Improving the current diabetic macular oedema screening programme

I Wong*, R Wong, R Gangwani, V Chong, R Kawasaki

KEY MESSAGES

1. The current diabetic retinopathy screening strategy is very effective at detecting maculopathy, but it has low sensitivity and positive predictive value.
2. Under the current strategy, up to 87.1% of patients referred to ophthalmologists for maculopathy screening were found to be false positives.
3. Three newly proposed screening strategies were compared with the current strategy in terms of sensitivity index and cost-effectiveness.
4. Strategy D that incorporated macular optical coherence tomography for all patients into the current strategy was most cost-effective.

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[1] **I Wong**, [2] **R Wong**, [1] **R Gangwani**, [3] **V Chong**, [4] **R Kawasaki**

[1] *Department of Ophthalmology, LKS Faculty of Medicine, The University of Hong Kong*
[2] *Department of Ophthalmology, The Hong Kong Eye Hospital*
[3] *Department of Ophthalmology, Oxford University, UK*
[4] *Department of Public Health, Yamagata University Graduate School of Medical Science, Japan*

* Principal applicant and corresponding author: wongyhi@hku.hk

Introduction

Diabetic retinopathy (DR) is a common cause of blindness. Diabetic macular oedema (DME) and proliferative diabetic retinopathy are the two major causes of vision loss in DR. Timely treatment is effective at preventing vision loss due to DME.[1] From a public health standpoint, prevention is more cost-effective than treatment.

In Hong Kong, the current DR screening strategy is based on fundus photograph grading.[2] Diabetic patients who attend general outpatient clinics are offered annual fundus photography screening. Those with maculopathy are referred for clinical assessment by ophthalmologists at specialist outpatient clinics. Those confirmed to have DME are offered treatments as appropriate.

Accurate diagnosis of DME requires stereopsis and detection of macular thickening. Even with stereo fundus photography, detection of DME may be difficult. Determining the presence of surrogate markers in the macula (ie, retinal exudates and/or haemorrhages) is the recommended first step in predicting the presence of macular oedema. Nonetheless, these surrogate markers may not be perfectly correlated with DME.

We have reported the DR screening results among 174 532 diabetic patients over 3.5 years.[2] The prevalence of DR was 39%. Of all patients, 8.6% (15 009) had fundus photographs graded as maculopathy. This accounted for up to 87.4% of all cases referred to specialist outpatient clinics during those 3.5 years.[2] This indicates that maculopathy is the most prevalent diagnosis of sight-threatening diabetic retinopathy among those with diabetes. Owing to the limitation of fundus photography to visualising retinal thickening in DME, false-positive maculopathy cases are a concern. Based on the current screening strategy, we devised three additional strategies to enhance the overall sensitivity and cost-effectiveness of screening. This study aimed to compare different screening strategies with the current strategy in terms of the sensitivity index and cost-effectiveness of DME detection.

Methods

Patients were recruited from the Diabetic Complications Screening Programme of the Hong Kong West Cluster, Hospital Authority from 1 February 2014 to 31 January 2016. Strategy A was the current screening protocol. Strategy B did not consider retinal haemorrhage in the macula as a surrogate marker for maculopathy; patients with haemorrhage only were not considered to have maculopathy. Strategy C used best-corrected visual acuity instead of visual acuity and used optical coherence tomography (OCT) for referred cases with suspicion of maculopathy only if positive for maculopathy. Strategy D used OCT of the macula for all cases in addition to all components of strategy A. The screening procedures have been reported previously.[2] Best-corrected visual acuity assessment and measurement of macular volume using OCT (Cirrus HD OCT 4000, Carl Zeiss Meditec, Dublin [CA], USA) were performed on all patients.

Reports of all patients were reviewed by investigators other than the initial grading optometrist(s). All assessments were reviewed separately by two independent investigators, and the results were recorded as the reference standard.

The current screening protocol (strategy A) was the benchmark and compared with the three other screening strategies. A model was formulated to simulate the current practice. The model estimated the costs for each patient until 12 months after being seen by an ophthalmologist. As there were no real-life data to show the exact probability that a patient underwent a particular management step, estimates were based on interviews with local retinal experts

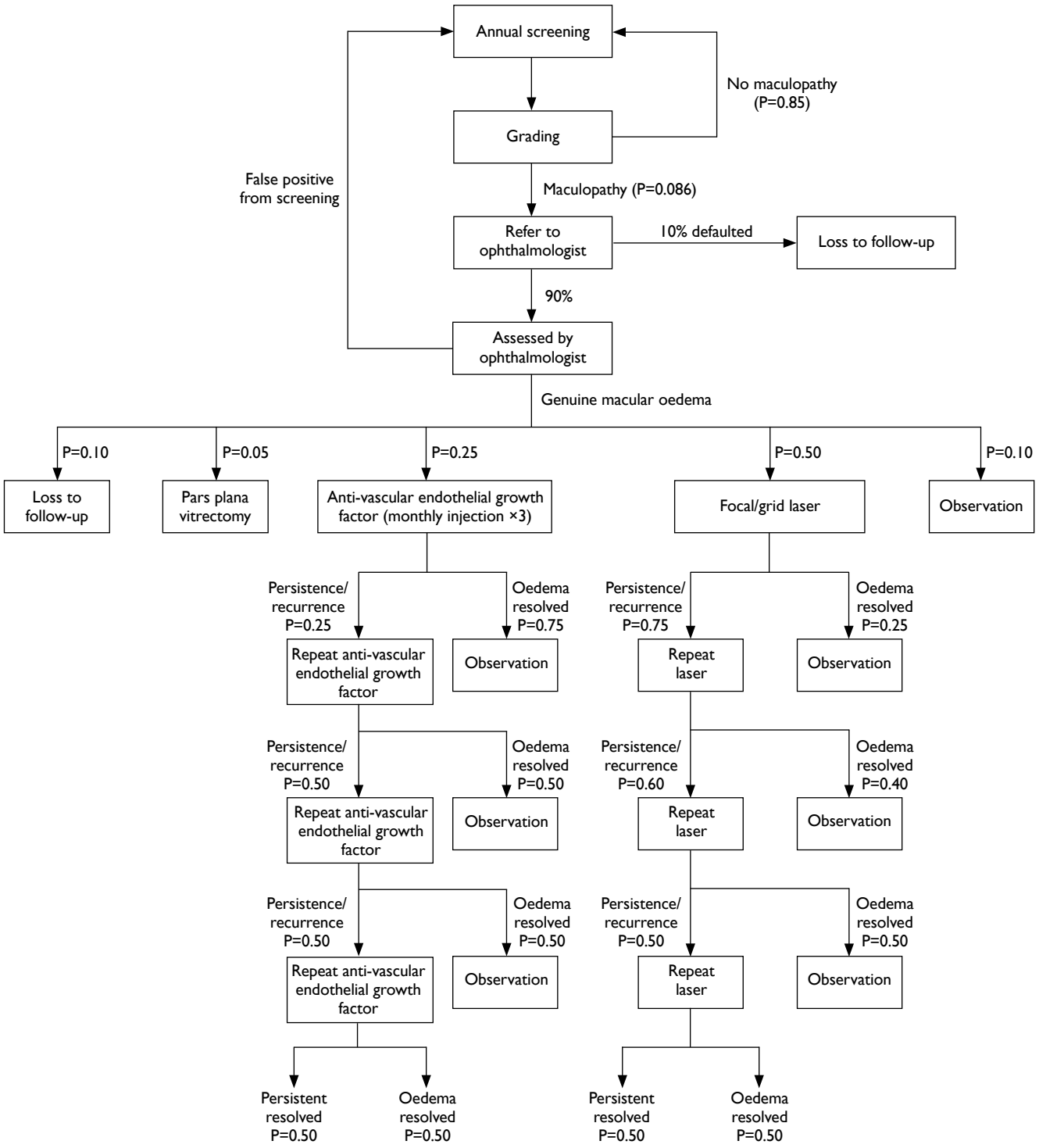

FIG. Model structure with probabilities of undergoing each step of management

and a review of medical records and the literature.[1] The per-person health provider costs of (1) the screening programme, (2) retinal examination at specialist outpatient clinics, and (3) treatment costs until 1 year after screening were used in the analysis (Fig).

The four strategies were compared in terms of sensitivity index, quality-adjusted life-years (QALYs) gained, and cost-effectiveness. Reference values were the gross domestic product (GDP) per capita of Hong Kong in 2014 (HK$310 113 or US$39 963)[5] and US$50 000/QALY gained.[3] Strategies that costs <1, 1 to 3, and >3 times the GDP per capita were considered as 'very cost-effective', 'cost-effective', and 'not cost-effective', respectively.[4]

Results

A total of 2277 patients (mean age, 62.80±11.75 years) were recruited; 996 (43.7%) of them were male. The outcomes and sensitivities of the four screening strategies are shown in Table 1. The QALY gained per patient was 0.45. The total QALY gained, costs involved, and incremental cost-effectiveness ratio for each strategy are shown in Table 2. The four strategies were all considered 'very cost-effective'; strategy D was the most cost-effective.

Discussion

We estimated the outcomes of each strategy for the same pool of screening-naïve diabetic patients. The difference in screening procedures resulted in varying sensitivity indices. With strategy A, the false-positive rate of maculopathy was high (87.1%) and resulted in unnecessary referrals (HK$740 [US$95.4] per consultation), the opportunity cost of using specialist outpatient clinics, and increased

TABLE 1. Outcomes of the four screening strategies for diabetic macular oedema (DME)*

Parameter	Strategy A		Strategy B		Strategy C		Strategy D	
	Normal	DME-positive	Normal	DME-positive	Normal	DME-positive	Normal	DME-positive
Fundus photograph grading								
Negative retinopathy, negative maculopathy	1007	38	1007	38	1007	38	1007	38
Positive retinopathy, negative maculopathy	874	24	1070	43	1165	33	1165	33
Positive retinopathy, positive maculopathy	291	43	95	24	0	34	0	34
Optical coherence tomography grading								
Negative	1881	62	2077	81	2172	71	2172	0
Positive	291	43	95	24	0	34	0	105
Sensitivity	40.95%		22.86%		32.38%		100.00%	
Specificity	86.60%		95.63%		100.00%		100.00%	
Positive predictive value	12.87%		20.17%		100.00%		100.00%	
Negative predictive value	96.81%		96.25%		96.83%		100.00%	

* Data are presented as No. of patients unless otherwise indicated

TABLE 2. Cost-effectiveness analysis of the four screening strategies*

	Strategy A	Strategy B	Strategy C	Strategy D
Quality-adjusted life-years gained, y	19.4983	10.8828	15.4173	47.6123
Total cost, HK$	1 125 408	710 893	715 986	1 517 867
Unit cost, HK$	494.25	312.21	314.44	666.61
Total cost, US$	145 213.9	91 728.1	92 385.3	195 853.8
Cost per quality-adjusted life-years gained, US$	7447.5	8428.7	5992.3	4113.5
Incremental quality-adjusted life-years gained, y	Reference	–8.62	–4.08	28.11
Incremental cost, US$	Reference	–53 485.8	–52 828.7	50 639.9
Incremental cost-effectiveness ratio, US$	Reference	6208.1	12 944.9	1801.2

* Cost estimates (per patient per visit): best-corrected visual acuity assessment HK$83.3, fundus photography HK$65.5, optical coherence tomography of the macula HK$208.3, ophthalmologist consultation HK$740, laser procedure HK$1500, anti-vascular endothelial growth factor injection HK$660, vitrectomy HK$30 000, hospital stay HK$3290.

waiting time for patients in need. Although the cost per QALY gained is still 'very cost-effective' from the health provider standpoint, strategy A has low sensitivity and positive predictive value. In strategy D, comprehensive OCT screening increases the sensitivity and positive predictive value. Although its total cost is highest, it yields the highest QALY gained. Strategy D's cost/QALY gained is US$4113.5, which is the lowest of the four strategies.

Given the fact that 95.4% of patients screened did not have DME, strategy D appears to waste OCT resources on normal diabetic patients. Nonetheless, every normal diabetic patient may be at risk of having developed DME by the next annual screening. A baseline OCT can be used as a reference for subsequent screening visits. In addition, when OCT is performed at the time of screening, specialists can read the report upon referral and make necessary decisions.

In strategy D, fundus photograph screening could be removed to save costs. Nonetheless, OCT is only good at detecting macular pathologies and cannot detect neovascularisation in sight-threatening diabetic retinopathy. Despite that, strategy D remained the most cost-effective of the four strategies. Strategies B and C were less cost-effective. For details on these two strategies, please refer to the full report.

There are limitations to the study. The disability weight of DR for DME differed from the genuine disability weight of DME. The disability weight reported in Global Burden of Disease was probably a combined disability weight of both sight-threatening diabetic retinopathy and DME. Nonetheless, in real-life situations, most referred cases of DR were due to DME. The cost estimates and probabilities of treatment were largely based on expert opinion and medical records, which may have been biased and incorrect.

More precise data on the epidemiology of DR in Hong Kong are needed. Validation of the costs and probabilities of treatment is needed, as are data on diabetic patients' compliance with the screening programme. A clear definition of cost-effectiveness specific to Hong Kong is important to facilitate interpretation of economic evaluation. In 2015, Hong Kong ranked 17th in the world in terms of GDP per capita; using this as a reference may not be reasonable. If the GDP per capita of China (US$7429.7) had been used as a reference,[5] strategies A and B would have become 'cost-effective', and strategies C and D would have remained 'very cost-effective'.

Conclusion

Strategy D that incorporates OCT of all patients in addition to all components of the current strategy is the most cost-effective of the four strategies investigated.

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