# Cost-effectiveness analysis of diabetic retinopathy screening with pharmacy-based tele-ophthalmology versus in-person eye examination

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**Acknowledgement:**

**Funding support:** AMOSO Innovation Fund: INN12-010 and Ontario Graduate Student Scholarship

**Conflict of Interest:** there is no any conflict of interest with any authors.

**Word count:** Abstract-23; Manuscript-2516 (not including abstract, tables, reference)

**Reference: 30**

**Keywords:** Cost-effectiveness, tele-ophthalmology, diabetic retinopathy screening

**Contributors:** Coronado, AC: conception, design, acquisition of data, analysis and interpretation of data, drafting the article; Zaric, GS: supervision; Martin, J: supervision; Malvankar-Mehta, MS: supervision; Si, F: obtaining funding, coordination, manuscript editing and submission; Hodge, WG: conception, design , interpretation, supervision, obtaining funding, final approval of the manuscript.

## ABSTRACT

**Objectives:** Diabetic eye complications are the leading cause of visual loss amongst working aged people. Pharmacy-based tele-ophthalmology has emerged as a possible alternative that may facilitate compliance with evidence-based recommendations and reduce barriers to specialized eye care. The objective of this study was to estimate the cost-effectiveness of mobile tele-ophthalmology screening compared to primary care examination for the diabetic population residing in non-urban areas of Southwestern Ontario.

**Methods:** A decision-tree was constructed using TreeAge Pro Suite 2013, to compare primary care examination (comparator program) versus pharmacy-based tele-ophthalmology (intervention program). The economic model was designed to identify patients with DR and corresponding to a Modified Airlie House Classification ≥20 on the reference standard.

**Results:** Cost-effectiveness was assessed as (1) cost per case detected, and (2) cost per case correctly diagnosed. For (1) the cost-effectiveness of in-person examination and tele-ophthalmology was $510 and $478.3, respectively, whereas for (2) was $107 for in-person examination and $73.2 for tele-ophthalmology. The incremental cost-effectiveness (ICER) was $314.1 per additional case detected and $102 per additional case correctly diagnosed

**Conclusions:** In a semi-urban community, our incremental cost of $314 per case may be considered too high to be implemented in a publicly funded healthcare system. This is largely due to the fact that the healthcare payer would still have to support in-person examination in addition to the new telescreening program, especially during early stages of program execution.

## Introduction

Diabetic retinopathy (DR) is a sight threatening complication in patients with diabetes mellitus, and is usually asymptomatic in early stages.[1] Diabetic eye complications are the leading cause of visual loss amongst working aged people.[2] Regular eye examination is fundamental to detect DR progression and to promote timely therapeutic interventions. Effective treatment for DR exists with over 50% of patients experiencing reduction of severe vision loss if they receive treatment after timely diagnosis of sight-threatening DR.[3]

Approximately 50% of diabetic patients do not receive the eye examination guidelines as recommended by the American Academy of Ophthalmology,[4] resulting in lost opportunities to prevent severe vision loss by means of timely treatment delivery.[5] Besides non-modifiable factors, limited availability of eye care specialists, travelling difficulties and time constraints also contribute to non-adherence, especially in non-urban areas.[6-7]

Within this context, pharmacy-based tele-ophthalmology has emerged as a possible alternative that may facilitate compliance with evidence-based recommendations and reduce barriers to specialized eye care.[8-9] In this program, retinal digital images are captured in a local pharmacy and securely transmitted electronically to a specialized reading centre, where photographs are graded by an eye specialist.[10] Patients with signs of DR can then be referred to an eye-care professional for comprehensive assessment.[11] Thus, the workload of routine eye examination is transferred to other (presumably less expensive) settings, optimizing the use of specialized eye-care services. In addition, this approach eliminates unnecessary traveling for patients and eye care professionals, and it may improve the consistency of community-based eye care delivery without geographic constraints.[12]

The cost-effectiveness of new technologies should be explored before implementation in specific settings in order to facilitate estimation of the eventual costs of introducing new technologies, as well as their potential benefits compared with competing alternatives.[13] Amongst cost-effectiveness studies conducted for DR screening , few have evaluated tele-ophthalmology as an alternative for in-person examination.[14] Thus, the objective of this study was to estimate the cost-effectiveness of mobile tele-ophthalmology screening compared to primary care examination for the diabetic population residing in non-urban areas of Southwestern Ontario (Canada). Our primary interest was to assess the additional cost per case of any diabetic retinopathy detected with pharmacy-based tele-ophthalmology on an annual basis from the health system perspective. Unlike previous studies, we consider a more realistic scenario in which the tele-ophthalmology program would not entirely replace in-person examination, while also accounting for the effects of performing a dilated or non-dilated examination with this technology.

## Methods

### Study setting

The economic analysis was designed for the South-western Ontario context, specifically non-urban areas at the Erie-St. Clair Local Health Integration Network (LHIN). Such non-urban areas have limited specialized eye-care and diabetic care, in which a pharmacy-based tele-ophthalmology system may be of benefit, as it would help reaching diabetic individuals who otherwise would not get an eye examination.[15] As of 2011, the census subdivision contemplated in this study (Chatham-Kent) reported a total of 103,671 habitants (population density of 14.2 people per $km^2$), from which 10,354 are type I or type II diabetic persons over 20 years old.[16] An explicitly urban model (ie Toronto) was not chosen based on the assumption that in-person exams would be relatively easy to access in this setting. An explicitly rural model (Canada’s far north) was not chosen since tele-ophthalmology may be the only alternative in such locations. However, there is true equipoise in understanding the cost-effectiveness of this program in a “semi-urban” context such as the Erie-St Clair or equivalent LHIN’s.

### Decision-tree model and study interventions

A decision-tree was constructed using TreeAge Pro Suite 2013 (TreeAge Software, Inc, Williamstown, Massachusetts), to compare primary care examination (comparator program) versus pharmacy-based tele-ophthalmology (intervention program). A simplified diagram of the decision-tree is provided in **Figure 1**. In the analytical framework, we assumed that the pharmacy-based tele-ophthalmology program coexisted along with the reference program, increasing the volume of DR examinations but did not entirely replace in-person examination. This assumption aligns with the purpose of the tele-ophthalmology program to complement existing eye-care services.

The model was tailored for a mixed cohort of adults with type I or type II diabetes. The outcome of interest was the detection of any diabetic retinopathy, manifested by at least one micro-aneurysm.[4]

Our interest focused on the potential ability of pharmacy-based tele-ophthalmology to strengthen diabetic retinopathy screening coverage at a reasonable cost. Thus, our analysis was restricted to the correct detection of DR cases (true positives), as opposed to incorporating treatment effects and disease progression into the model. A heath care system perspective was adopted, where consequences and direct costs pertaining to each program were included based on a 12-month time frame.

*Intervention: Pharmacy-based tele-ophthalmology*

The economic model was designed for the evaluation of a tele-ophthalmology screening program, used to identify patients with no (or minimal) DR and patients with more than minimal DR, corresponding to a Modified Airlie House Classification ≥20 on the reference standard.[17] We considered the introduction of a part-time mobile retinal unit, operating on a rotational basis among regional pharmacies at the main municipalities of Chatham-Kent. In this model, clinical history and 45 degree digital photographs were taken from each eye by an ophthalmic photographer and pharmacologic dilation with tropicamide or phenylephrine was optional. Readable digital images were sent via electronic communications to the reading center at St. Joseph's hospital in London (ON) for assessment by a retina specialist. Patients with positive findings were referred to a retina specialist for a diagnostic confirmation with angiography and optical coherence tomography. Similarly, patients with unclear fundus photographs were referred to in-person examination with the retina specialist for further assessment.

*Comparator: In-person examination (primary care)*

The primary care screening was defined as a dilated fundus examination performed by a primary care eye specialist (either an optometrist or ophthalmologist). Patients with positive results were referred to a retina specialist for a comprehensive eye examination with angiography and optical coherence tomography.

**Identification and calculation of model probabilities**



Probabilities used in the base-case model are shown in **Table 1**. Prevalence of any DR (22.5%) was calculated using public reports by the Public Health Agency of Canada and the National Coalition for Vision Health.[18-19] Screening rate with the reference program ($P_{(ref)}$) was considered to mirror  the eye examination rate after diagnosis of diabetes in Ontario (51.1%).[20] After the introduction of the new screening intervention, the patient could choose between two screening alternatives, namely in-person examination or telescreening, or no screening at all. To calculate the screening rate of tele-ophthalmology examinations ($P_{(tele)}$), we used the following formula that considered the increased screening compliance after the introduction of tele-ophthalmology (V) and the proportion of screening examinations with tele-ophthalmology based on screening preference (T), as follows

$$\mathbf{P_{(tele)} = T\,(\,P_{(ref)} \times V\,)} \quad , V \geq 1,\ P_{(tele)} < 1 \qquad (1)$$

In this equation, "$P_{(ref)} \times V$" is the overall screening rate after the introduction of the tele-ophthalmology program (in-person examination and tele-ophthalmology combined), and "$P_{(tele)}$"  is the proportion of those examinations that correspond to tele-ophthalmology screening.

Both patients' preferences (T) and screening compliance after tele-ophthalmology (V) were derived from published literature. For the base-case model, the volume increase in DR examinations after tele-screening (V) was set to 10%, with 40% of patients favoring pharmacy-based telescreening examination over the comparator.[21] Hence, the base-case screening probability for the tele-ophthalmology arm was 0.562.

Estimates of the diagnostic performance of tele-ophthalmology were obtained from a recent meta-analysis[22] that separately reported the summary results according to diagnostic threshold. Therefore, we used the summary sensitivity and specificity corresponding to the assessment of any DR. We also used this data to calculate the proportion of unreadable images with tele-ophthalmology with and without pharmacologic dilation. Finally, the proportion of dilated examinations was obtained from a study that used pharmacy-based tele-ophthalmology for DR screening across Canadian provinces.[22] It was assumed that pupil dilation with tropicamide or phenylephrine was performed by the pharmacist at the patient's discretion.



**Identification and calculation of model costs**

Data sources for estimates of costs included published literature, market prices, vendor's quotations, official government reports and administrative information from St. Joseph's Healthcare in London (ON). Only direct costs were incorporated into the model and presented in 2013 Canadian dollars. Cost information is provided in **Table 2**. Costs related to equipment and maintenance were obtained directly from the vendor assuming a 5 year life (written communication, 2013). Capital costs were annualized at a 5% discount rate per year, corresponding to the rate for Ontario government bonds. Fuel costs were obtained from the Ontario Ministry of Energy report and reflected the cost per gallon in Ontario.[23] Pharmacy overhead costs were calculated from the annual Pharmacy Trends Reports, which provided information on annual operating expenses per square foot among Canadian pharmacies.[24]

To estimate the labor cost per patient assessment, a structured literature search was conducted to find economic studies on DR screening that reported information on average minutes of labor cost per patient. Studies calculated the average minutes spent by personnel for taking and/or assessing eye photographs, which varied between 5 and 15 minutes.[25] In-person consultation fees for major eye examination were obtained from the Schedule of

Benefits of Physician Services by the Ontario Ministry of Health and Long-term care.[26] The ophthalmic reader fee was based on the tele-consultation fee provided by the Alberta Healthcare Insurance Plan for pediatricians and related subspecialties.[27] It was assumed that an Ontario tele-consultation fee for DR assessment would resemble that of Alberta for tele-consultation in pediatric specialties.

**Cost-effectiveness evaluation and sensitivity analysis**

Two measures of effectiveness were analyzed in this study; (1) cases of any DR detected (true positives) and (2) cases correctly diagnosed (including true positives and true negatives). A case of DR was defined as any DR beyond very mild non-proliferative DR, corresponding to a Modified Airlie House Classification ≥20 on the reference standard.[17] Cost-effectiveness was calculated as total cost divided by number of cases detected (or number of cases correctly diagnosed). Thus, the Incremental Cost Effectiveness Ratio (ICER) was calculated as the extra cost needed to identify (1) an additional case of DR or (2) an additional case correctly diagnosed after the implementation of pharmacy-based tele-ophthalmology.

**Deterministic Sensitivity Analysis**

Parameters considered as potential drivers of the model were included in sensitivity analysis, and were assigned plausible ranges based on 95% confidence intervals or upper and lower 25% limits around the base-case value. For simplicity we limited the reporting of sensitivity analyses to the cost per case detected per year.

One way sensitivity analyses were conducted for most data elements to investigate the extent to which each variable's uncertainty affected the model results. Variables considered for one-way sensitivity analysis with their respective ranges are listed in **Table 1** (model probabilities) and **Table 3** (model costs). A multi-way sensitivity analysis was also performed, where model parameters were varied simultaneously to generate extreme scenarios.

## Results

### Base-case analysis

Base-case parameters are outlined in Table 1. Considering a population of 10,354 diabetic patients, the tele-ophthalmology program would correctly detect additional 136 cases compared to in-person examination only (**Table 4**). Cost-effectiveness was assessed as (1) cost per case detected, and (2) cost per case correctly diagnosed. For (1) the cost-effectiveness of in-person examination and tele-ophthalmology was $510 and $478.3, respectively, whereas for (2) was $107 for in-person examination and $73.2 for tele-ophthalmology. The incremental cost-effectiveness (ICER) was $314.1 per additional case detected and $102 per additional case correctly diagnosed (**Table 5**). In both instances the programs were non-dominant; hence, tele-ophthalmology was always more costly, but more effective than in-person examination alone. (**Figure 2**).

### Sensitivity analyses

Sensitivity analyses assessed uncertainties of model parameters, including diagnostic accuracy, DR prevalence, compliance and costs. Results of multiple one-way sensitivity analyses are outlined in **Table 6**. We found that the model was stable with regards to sensitivity, specificity and prevalence variations. Workforce wages played a significant role in the cost-effectiveness of both screening programs. For the base-case scenario we used a proxy code from the Alberta Schedule of Medical Benefits (code 03.05JJ).[27] Other influential variables in the tele-ophthalmology program included the proportion of unreadable images (without pupil dilation) and the grader fee.

A two-way sensitivity analysis was conducted to estimate the joint influence of screening volume and patients' preferences on the cost-effectiveness of pharmacy-based tele-ophthalmology (**Figure 3**).

## Discussion

### Cost-effectiveness of tele-ophthalmology

The detection of DR by means of tele-ophthalmology programs has proven to be a cost-effective alternative amongst isolated communities, generating savings through lower transportation and personnel costs.[6,7] In our study, in the Chatham-Kent context, the introduction of tele-ophthalmology was more expensive than in-person examination (approximately $50) but detected 15% more cases of any DR at $314.1 per additional case.

A previous study assessed the cost-effectiveness of systematic photographic screening versus opportunistic eye examination in the UK.[28] Adjusted to 2013 Canadian dollars, the incremental cost per additional DR case detected was $83, which was regarded as cost-effective within the British healthcare system. In comparison, the incremental cost-effectiveness of tele-ophthalmology in our study of $314.1 may be too high to consider its implementation in a semi-urban context. However, if an exclusive use of tele-ophthalmology is assumed, the ICER would be reduced to $192 per case detected, almost half of the base-case value and closer to the acceptable cost-effectiveness estimate reported by James and colleagues.[28]

### Sensitivity analyses

Sensitivity analyses showed an important influence of healthcare specialists' fees for in-person examination and interpretation of retinal images. As expected, the ICER increased as the fee of retinal image readers increased up to 15% its base-case value. Alternatively, when in-person examination cost reached $78 per patient, tele-ophthalmology became less costly and more effective, dominating over in-person examination.

Undilated tele-screening examinations showed a higher rate of unreadable images, which affected the incremental cost-effectiveness of the program. Although pupil dilation may improve image quality and lower the costs, it may prevent patients form accepting eye-screening at the pharmacy, as has been previously reported.[29]

## Comparison to previous evidence

In contrast to our findings, other studies have reported tele-ophthalmology to be highly cost-effective or even dominant at the base-case analysis.[14,30] However, comparisons of our results with prior published studies are not straightforward due to differences in effectiveness outcomes, model assumptions and geographical settings.

## Study applicability

In a semi-urban community, the implementation of tele-ophthalmology would be more expensive compared to a context where the tele-ophthalmology program is assumed to be exclusive. Our incremental cost of $314 per case may be considered too high to be implemented in a publicly funded healthcare system. This is largely due to the fact that the healthcare payer would still have to support in-person examination in addition to the new telescreening program, especially during early stages of program execution.

If stakeholders are interested in investing on a telescreening program in a semi-urban context, a comprehensive discussion about potential strategies to reduce screening costs should be in order. From the sensitivity analyses, we found that eye specialist fees and pupil dilation are the most influential factors in the cost-effectiveness of the tele-ophthalmology program. Given that pharmacologic dilation reduces the proportion of unnecessary referrals due to unreadable images, a program with pupil dilation to all patients will improve cost-effectiveness. Also, the automated detection of DR lesions may be an alternative to the manual assessment of digital images by a specialist.

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## Figures

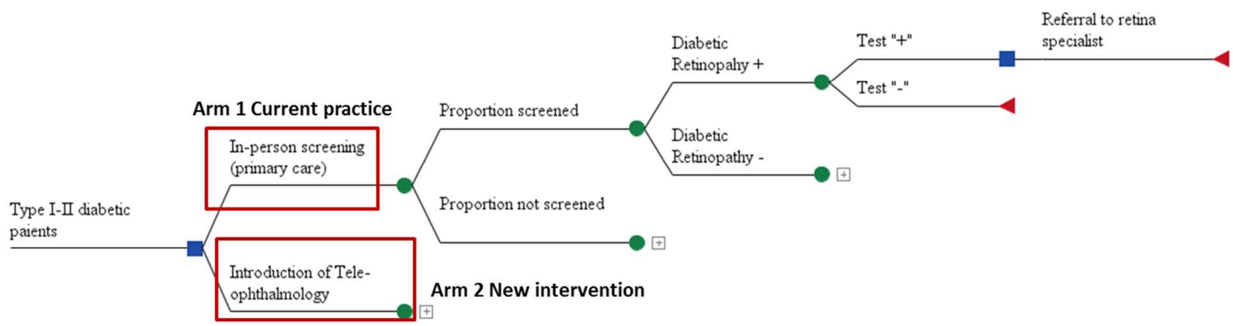


**Figure 1.** Illustration of a portion of decision tree showing competing alternatives for diabetic retinopathy screening. Arm 1 corresponds to current practice (in-person examination); Arm 2 corresponds to the new intervention evaluated in the model (pharmacy-based tele-ophthalmology)

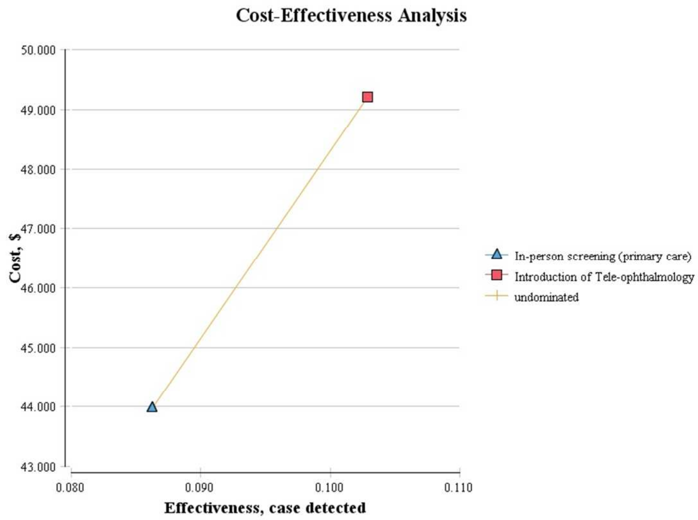


**Figure 2.** Cost-effectiveness plane. In-person examination versus introduction of tele-ophthalmology

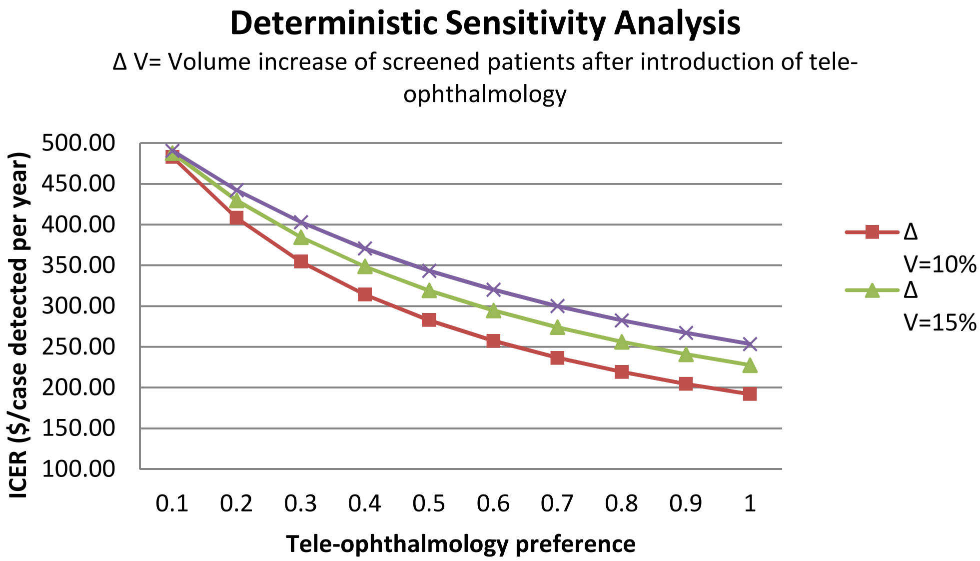


**Figure 3.** Two way sensitivity analysis. Influence of tele-ophthalmology preference and increased patience compliance after introduction of tele-ophthalmology on the incremental cost-effectiveness ratio (ICER)

## Tables

**Table 1.** Base case model parameters and parameter ranges

| Parameter | Value | Range (interval for DTA) |
|---|---|---|
| ***Fixed Data Elements*** | | |
| Diabetic population in study setting | 10,354 patients | - |
| Eye examination rate with current practice | 0.511 | - |
| Volume increase of screening compliance after tele-ophthalmology is implemented | 10% increase | - |
| **Variable Data Elements** | | |
| Prevalence of any DR in Canada | 0.225 | 0.169 to 0.281 |
| *a) Screening intervention parameters (tele-ophthalmology)* | | |
| Proportion prefers tele-ophthalmology for DR screening | 0.40 | 0.50; 0.60; 0.70 |
| Proportion examined with tele-ophthalmology* | 0.225 | 0.169 to 0.281 |
| Sensitivity | 0.84 | (95% CI) 0.76 - 0.91 |
| Specificity | 0.94 | (95% CI) 0.90 - 0.97 |
| Proportion of dilated examinations | 0.337 | (95% CI) 0.25-0.47 |
| Proportion of unreadable images with pupil dilation | 0.054 | (95% CI) 0.033-0.076 |
| Proportion of unreadable images without pupil dilation | 0.287 | (95% CI) 0.139-0.435 |
| *b) Current practice parameters (in-person examination)* | | |
| Proportion examined with current practice (Pc) after introduction of tele-ophthalmology* | 0.337 | 0.253 to 0.421 |
| Sensitivity | 0.75 | (95% CI) 0.67-0.83 |
| Specificity | 0.82 | (95% CI) 0.79-0.86 |
| DTA=Deterministic sensitivity analysis; DR=Diabetic Retinopathy | | |
| * Based on published data estimates about proportion of patients screened after introduction of tele-ophthalmology and patient preferences towards examination with tele-ophthalmology. | | |

**Table 2.** Estimated costs for in-person examination and pharmacy-based tele-ophthalmology

| **Item** | **Cost per unit** | **Unit description** | **Total cost** |
|---|---|---|---|
| ***Capital costs**** | | | *Cost/year* |
| Digital Camera | $ 17,458.50 | One retinal camera | $ 4,032.45 |
| Table Lift | $ 1,045.25 | One table lift | $ 241.43 |
| Software | $ 1,610.25 | One software package | $ 371.93 |
| Carrying case | $ 1,299.50 | One carrying case | $ 300.15 |
| Maintenance | $ 460.00 | Annual maintenance | $ 460.00 |
| ***Camera transportation costs*** | | | *Cost/year* |
| Van rent | $ 91.07 | One cargo van | $ 1,092.84 |
| Fuel | $ 1.27 | One litre | $ 76.26 |
| ***Overhead costs†*** | | | *Cost/year* |
| Pharmacy overhead costs | $ 155.00 | Annual expenditures per square foot | $ 775.00 |
| ***Labour costs*** | | | *Cost/patient* |
| Tele-ophthalmology coordinator | $ 24.18 | Hourly wage[£] | $ 4.03[ϕ] |
| Photographer | $ 24.18 | Hourly wage[£] | $ 6.05[ϕ] |
| Grader (ophthalmologist) | $ 31.66 | Consultation per patient | $ 31.66 |
| Eye care specialist | $ 51.10 | Consultation per patient | $ 51.10 |
| ***Consumables*** | | | *Cost/patient* |
| Referral to retina specialist | $ 111.31 | Examination per patient | $ 111.31 |
| Dilation drops- Tropicamide 1% | $ 16.15 | Cost per unit (15 ml) | $ 0.54 |
| Dilation drops- phenylephrine 2.5% | $ 4.82 | Cost per unit (5 ml) | $ 0.120 |
| Chin covers | $ 56.50 | Cost per pack (500) | $ 0.113 |

*Annualized based on a 5-year life equipment and a 5% depreciation rate

†Based on average annual pharmacy overhead expenditures for 5 square feet, adjusted to inflation

[£]Based on a part-time annual salary of $21,762.

[ϕ]Part-time salary was extrapolated according to the number of patients per hour. Workload estimation was defined based on literature searches (see appendix K)

**Table 3.** Cost ranges used for Deterministic Sensitivity Analysis

| Item | Unit description | Cost | Value or Range† (for DSA) |
|---|---|---|---|
| *Capital costs* | | | |
| Digital Camera | One retinal camera | $ 17,458.50 | $ 29,798.10 |
| *Labour costs* | | | |
| Tele-ophthalmology coordinator | Consultation per patient | Hourly wage | $24.18 |
| Photographer | Consultation per patient | Hourly wage | $24.18 |
| Grader (ophthalmologist) | Consultation per patient | $ 31.66 | $ 23.75 to $ 55.41 |
| Eye care specialist | Consultation per patient | $ 51.10 | $ 38.33 to $ 89.43 |

† Range based on upper and lower 25% limits

**Table 4.** Examination outcomes of pharmacy-based tele-ophthalmology and in-person examination programs per 10,354 diabetic patients in the study model

| | In-person examination | Introduction of tele-ophthalmology |
|---|---|---|
| **Patient compliance (%)** | 51.1% | 56.2% |
| **True positive** | 893 | 1029 |
| **True negative** | 3362 | 3914 |
| **False positive** | 738 | 595 |
| **False negative** | 298 | 280 |
| Total patients screened | 5291 | 5819 |

**Table 5.** Incremental cost-effectiveness results for in-person examination versus introduction of tele-ophthalmology

| Screening stategy | Cost per patient | Incremental cost per patient | Effectiveness (case detected) | Incremental effectiveness | ICER | Dominance |
|---|---|---|---|---|---|---|
| *In-person screening (primary care)* | $43.98 | | 0.086 | | | Undominated |
| *Introduction of Tele-ophthalmology* | $49.22 | $5.24 | 0.103 | 0.017 | **$314.1** | Undominated |

**Table 6.** One-way deterministic sensitivity analysis results

| Parameter | Base-case value | Range | ICER ($/case detected per year) |
|---|---|---|---|
| Prevalence of any diabetic retinopathy | 0.225 | 0.169 to 0.281 | $ 394.4 to $ 265.89 |
| Patient preference for pharmacy-based tele-ophthalmology | 0.40 | 0.40 to 0.70 | $ 314.15 to $ 236.56 |
| Diagnostic accuracy in-person examination | | | |
| *Sensitivity* | 0.75 | 0.67 to 0.83 | $ 282.0 to $ 361.2 |
| *Specificity* | 0.82 | 0.79 to 0.86 | $ 287.0 to $ 350.2 |
| Diagnostic accuracy tele-ophthalmology | | | |
| *Sensitivity* | 0.84 | 0.76 to 0.91 | $ 405.9 to $ 304.9 |
| *Specificity* | 0.94 | 0.90 to 0.97 | $ 350.9 to $ 286.6 |
| Proportion of dilated examinations (tele-ophthalmology) | 0.337 | 0.25 to 0.47 | $ 333.9 to $ 321.5 |
| Rate of unreadable images (tele-ophthalmology) | | | |
| *With pupil dilation* | 0.054 | 0.033 to 0.076 | $ 306.6 to $ 321.5 |
| *Without pupil dilation* | 0.287 | 0.139 to 0.435 | $ 209.9 to $ 411.2 |
| Grader fee per patient (tele-ophthalmology) | $31.66 | $ 23.75 to $ 55.41 | $ 207.6 to $ 633.9 |
| Tele-ophthalmology coordinator fee per patient | $4.03 | $3.02 to $5.04 | $300 to $327.8 |
| Ophthalmic photographer | $6.05 | $4.54 to $7.56 | $300.05 to $327.8 |
| In-person consultation | $51.10 | $ 38.33 to $ 89.43 | Tele-ophthalmology dominates at $ 77 |
| Referral to retina specialist | $111.31 | $ 83.48 to $ 139.14 | $ 252.5 to $ 375.8 |