib and rosiglitazone. Previous work found that the probability of new drugs either acquiring a black box safety warning or being withdrawn for safety reasons was 20% over a 25-year period[1] and that oncology drugs that were granted a priority review were more likely to be subject to labeling changes than were drugs with a standard review.[2]

This study was undertaken to answer 2 questions. What is the percentage of drugs approved in Canada that subsequently either acquire serious safety warnings or have to be withdrawn from the market for safety reasons (hereafter referred to collectively as serious safety issues)? Is there a difference between priority and standard review drugs according to this measure, and if so, what is the main reason for this difference: the length of the review time, the inherent characteristics of the drug, or the disease for which the drug is approved?

See Invited Commentary at end of letter

Methods. A list of new active substances (NASs) (the equivalent of new molecular entity) approved between January 1, 1995, and December 31, 2010, was compiled from the annual reports of the Therapeutic Products Directorate and the Biologic and Genetic Therapies Directorate (available from publications@hc-sc.gc.ca). All serious safety warnings (those using boldface black print or boxed warnings) and drug withdrawals for the period January 1, 1995, to October 31, 2011, were identified from the MedEffect Canada website (http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/index-eng.php). Kaplan-Meier survival curves were calculated to estimate the probability that any NAS would have a serious safety issue during the study period and separately for an NAS with a priority and a standard review.

The characteristics of drugs with a priority approval might account for differences in the percentage with safety issues compared with drugs with standard reviews. Drugs that received a priority approval but were not considered to be major therapeutic advances were compared with drugs that received a standard review.

Drugs are usually assigned a priority review for important clinical problems and may be licensed with a lower benefit to harm threshold, leading to a higher rate of safety warnings. Drugs with priority reviews for 5 serious diseases—cancer, human immunodeficiency virus/AIDS, inborn errors of metabolism, multiple sclerosis, and the prevention of transplant rejection—were compared with drugs with standard reviews for the same diseases. Kaplan-Meier survival curves were calculated using XLSTAT add-in for Excel (Addinsoft).

Results. A total of 434 NASs were approved from January 1, 1995, to December 31, 2010; 84 (19.4%) had a serious safety issue. The probability of an NAS acquiring a serious safety issue was 23.7% (95% CI, 19.1-28.3) (**Figure**).

Three hundred twenty-one NASs (74.4%) had a standard review, and 112 (25.6%) had a priority review. (The approval status of 1 product could not be determined.) For products with a standard review, there was a 19.8% (95% CI, 14.8-24.8) estimate of acquiring a serious safety