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Cost-Effectiveness of Screening for Intermediate Age-Related Macular Degeneration during Diabetic Retinopathy Screening

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Purpose: To determine whether screening for age-related macular degeneration (AMD) during a diabetic retinopathy (DR) screening program would be cost effective in Hong Kong.

Design: We compared and evaluated the impacts of screening, grading, and vitamin treatment for intermediate AMD compared with no screening using a Markov model. It was based on the natural history of AMD in a cohort with a mean age of 62 years, followed up until 100 years of age or death.

Participants: Subjects attending a DR screening program were recruited.

Method: A cost-effectiveness analysis was undertaken from a public provider perspective. It included grading for AMD using the photographs obtained for DR screening and treatment with vitamin therapy for those with intermediate AMD. The measures of effectiveness were obtained largely from a local study, but the transition probabilities and utility values were from overseas data. Costs were all from local sources. The main assumptions and estimates were tested in sensitivity analyses.

Main Outcome Measures: The outcome was cost per quality-adjusted life year (QALY) gained. Both costs and benefits were discounted at 3%. All costs are reported in United States dollars ($).

Results: The cost per QALY gained through screening for AMD and vitamin treatment for appropriate cases was $12 712 after discounting. This would be considered highly cost effective based on the World Health Organization's threshold of willingness to pay (WTP) for a QALY, that is, less than the annual per capita gross domestic product of $29 889. Because of uncertainty regarding the utility value for those with advanced AMD, we also tested an extreme, conservative value for utility under which screening remained cost effective. One-way sensitivity analyses revealed that, besides utility values, the cost per QALY was most sensitive to the progression rate from intermediate to advanced AMD. The cost-effectiveness acceptability curve showed a WTP for a QALY of $29 000 or more has a more than 86% probability of being cost effective compared with no screening.

Conclusions: Our analysis demonstrated that AMD screening carried out simultaneously with DR screening for patients with diabetes would be cost effective in a Hong Kong public healthcare setting. *Ophthalmology 2015;122:2278-2285 © 2015 by the American Academy of Ophthalmology.*

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Age-related macular degeneration (AMD) is a major cause of blindness in developed countries with a prevalence of 8.7% worldwide.[1,2] Age-related macular degeneration ranks globally as the third highest cause of visual impairment predominantly affecting individuals 50 years of age and older.[1,3,4] From approximately 37 million people affected worldwide in 2010, population ageing will increase the number of individuals with AMD to approximately 47 million people (>1% of the world's population) by 2020.[5]

The early stages of AMD often are asymptomatic, and there is no current treatment for early AMD. However, treatment using high-dose antioxidant vitamins and zinc supplements has been shown to be effective for intermediate AMD. The Age-Related Eye Disease Study (AREDS)[6] found that intake of high-dose vitamin supplements containing a combination of vitamin C, vitamin E, β-carotene, and zinc could reduce progression from intermediate to advanced AMD by 25% (odds ratio, 0.75; 99% confidence interval, 0.45−1.24) over a 5-year period. In a population-based cohort study,[7] this regimen was associated with a reduction of 35% (hazard ratio, 0.65; 95% confidence interval, 0.46−0.92) in incident AMD after a mean follow-up of 8 years (range, 0.3−13.9 years). The existence of a possible treatment therefore raises the question of whether screening for intermediate AMD would be cost effective.

Hopley et al[8] examined the cost effectiveness of screening and treatment for intermediate AMD in the Australian population using a decision-analytic model and outcome data from AREDS. This evaluation, from a provider's perspective, demonstrated a cost of £22 722 ($34

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500 United States dollars [US$]), or £18 948 (US$28 770) when treatment cost savings were included, per quality-adjusted life year (QALY) gained for those 65 years of age or older. The authors considered this to be moderately cost effective. Rein et al[9] also used the AREDS outcomes and estimated that, in the United States, vitamin therapy for all those older than 50 years who may benefit from it would cost US$21 387 per QALY gained compared with no therapy from a provider's perspective. The authors considered this a reasonable use of resources compared with other treatments. In these previous studies, the screening for AMD took place during a visit to an ophthalmologist[9] or optician.[8]

Currently, there is no screening for AMD in Hong Kong. A recent study[10] in Hong Kong found that among patients with diabetes who attended a diabetic retinopathy (DR) screening program, the age-standardized prevalence of early and advanced AMD was 17.9% and 0.1%, respectively. Given that many people with diabetes already undergo regular screening for DR with digital retinal photographs, there is an opportunity to look for signs of AMD from these existing photographs. Many of these subjects with diabetes are at the age when they would be at risk of AMD. Therefore, it is interesting to determine whether screening for AMD at the same time as screening for DR could be cost effective for this subpopulation of people with diabetes. To answer this, we modeled costs and effects using data obtained largely from a study of DR screening in Hong Kong[11] and incorporating the outcome estimates from AREDS as reported by Rein et al.[9]

Methods

Cost-Effectiveness Model Structure

The model was based on a cohort of subjects with diabetes who undergo regular screening for DR using a retinal fundus camera. A cost-effectiveness model was built to incorporate costs and benefits of screening and treatment for intermediate AMD in terms of incremental cost per QALY gained and sight-years gained. The provider's perspective was used for the costing and only direct costs associated with grading of AMD fundus photographs, referral visits to the ophthalmologist and supervision of the treatment were included. Subjects purchased the supplements themselves as is the normal practice in Hong Kong. Costs are presented in 2009 US$.

A Markov state-transition cohort model was used to assign health states to the subjects in the cohort starting with no sight-threatening DR (STDR) and therefore eligible for DR screening. Those subjects with STDR are already followed up by eye specialists, and other eye diseases, if detected, would be dealt with there. The non-STDR subjects could be in 1 of the 4 AMD states initially, and the proportion in each state was determined according to the prevalence of AMD states found at DR screening in Hong Kong in 2009 (Fig 1). The simulated cohort had a mean age of 62 years and underwent yearly transitions between states until death or age 100 years. Each health state was associated with a cost and a utility level. The final stage in this model was advanced AMD, and it was assumed that subjects in this stage would have utility loss. The impact on quality-of-life changes in visual acuity (VA) associated with early and intermediate AMD was not considered in the model because such changes in VA are unlikely and their magnitude is unknown. In the model, AMD progression in each cycle, if any, occurred before screening. A mortality rate was applied to each cycle based on the general population age-specific mortality rates for men and women in 2009.[12] Age-related macular degeneration state transition probabilities were based on the Rotterdam study[13] and AREDS trial,[6] and both used categories of AMD similar to those we used in the model (Fig 1).

We compared a cohort that was offered screening plus treatment versus a cohort with no AMD screening. The treatment option was antioxidants and zinc for nonsmokers and antioxidants minus β-carotene and zinc for smokers, and the supplements were purchased by the subjects. One annual specialist clinic visit was assumed for all treated subjects. In the absence of evidence that diabetes or DR is associated with the progression of AMD, we assumed they were independent. The model was built in Microsoft Excel 2007 (Microsoft, Redmond, WA).

Model Parameters

Many of the model parameters were obtained from a local study of screening for DR.[11,14] Those subjects attending 2 primary care government outpatient clinics in Hong Kong for monitoring and treatment of diabetes were included in a new DR screening program between February and August 2009. Of the 4619 in the target group, 2218 attended for DR screening, of whom 2003 (90.4%) were 50 years of age or older. The average characteristics of this group were used as the characteristics of the modeled cohort.

Screening Process and Fundus Photography

In the DR screening, each subject underwent biomicroscopic examination of the anterior segment, a test to rule out narrow angles, and mydriatic fundus photography. Two retinal images were captured for each eye, the first centered on the macula and the second centered on the optic disc, using a Canon CR-DGI non-mydriatic retinal camera. (Canon, Tokyo, Japan). All fundus photographs were graded for DR and AMD by the trained optometrists and ophthalmologists (R.A. Gangwani) at the Eye Institute of the University of Hong Kong. Only the images centered on the macula were used for AMD grading. Subjects were graded for DR according to the English National Screening Programme for Diabetic Retinopathy.[15] In this grading scheme, STDR includes the categories of preproliferative retinopathy (R2), proliferative retinopathy (R3), maculopathy (M1), previous laser photocoagulation (P), or a combination thereof. Subjects graded

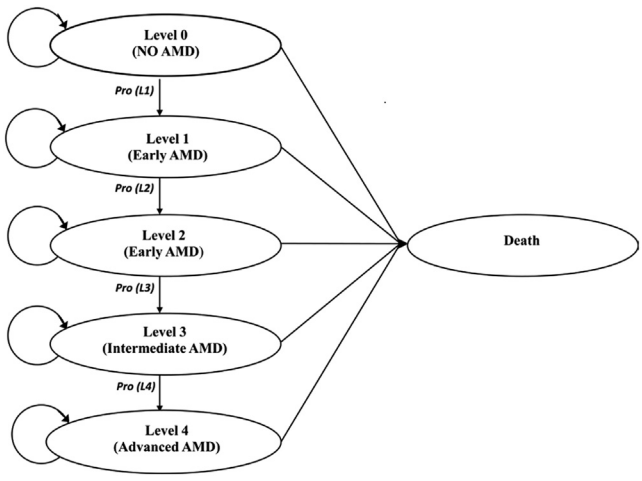

Figure 1. Diagram showing the natural disease progression of age-related macular degeneration (AMD).