**TITLE: Tele-Ophthalmology for Detecting Eye Diseases: Clinical and Cost-Effectiveness**

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## CONTEXT AND POLICY ISSUES:

Screening and detection of various ocular diseases is an important way to prevent blindness. People with diabetes are 25 times more likely to develop blindness than individuals without diabetes.[1] Diabetic retinopathy (DR) is the most common cause of vision loss among the working-age population of developed countries yet a clinical trial conducted in the UK reported that approximately 26% of patients with type 1 diabetes and 36% of patients with type 2 diabetes have never had their eyes examined.[2,3] Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in the western world. In Canada, it is estimated that by 2026 over 300,000 people will have severe exudative AMD.[4] Glaucoma is the second most common cause of blindness[5], and previous studies have reported a positive association between diabetes and primary open-angle glaucoma[6].

Accurate and timely access to diagnosis and treatment for DR, AMD, and glaucoma may slow the development and progression of these diseases, and therefore result in a better prognosis. Screening and detection of ocular disease usually includes a comprehensive annual eye examination, including measurement of visual acuity, intraocular pressure, and an examination of the retina, usually with the pupils pharmacologically dilated.[1] These tests are usually performed by an optometrist or ophthalmologist.[1] However, early detection of ocular disease and regular follow-ups is not easy to achieve due to limited health care resources, especially for people living in remote or rural areas.

Telemedicine is the use of telecommunications technology for diagnostic, monitoring, or therapeutic purposes where distance and/or time separates the patient from the health care provider.[7] Ocular telemedicine has the potential of delivering eye care to those with limited access to health care resources.[2] In general, the equipment required in tele-ophthalmology consists of image acquisition hardware (including computers and cameras), systems for retinal image transmission, storage and retrieval, and software applications for image analysis and clinical workflow management.[2] Digital retinal imaging is a relatively new tool for assessing patients with eye conditions.[2] With digital fundus photography, the image may be processed to enhance the quality of the image and the images may be stored and retrieved more easily than conventional film.[1] Images may then be transferred electronically to a retinal specialist to detect or diagnose disease.[1] Several commercial retinal cameras, such as the Canon CF-1[8] and the Topcon TRC-NW8 and TRC-50 DX models [9,10], have obtained approval from Health Canada for detecting certain eye diseases.

The purpose of the current report is to evaluate the evidence for the clinical and cost-effectiveness of tele-ophthalmology for detecting DR, AMD, and glaucoma.

**RESEARCH QUESTIONS:**

1. What is the clinical effectiveness of tele-ophthalmology for the detection of eye disease?

2. What is the cost-effectiveness of tele-ophthalmology for the detection of eye disease?

**METHODS:**

A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library ( Issue 4, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. Results include articles published between 2003 and November 2008, and are limited to English language publications only. Filters were applied to limit the retrieval to systematic reviews, health technology assessments, meta-analyses, randomized controlled trials, economic studies, and observational studies.

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by economic evaluations, randomized controlled trials, observational studies, and evidence-based guidelines.

**SUMMARY OF FINDINGS:**

One systematic review, two randomized controlled trials, four observational studies, and three economic studies were identified examining the clinical and cost-effectiveness of tele-ophthalmology for DR, glaucoma, and AMD.

*Systematic reviews and meta-analyses*

One systematic review was identified.[7] Hersh and coworkers performed an update to an existing systematic review of telemedicine services that substitute for face-to-face medical diagnosis and treatment. They included 106 studies in many specialties. The included studies were critically appraised using different scales based on the various types of outcome measures. The following endpoints were addressed: clinical outcomes, diagnostic accuracy, and access to care. Six studies examined the diagnostic accuracy of tele-ophthalmology. Of these, four studies evaluated digital imaging examinations for patients with DR and showed that a high accuracy of diagnosing DR could be obtained. The review did not specify details of which retinal cameras were evaluated. Two of the four studies reported class I evidence (defined as "case series of consecutive patients from relevant population of individuals who would use telemedicine, using an objective gold standard with blinded interpretation of results; with inter-observer analysis"); the other two studies reported class II evidence (defined as "case series of patients from relevant population of individuals who would use telemedicine; using an objective gold standard"). Only one study evaluated the effect of tele-ophthalmology on access to care. It was of low quality ("case series not from relevant population or not using appropriate methodology for diagnostic test evaluation") and did not report whether the care provided by the telemedicine service was adequate, or collect any follow-up information on the screened patients. The authors of the systematic review concluded that the quality of studies in the domain of tele-ophthalmology was slightly higher than in other specialties such as dermatology, and the evidence for the effectiveness in detecting eye diseases was mixed. Results indicated that tele-ophthalmology may provide high rates of diagnostic accuracy for DR. However, there were a number of diagnoses for which it fared less well, and it was often unusable altogether when certain patient characteristics were present, such as cataracts and other lens abnormalities.

*Randomized controlled trials (both on DR)*

Two randomized controlled trials were identified.[11,12] Details of these trials are presented in Table 1.

Conlin *et al*. studied whether nonmydriatic digital retinal imaging with remote interpretation in the ambulatory care setting affected adherence to annual dilated eye exams among diabetic patients.[11] Participants were randomly assigned to teleretinal imaging or usual care. Teleretinal imaging and eye exam results showed significant correlation and moderate agreement. Significantly more patients in the teleretinal imaging group were adherent to follow-up dilated eye exams when compared to the control group. The authors concluded that nonmydriatic teleretinal imaging improved adherence to annual eye exams in patients with diabetes.

Davis *et al.* examined whether telemedicine in a primary care setting improved retinal examination rates for DR in a rural and ethnically diverse community in the United States (US).[12] No details on study design and follow-up were provided. Furthermore, this study enrolled a small number of participants. The authors reported that patients who had the opportunity to receive their eye examination via telemedicine were approximately six times more likely to obtain a screening eye examination than those who were simply reminded to schedule examinations with their usual eye-care provider.

*Observational studies (two on DR, one on glaucoma, one on AMD)*

Four observational studies were identified. Only studies evaluating various models of the Topcon retinal camera were included. Details of these trials are presented in Table 1.

Pasquale *et al.* conducted a retrospective study in a group of diabetic patients, to assess the accuracy of a tele-ophthalmology program for detecting glaucoma-like optic discs.[6] Retinal images were captured using a Topcon TRC NW-55 nonmydriatic digital fundus camera, then transmitted to an ocular telehealth center for evaluation. All the patients had a subsequent comprehensive eye examination. The result reader was not masked to patient medical information. One hundred and seventy-five patients labeled as glaucoma suspects by the tele-ophthalmology program were compared with another 175 patients from the same imaging pool for which the optic discs were not regarded as glaucomatous damage. Results indicated that assessment of clinical data obtained after the tele-ophthalmology exam found that 103 of 175

(59%) glaucoma suspects had glaucoma-suspicious optic discs, while in the comparison group, only 7 of 175 (4%) had glaucoma-suspicious optic discs. The authors concluded that although specificity was high (96%), modifications in diabetes teleretinal imaging programs are needed to improve the sensitivity of detecting glaucoma-like optic discs.

Massin *et al*. conducted an observational study[13] comparing patients examined by a digital nonmydriatic camera with those examined by dilated eye fundus exam. The baseline characteristics of the included patients were comparable in each group. Results indicated that the proportion of screened patients for whom primary care physicians received a screening report within six-month follow-up period did not differ significantly between the two groups. The authors concluded that DR screening using fundus photography is effective for providing primary care physicians with information about eye disease status.

Pirbhai *et al.* compared the effectiveness of mydriatic non-stereoscopic digital color fundus photographs with clinical examination and fluorescein angiography for identifying and classifying exudative AMD.[4] The result reader was masked to patient medical information. The agreement between the two exams and the diagnostic accuracy of digital color fundus photographs using fluorescein angiography as reference suggested that the telemedical approach was sensitive as a screening tool for AMD.

One study performed by Saari *et al*. compared three digital fundus cameras for DR screening.[14] The investigated technologies were compared with results from an ophthalmologist exam. The results showed that the Topcon TRC 501A and the Canon CR6-54 NM digital cameras were suitable for DR screening but the MediTell videocamera was not.

**Table 1. Clinical Trials Identified on the Effectiveness of Tele-ophthalmology**

| Studies | Patients | Interventions and comparator, n | Results | Conclusions |
|---|---|---|---|---|
| *Randomized Controlled Trials* | | | | |
| Conlin *et al*., 2006[11] | RCT<br><br>Pts with diabetes and a Veterans Affairs-based primary care provider | Topcon TRC-NW5S (teleretinal imaging group), 223<br><br>Usual care (control group), 225 | Number of pts who were adherent to follow-up dilated eye exams by eye-care professional during the 12-month following the randomization:<br>Topcon: 87%<br>Usual care: 77%<br>($p<0.01$)<br><br>For pts with both exams, results of the follow-up dilated eye exams were significantly correlated with teleretinal imaging ($r$=0.60, $p<0.001$), with moderate agreement ($k$=0.42, $p<0.01$).<br><br>Pts reported high satisfaction with nonmydriatic teleretinal imaging. | Nonmydriatic teleretinal imaging improves DR assessment rates. |

| Studies | Patients | Interventions and comparator, n | Results | Conclusions |
|---|---|---|---|---|
| Davis *et al*., 2003[12] | RCT<br><br>Pts with diabetes living in a rural and ethnically diverse community | Telemedicine retinal screening program using a nonmydriatic retinal camera (not specified), 30<br><br>Usual care, 29 | Frequency of eye exams:<br>Nonmydriatic retinal camera group: 77%<br>Usual care pts: 14%<br>(relative risk 5.56, 95%CI 2.19 – 14.10) | The telemedicine program elicited greater adherence to vision care guidelines for pts with diabetes living in an under-served and ethnically diverse community |
| *Observational Studies* | | | | |
| Pasquale *et al*., 2007[6] | Pts with diabetes who did not have comprehensive eye exam within the previous 11 months | All pts were examined using a Topcon TRC NW-55 retinal camera, followed by a comprehensive eye exam. Pts labeled as GC suspects by tele-ophthalmology (group 1) were compared with those not labeled as GC suspects from the same imaging pool (group 2)<br><br>Group 1: 175<br>Group 2: 175 | Pts had disc features that met criteria for GC-like optic discs based on comprehensive eye exam:<br>Group 1: 103/175 (59%)<br>Group 2: 7/175 (4%) | The teleretinal program showed low-to-moderate sensitivity and high specificity in detecting GC-like optic discs. |
| Massin *et al*., 2005[13] | Pts with type 1 or type 2 diabetes | Topcon TRC-NW6S (nonmydriatic camera), 358<br><br>Reference: dilated eye fundus exam, 320 | Proportion of screened pts for whom primary care physicians received a screening report within 6-month follow-up:<br>Topcon: 74.1%<br>Reference: 71.5%<br>($p>0.05$)<br><br>Accessibility to the oph. office was considered not difficult or only slightly difficult:<br>Topcon: 82%<br>Reference: 93% ($p<0.001$)<br><br>99.1% pts in Topcon group were ready to have the next annual screening exam performed with the nonmydriatic camera. | The telemedical approach to DR screening proved to be effective in providing primary care physicians with information about their pts' eye status; the nonmydriatic camera was found of little inconvenience by pts. |

| Studies | Patients | Interventions and comparator, n | Results | Conclusions |
|---|---|---|---|---|
| Pirbhai *et al*., 2005[4] | Patients seen in an AMD clinic | Topcon TRC 50IX retinal camera<br><br>Reference: clinical exam and fluorescein angiography<br><br>118 pts had both exams | Against the reference: Sensitivity: 82.1%<br>Specificity: 79.1%<br>Positive predictive value: 70.4%<br>Negative predictive value: 88.0%<br><br>When comparing clinical recommendations based on digital photo assessment against the final clinical assessment, exact agreement was 80.3%; *k*=0.59 (95%CI 0.49-0.70) | Digital non-stereoscopic color fundus photographs were highly sensitive and had a high negative predictive value as a screening tool. Very few treatable lesions were missed using telemedicine in AMD. |
| Saari *et al*., 2004[14] | 70 subjects (42 pts with diabetes, 28 healthy control) | Topcon TRC 50 IA fundus camera to take color images, 106 eyes<br><br>Topcon TRC 50 IA fundus camera to take red-free image, 106 eyes<br><br>Canon CR6-45NM to take color images, 29 eyes<br><br>MediTell videocamera to take color images, 44 eyes<br><br>Reference: combined results of the oph. exam including 3-mirror lens funduscopy and digital color and red-free black-and-white images of the ocular fundus. | Sensitivity vs. reference:<br>Topcon color: 94.0%<br>Topcon red-free: 97.7%<br>Canon: 88.9%<br>MediTell: 6.9%<br><br>Specificity vs. reference:<br>Topcon color: 99.0%<br>Topcon red-free: 98.9%<br>Canon: 100%<br>MediTell: 50% | Topcon TRC 50 IA and Canon CR6-45 NM were suitable for DR screening, whereas MediTell videocamera was not sufficiently accurate for DR screening |

AMD – age-related macular degeneration; CI – confidence interval; DR – diabetic retinopathy; GC – glaucoma; *k* – kappa; oph. – ophthalmologist; pt – patients; RCT – randomized controlled trial

*Economic evaluations*

Three cost-effectiveness analyses were identified from the literature search.[15-17]

A modeled economic analysis was performed to examine the cost-effectiveness of a nonmydriatic digital tele-ophthalmology system (Joslin Vision Network, JVN) for detecting proliferative DR in diabetic patients served by the Indian Health Service, the Department of Veterans Affairs, and the Department of Defense in the US.[15] The JVN system was compared with clinic-based ophthalmologic examinations with pupil dilation to detect proliferative DR and its complications. The authors designed agency-specific cost-effectiveness decision models by using Monte Carlo simulations for three outcomes: the number of true positive cases of proliferative DR detected by each modality, the number of patients identified by each modality who required treatment with panretinal laser photocoagulation, and the number of cases of severe vision loss averted. Results showed that the JVN system was less costly but more effective in seven of the nine modeled scenarios. This economic analysis predicted that the JVN was likely to result in better outcomes for patients with proliferative DR served by the three health services, and it could deliver these improvements at lower costs than clinical ophthalmoscopy in most scenarios. These findings indicate that the JVN system shows promise as an alternative method of detecting proliferative DR.

Aoki *et al*. developed a Markov model to compare a tele-ophthalmology strategy with a non-tele-ophthalmology strategy in American prison inmates with type 2 diabetes.[16] They used a health care system perspective for the cost-effectiveness analysis. The telemedicine system (composed of Topcon NW6S nonmydriatic retinal camera, JVC 3-chip CCD color video camera, Windows 2000-based Intel Pentium III computer and monitor, and Topcon IMAGEnet 2000 Lite software) was compared with screening and follow-up evaluation performed by eye care providers. The major outcome measures in this study were quality-adjusted life-years (QALYs) gained and costs generated. The tele-ophthalmology strategy proved to be more cost-effective with US$16,514 per18.73 QALYs gained versus US$17,590 per 18.58 QALYs gained for non-teleophthalmology. Ninety percent of the Monte Carlo simulations showed cost effectiveness (annual cost per QALYs gained of less than US$50,000) in the tele-ophthalmology strategy based on an assumed inmate population. Tele-ophthalmology was the more cost-effective strategy if the number of diabetic inmates in the prison community was greater than 500. The authors concluded that tele-ophthalmology holds great promise to lower the cost of inmate care and reduce blindness caused by DR in type 2 diabetic patients.

Johnston *et al.* conducted an analysis to evaluate the costs and benefits to patients and practitioners associated with a technology transfer project between the hospitals in the United Kingdom (UK) and South Africa.[17] Tele-ophthalmology was used as the mode of technology transfer. The hospital in the UK provided specialist advice as part of the technology transfer project. Cost-effectiveness was measured in terms of cost per disability-adjusted life year (DALY) averted, which was based on the changes in visual acuity. Costs included the set-up (including equipment, installation and training) and running costs of tele-ophthalmology. Changes in costs attributable to tele-ophthalmology in terms of clinical examinations, tests, investigations and inpatient admission were calculated. Data of 90 patients with various eye diseases attending a hospital in South Africa was used in the report. The average DALYs averted for the 90 patients was 6.8. Results showed the average cost per patient for the tele-ophthalmology project was £359 and the cost per DALY averted was £53. Sensitivity analyses showed that increasing the duration of disability from 10 years to 20 years led to a higher cost per DALYs averted (£73). The authors concluded that technology transfer using telemedicine was cost-effective.

*Limitations*

1. Limited evidence was identified in the search time frame evaluating the effectiveness of tele-ophthalmology for detecting DR, glaucoma and AMD;
2. Quality of the included studies varied and some were of low quality due to small sample size or study design;
3. None of the clinical trials examined clinically relevant outcomes such as a reduction in number of patients with vision loss;
4. None of the economic studies were conducted in a Canadian setting;
5. None of the studies examined the specific retinal camera of interest (Topcon TRC-NW8).

**CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:**

The evidence for effectiveness of tele-ophthalmology for screening patients with certain eye conditions is limited. The majority of the included studies focused on DR. All the clinical studies examined diagnostic accuracy or access to care, but there is currently no evidence for the effect of tele-ophthalmology on clinically relevant outcomes such as the potential reduction in vision loss.

Based on the evidence identified, tele-ophthalmology appears to have acceptable diagnostic accuracy as a screening tool for detecting DR and AMD. Evidence from economic evaluations indicates that tele-ophthalmology may be a cost-effective option, especially for patients in remote or rural settings. Tele-ophthalmology also increases access to eye care specialists as majority of patients feel it is more convenient for them to take a teleophthalmologic exam instead of a face-to-face visit with an ophthalmologist. There is also evidence that tele-ophthalmology leads to enhanced adherence to follow-up exams required for DR or other eye conditions.

The American Diabetes Association (AMA) recommends that patients with diabetes should undertake eye examinations on a regular basis.[1] Examinations can be done by the taking of retinal photographs (with or without dilation of the pupil) and have these read by experienced experts in this field.[1] The AMA also states that tele-ophthalmology has its greatest potential in areas where qualified eye care professionals are not available.[1]

Tele-ophthalmology is a promising screening tool in detecting DR, AMD, or other eye diseases. However, further well-designed clinical and economic studies are warranted to provide more compelling evidence to estimate effectiveness and utilization for patients with eye diseases in various clinical settings.

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