Cost-effectiveness and cost-utility of traditional and telemedicine combined population-based age-related macular degeneration and diabetic retinopathy screening in rural and urban China

Ruyue Li, Ziwei Yang, Yue Zhang, Weiling Bai, Yifan Du, Runzhou Sun, Jianjun Tang, Ningli Wang, Hanruo Liu

Summary

Background To assess the cost-effectiveness and cost-utility of a population-level traditional and telemedicine combined age-related macular degeneration (AMD) and diabetic retinopathy (DR) screening program in rural and urban China.

Methods Decision-analytic Markov models were conducted to evaluate the costs and benefits of traditional and telemedicine combined AMD and DR screening from a societal perspective. A cohort of all participants aged 50 years old and above was followed through a total of 30 1-year Markov cycles. Separate analyses were performed for rural and urban settings. Relevant parameters such as the prevalence of AMD and DR, transition probability, compliance with screening and treatment, screening sensitivity, specificity, utility, and mortality were collected from published studies specific to China, other Asian counties, or unpublished data sources such as the National Committee for the Prevention of Blindness. Costs of screening, full examination, and treatment come from the real medical environments and unified pricing of Beijing Municipal Medical Insurance Bureau. Primary outcomes were incremental cost-utility ratios (ICURs) using quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs) using years of blindness avoided. One-way deterministic and simulated probabilistic sensitivity analyses were conducted to reflect uncertainty.

Findings Under the status quo, the total expected medical costs for a 50-year-old patient with AMD or DR were $869.59 and $1,514.18 in rural and urban settings, respectively. Both traditional and telemedicine screening were highly cost-effective. In rural settings, ICURs were $191 (95% confidence interval [CI]: $66 to $239) and $199 (95% CI: $-12 to $217), and ICERs were $2,436 (95% CI: $1,089 to $3,254) and $2,441 (95% CI: $1,452 to $3,900) for traditional and telemedicine screening separately. Even more surprising, both screening strategies dominated no screening in urban settings. Our results were insensitive and robust to extensive sensitivity analyses. Among all acceptable screening intervals (from 1 to 5 years), annual screening could not only produce biggest benefits but also keep ICERs less than three times and one time the per capita gross domestic product (GDP) in rural and urban settings separately. When compared with traditional screening, ICERs of telescreening were less than three times the per capita GDP in rural settings ($2,559 to $8,809) and less than one time the per capita GDP in urban settings (less than $5,564), annual telescreening produced the biggest benefits, it could avert 119 and 270 years of blindness in rural and urban areas separately when 100,000 people were screened.

Interpretation We performed decision-analytic Markov models for combined AMD and DR screening in rural and urban China, and the results showed that population-level combined screening for AMD and DR is likely to be highly cost-effective in both rural and urban China for people over 50 years old. Optimal screening may have an interval of every year based on teleophthalmology platforms. In the future, China should pay more attention to

*Corresponding author at: School of Agricultural Economics and Rural Development, Renmin University of China, Beijing 100000, China.
**Corresponding authors at: Beijing Institute of Ophthalmology, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing Key Laboratory of Ophthalmology and Visual Sciences, Beijing Institute of Technology, Beijing, 100000, China.

E-mail addresses: j.tang@ruc.edu.cn (J. Tang), wningli@vip.163.com (N. Wang), hanruo.liu@hotmail.co.uk (H. Liu).
chronic eye diseases and the government should establish a sound chronic disease management system and make every patient enjoy equal medical services.

**Funding** National Natural Science Foundation of China, NSFC (82171051); the Major Innovation Platform of Public Health & Disease Control and Prevention, Renmin University of China and Beijing Nova program (Z191100001119072).

**Copyright** © 2022 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

**Keywords:** Cost-effectiveness; Cost-utility; Age-related macular degeneration; Diabetic retinopathy; Telemedicine screening

---

**Research in context**

**Evidence before this study**

We searched PubMed for studies published until 2 November 2020, with terms specifications defined (“cost-effectiveness” OR “cost-utility”) AND (“AMD” OR “DR” OR “age-related macular degeneration” OR “diabetic retinopathy”) AND “screening” AND (“China” OR “Chinese”). We also searched references listed in the identified papers. There were no cost-effectiveness analyses of combined AMD and DR screening in Chinese mainland. Previous studies have focused on cost-effectiveness analyses of single AMD or DR screening. Studies in developed and some developing countries have demonstrated the cost-effectiveness of annual screening for DR, especially telemedicine screening. However, it is unclear whether early screening for AMD is cost-effective. As population aging and increases in the prevalence of metabolic diseases, the incidences of AMD and DR remain high and they are the leading causes of visual impairment and blindness worldwide. As the world’s most populous country, China has a large number of elderly patients with eye diseases, and the national and family burden of these chronic eye diseases is likely to continue to increase in the future. At present, China lacks a complete chronic disease management system, and the public does not pay enough attention to the common blindness-causing eye diseases, which leads to a large number of AMD and DR patients without early diagnosis and treatment. Because AMD and DR mostly occur in elderly people, both diseases can be diagnosed by a single fundus photograph, and regular screening can improve patients’ awareness of the disease and avoid severe complications and blindness, it is necessary to testify the cost-effectiveness of combined AMD and DR screening in China.

**Added value of this study**

To the best of our knowledge, this is the first cost-effectiveness analysis that simulated the natural progression of AMD and DR and evaluated the costs and effectiveness of AMD and DR combined screening programs in different settings of Chinese mainland from a societal perspective. For participants aged >50 years, combined AMD and DR screening is highly cost-effective in rural and urban China. ICURs and ICERs of traditional and telemedicine screening in rural areas were less than one time the per capita GDP in base-case analysis. Even more surprising, both screening strategies dominated no screening in urban settings. What’s more, our study compared the cost-effectiveness between traditional face-to-face community screening and telemedicine screening, and we recommended annual screening based on telemedicine platform as the optimal screening strategy for either rural or urban settings.

**Implications of the available evidence**

Our findings highlight the importance of early screening and intervention for AMD and DR in general population. It is necessary to incorporate telemedicine-based combined AMD and DR screening into routine national physical examination projects and establish a complete telemedicine-based chronic eye disease management system which includes screening, referral, treatment and follow-up to realize the sustainable management of chronic eye diseases. What’s more, our findings provide practical recommendations for other developing countries where blindness-causing eye diseases are prevalent and regular screening programs are not widely popularized.

---

**Introduction**

Age-related macular degeneration (AMD) and diabetic retinopathy (DR) are the leading causes of vision impairment (VI) and blindness worldwide, with 1.8 and 0.86 million cases of blindness caused by AMD and DR among people aged 50 years and older in 2020. As the world’s most populous country, China is home to a large population with age-related eye diseases. In 2019, the number of patients with blindness caused by AMD and DR in China was 0.32 and 0.23 million respectively. Currently, the burden of chronic eye diseases continues to increase as a result of population...
aging and increases in the prevalence of metabolic diseases; moreover, the slow natural progression and asymptomatic early stages of AMD and DR make patients unaware of their vision changes until they have had the disease for a long time, which also imposes a significant economic burden on both individuals and society.

Both AMD and DR met the requirements of early screening according to the Wilson-Jungner screening principles recommended by the World Health Organization (WHO). They are both important public health problems; the natural progression history of these diseases are fully understood and both have early and identifiable signs; fundus photograph is a feasible method of early screening, which is fast and non-invasive and accepted by the public; anti-vascular endothelial growth factor (VEGF) drugs is an effective treatment for neovascular AMD (NVAMD) and diabetic macular edema (DME), which can improve vision and quality of life; and regular follow-up of early AMD and DR can prevent the occurrence of severe complications and blindness to some extent.

At present, many economic studies have proved the cost-effectiveness of DR screening in diabetic population in both developed and developing countries, especially telemedicine-based DR screening. Real-world DR screening program has been also recommended and nationally conducted among diabetes mellitus (DM) patients in China. Notably, the “Health Express-Diabetic Retinopathy Screening Project” and “China Diabetic Retinopathy Screening and Prevention Project” have helped a large number of undiagnosed DR patients to get screening and timely treatment. However, previous DR screening programs were mostly single-center studies targeted at the diabetic population and there is still a lack of population-based national DR screening program in China. As for AMD screening, there is limited evidence of real-world screening programs and cost-effectiveness analyses of AMD worldwide. Not to mention the combination of AMD and DR screening. We believe that combined screening may be a cost-effective option because it can not only detect a large number of patients with AMD or DR at early stage and enable them to receive early treatment, but also do not require additional medical costs. Although there have been implications that combined AMD and DR screening could be potentially cost-effective, there are also many challenges and barriers to carry out population-based large-scale screening programs across the country. It takes a lot of workforces of manpower and time to organize a nationwide screening program. Given the country’s complex national conditions such as large population, vast territory and uneven distribution of medical resources, it is difficult to carry out large-scale face-to-face screening programs in China. However, the rapid development of telemedicine has made it possible to achieve large-scale population-based screening. To date, the economic studies of combined traditional or telemedicine-based AMD and DR screening, which health care providers and policymakers required to consider, were inadequate. Our study evaluated the cost-effectiveness of population-based combined AMD and DR screening among Chinese participants aged 50 years and older in rural and urban settings separately, and compared the cost-effectiveness between traditional face-to-face screening and telemedicine-based screening. The results of our study may provide a reference for policy makers in planning eye disease screening programs.

Methods

Model overview

We built Markov models using TreeAge Pro (TreeAge Software; Williamstown, MA, USA) to evaluate the economic effects of traditional and telemedicine screening, and the primary results were incremental cost-effectiveness ratios (ICERs) and incremental cost-utility ratios (ICURs). To minimize the influence of the environment on the results, we set up Markov models for rural and urban areas and described the results separately.

The model was based on a hypothetical cohort of individuals from the age of 50 years through a total of 30 1-year Markov cycles. Individuals were allowed to enter the model as either healthy (free of AMD and DR) or unhealthy (affected by AMD or DR) and could transition to death from any health state. The classifications of AMD and DR were based on international classification systems and were appropriately modified to fit our model (The Markov models for AMD and DR are shown in Appendix Figure 11). The Markov model for AMD was based on The Age-Related Eye Disease Study, which comprised 4 stages (from level 1 to 4). In our study, level 1 and 2 were considered early AMD, level 3 was considered geographic atrophy (GA), and level 4 was considered NVAMD. Similarly, the Markov model for DR was modified according to the English National Screening Programme for Diabetic Retinopathy, which included non-sight-threatening DR (non-STDR), sight-threatening DR (STDR) and DME. Notably, because of incomplete data regarding unilateral and bilateral blindness, we combined the two stages, and defined blindness as presenting visual acuity <3/60 or visual field around central fixation <10% based on the better eye. During each cycle, an individual either stayed in the same state or transitioned to a more severe phase. Treatment could reduce the risk of progressing from one state to another. Relevant parameters such as the prevalence of AMD and DR, transition probability, compliance with screening and treatment, screening sensitivity, specificity, utility, and mortality were collected from published studies specific to China, other Asian counties’ studies, or unpublished data sources (such as
the National Committee for the Prevention of Blindness and the China Diabetic Retinopathy Screening and Prevention Project). Costs of screening, full examination, and treatment come from real-world eye disease screening programs, Beijing Tongren Hospital and unified pricing of Beijing Municipal Medical Insurance Bureau. The basic parameters and detailed ranges of fluctuations for the sensitivity analyses are listed in Appendix Tables 1–4.

Overview of screening strategies
No screening program. Patients did not receive a routine ophthalmic screening examination but might be opportunistically diagnosed and treated upon presenting at a hospital for another concern.

Traditional community screening. The entire study population aged 50 years or older living in this community was invited to participate in a combined AMD and DR screening program in local medical examination centers or community hospitals by trained volunteers or posters. All the participants underwent a series of detailed ophthalmic examinations by eye care professionals (optometrists, ophthalmic technicians and ophthalmologists). The examination process included: detailed medical history inquiry, vision acuity measurement, intraocular pressure measurement using a full auto tonometer, anterior segment examination through a slit lamp, and fundus photos with a nonmydriatic fundus camera. Finally, the ophthalmologist gave real-time diagnosis and referral recommendation. As a result, test positive patients were referred to tertiary hospitals or specialized ophthalmic hospitals for a detailed reexamination (the screening and referral pathway is shown in Appendix Figure 5). Those who were eventually diagnosed with AMD or DR were assumed to receive appropriate treatment and routine clinical care depending on the severity of the disease, antioxidant vitamins and zinc supplements were prescribed to patients with early AMD,17 patients with NVAMD or DME were treated with anti-VEGF drugs,18 scatter or panretinal photocoagulation was recommended for patients with STDR.19

Telemedicine screening. Residents aged 50 years or older were invited to participate in a combined AMD and DR telescreening program in primary medical institutions (local medical examination centers or community hospitals). All examination programs were performed by primary eye care staff (nurses or medical assistants). It included auto-optometry, intraocular pressure measurement, and anterior segment and fundus photography using a digital nonmydriatic retinal camera. When all the tests were done, data were timely transmitted to a high-level hospital telemedicine platform via a secured network system (in line with the standards of Health Insurance Portability or Accountability Act or Privacy Information Management System Certification). Then two trained graders assessed the severity of the retinal images. Subsequently, one ophthalmologist made final diagnosis and sent the assessment report back to the primary care settings. Participants usually came back to collect their assessment report in two days. The further management of positive subjects was the same as that described for traditional screening programs. Under telescreening system, ophthalmologists did not come to the community and examine the participants face to face, which greatly saved time and money. Therefore, we assumed that more participants could be detected during the same time span than traditional screening.

Prevalence and transition probabilities
We searched relevant studies on the epidemiology of AMD and DR in China published in the National Knowledge Infrastructure, Wanfang, PubMed, and Medline, using the following combined terms: “AMD” or “aged-related macular degeneration” or “diabetic retinopathy” or “DR” and “prevalence” or “epidemiology” and “China” or “Chinese”. The prevalence data were collected from large-scale epidemiological surveys of people over 50 years old in rural and urban China in the last few years. Transition probabilities took place over a 1-year cycle. In studies that reported multiyear incidences, the 1-year incidence was calculated using the formula $r = -\log(1 - p)/t$, where $r$ denoted the 1-year incidence, and $p$ represented the cumulative incidence over interval $t$.44 Most transition data were obtained from published studies specific to China (including Hong Kong); however, few data are available on the transition probabilities from one stage to the next stage for Chinese patients, several parameters were obtained from other Asian countries or unpublished data sources (the National Committee for the Prevention of Blindness and the China Diabetic Retinopathy Screening and Prevention Project).

Screening and intervention costs
Our study was analyzed from a societal perspective which included both direct and indirect costs. Direct medical care costs consisted of the charges related to screening, examination and treatment, direct non-medical care costs included costs of transposition, food and accommodation associated with visits to hospitals, indirect costs included components such as family members’ time associated with the visits and their wage loss. All of the costs were collected in Chinese yuan and converted into US dollars at an exchange rate of 6.705 yuan per dollar (2 November 2020). All data related to costs are listed in Table 1.

According to “Handan Eye and General Health Study” and “Beijing Tongren Eye Centre Ocular Reading Centre and China Intelligent Ophthalmology Big Data Research Centre”, the procedures of traditional
and telemedicine screening were defined. Screening costs included equipment purchase and maintenance costs, labour costs for medical personnel, and residents’ costs for transportation. The annualized cost for fixed assets was calculated by assuming a life span of 5 years and no salvage value and they were collected from the Finance Department and Procurement Center of Beijing Tongren Hospital. The construction and maintenance cost of the telemedicine platform came from Beijing Tongren Eye Centre Ocular Reading Centre and China Intelligent Ophthalmology Big Data Research Center. We assumed that under traditional screening mode, each patient’s visit time was 20 min, eye care professionals worked 8 h a day for 250 days a year, so about 20,000 patients were screened annually. In tele-screening mode, each patient was examined for 5 min by primary eye care staff, and a total of about 30,000 patients were screened annually. Since the participants were older than 50 years old, we assumed that they did not produce wage loss. Furthermore, the wage loss for accompanying family members were also not included in screening costs. The total costs per person for traditional screening were $2.79 and $2.64 in rural and urban settings, respectively, and the cost of telescreening in both settings was $1.52.

The detailed compositions of Screening costs are provided in Appendix Table 6.

For further thorough examination, direct medical costs included the costs of ophthalmic examinations, equipment and wage for medical personnel; direct non-medical costs included costs of transposition, food, accommodation associated with the visits; indirect costs consisted of one accompanying family member’s wage loss according to time spent and per capita daily income in rural and urban areas. The costs of full examination were collected from unified pricing of Beijing Municipal Medical Insurance Bureau and the health care costs were under the Chinese government’s control and varied little from institution to institution. Due to the different examination items, the costs for AMD and DR patients were slightly different. What’s more, we assumed that rural patients needed to spend more time and transportation costs to go to tertiary hospitals or specialized ophthalmic hospitals for examination than urban patients. The detailed compositions of hospital-based examination costs are provided in Appendix Table 7.

Initial and follow-up treatment costs varied according to the severity of the disease, and the costs for the medications and surgeries were obtained from Beijing Tongren Hospital. Patients with early AMD were treated with antioxidant vitamins and zinc supplements and had annual ophthalmoscopic examinations in subsequent years. Patients with NVAMD or DME received three anti-VEGF treatment in the first year, followed by annual outpatient review and necessary anti-VEGF treatment according to disease progression. Scatter or panretinal photocoagulation and annual examination and necessary anti-VEGF treatment were recommended for patients with STDR. We assumed that the total economic burden for blind patients in the first year was $8,920, including 53.2% of direct medical costs, 6.4% direct non-medical costs, and 40.4% indirect costs (loss of labour resources for family members, low-vision

|                      | Rural Treatment costs per person for the first year (US$) | Annual maintain costs per person in follow-up years (US$) | Urban Treatment costs per person for the first year (US$) | Annual maintain costs per person in follow-up years (US$) |
|----------------------|-----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
| Screening costs      | Traditional screening                                     | 2.79                                                     | NA                                                       | 2.64                                                     | NA                                                       |
|                      | Telemedicine screening                                    | 1.52                                                     | NA                                                       | a                                                        | NA                                                       |
| Full examination costs | Normal                                                   | 176.29                                                   | NA                                                       | 62                                                       | NA                                                       |
|                      | AMD                                                      | 216.29                                                   | NA                                                       | 102                                                      | NA                                                       |
|                      | DR                                                      | 226.29                                                   | NA                                                       | 112                                                      | NA                                                       |
| Treatment costs      | Early AMD                                                | 347.14                                                   | 130                                                      | 111.43                                                   | 51.43                                                   |
|                      | NVAMD                                                    | 2,338.29                                                 | 774.71                                                   | 2,102.57                                                 | 698.71                                                   |
|                      | STDR                                                     | 2,638.29                                                 | 784.71                                                   | 2,402.57                                                 | 708.71                                                   |
|                      | DME                                                      | 2,338.29                                                 | 784.71                                                   | 2,102.57                                                 | 708.71                                                   |
|                      | Blindness                                                | 8,920                                                    | 3,603.68                                                 | a                                                        | a                                                        |

Table 1: Costs of AMD and DR related screening, full examination and treatment in rural and urban settings.

AMD=age related degeneration. DR=diabetic retinopathy. NVAMD=neovascular AMD. STDR=sight-threatening DR. DME= diabetic macular edema. NA=not applicable.
a=same with the rural setting.

Costs are given in US dollars.

* Detailed calculations on screening costs can be found in Appendix Tables 6—9.

www.thelancet.com Vol 23 Month June, 2022 5
services costs like modification costs, etc., and there were only indirect costs in follow-up years. Since we considered the societal costs of medical care, specific reimbursement rates were not relevant. The detailed compositions of treatment costs are provided in Appendix Tables 8 and 9.

Utilities and quality-adjusted life-years
To calculate quality-adjusted life-years (QALYs), we estimated utilities for each stage. The utility values were based on several published economic studies specific to China or other Asian countries such as Japan and India. Utilities were assumed to be 1 for participants without AMD and DR, 0.97 for those with early AMD, 0.85 for those with GA, and 0.7 for those with NVAMD. Patients with non-STDR were assumed to have a utility value of 0.87, and patients with DME and STDR were assumed to have utility values of 0.83 and 0.7, respectively. Patients with blindness were assumed to have a utility value of 0.26. All of the values for the base and sensitivity analyses are shown in Appendix Table 3.

Other parameters
Screening sensitivities and specificities at different stages, compliance with participating community screening, and adherence to referral to the hospital for definitive examination and treatment were collected from previous studies. We first used data from studies conducted in China and then considered data from other countries with similar conditions to China. A recent Chinese study suggested that telescreening could improve patients’ satisfaction and compliance to screening. Since compliance with traditional community screening was 90–97% in rural settings and 82–95% in urban settings, we assumed increases in compliance with telemedicine screening to 95% and 96% in rural and urban settings, respectively. Since the role of telescreening was to widely screen patients who may have diseases in the population, the sensitivities of tele-screening were the same as or higher than those of face-to-face screening but that the specificity was still lower than that of traditional screening. Natural mortality could occur at any stage in our model, and we used natural age-specific mortality rates. Moreover, we considered the increased odds of mortality for patients with severe disease.

In our study, both costs and utility values were discounted at 3.5% per annum in the base-case analysis. In terms of the cost-effectiveness threshold, the WHO defined interventions that cost less than the per capita gross domestic product (GDP) as highly cost-effective, interventions that cost between one to three times the per capita GDP as cost-effective, and interventions that cost more than three times the per capita GDP as not cost-effective. We calculated the per capita GDP for rural ($7,000) and urban ($12,000) China in 2020 according to the overall per capita national GDP ($10,137.98), urbanization rate (0.61), and urban-rural ratio (2.64) of per capita disposable income (The detailed calculations are shown in Appendix Figure 1). We assumed a willingness to pay (WTP) of $21,000 per QALY gained for rural settings and $36,000 per QALY gained for urban settings.

Main outcomes
The main outcomes were ICURs and ICERs, calculated using the following formulas:

$$ICURs = \frac{\text{incremental cost}}{\text{quality adjusted life years gained}}$$

$$ICERs = \frac{\text{incremental cost}}{\text{years of blindness avoided}}$$

Sensitivity analysis
We performed extensive 1-way deterministic and simulated probabilistic sensitivity analyses to account for the uncertainties of ICURs and ICERs. Probability-related data (i.e., prevalence, utility, sensitivity, specificity, compliance, and transition probability) were mostly derived from previously published literature, a change of 10% was therefore used. In terms of costs, the majority of treatment-related costs were provided by China’s real eye disease screening program and tertiary hospitals, so a floating range of 20% was adopted. Since the specific composition of eye disease screening programs varied from region to region and costs for blind people were drawn from previous literature, we allowed these uncertain parameters to vary within a large floating range (50%). The widths of the bars in the tornado diagrams represent the 5 factors that had the greatest influence on ICURs. A probabilistic sensitivity analysis enabled uncertainty across all of the variables to vary simultaneously. It was evaluated by taking 10,000 random draws from the probability distribution of each parameter, and the upper and lower bounds used in the 1-way probabilistic sensitivity analysis were used to define the distribution parameters. The reporting of methods and results conformed to the Consolidated Health Economic Evaluation Reporting Standards (Appendix Table 10).

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.
Results

The cost-utility analysis showed that programmatic combined AMD and DR screening was highly cost-effective in both rural and urban China. Under the status quo, the total expected medical cost for a 50-year-old patient with AMD or DR was $869.59, and the total expected QALYs gained were 16.06952 over the next 30 years in rural settings; the figures for urban environments were $1,514.18 and 15.70452, respectively. In rural settings, although combined screening required extra financial investment, it was very cost-effective since traditional screening resulted in a gain of 1 QALY at a cost of $191 (95% CI: $66 to $239), and telescreening resulted in a gain of 1 QALY at a cost of $199 (95% CI: $-12 to $217) compared with no screening. Even more incredible, screening for AMD and DR with either traditional screening or telescreening resulted in fewer costs and more QALYs than no screening in urban areas, indicating that combined AMD and DR screening dominated no screening in urban settings (Table 2).

Parallel to the cost-utility analysis, the cost-effectiveness analysis reached a similar conclusion. In rural areas, to avoid a year of blindness, the costs were $2,436 (95% CI: $1,089 to $3,254) and $2,441 (95% CI: $1,452 to $3,900) for traditional and telemedicine screening, respectively, satisfying the criteria for a highly cost-effective health intervention. Moreover, both traditional and telemedicine screening dominated no screening in urban areas since ICERs were negative (Table 2).

Extensive sensitivity analyses were performed to test the robustness of our model outcomes. The base-case results were not sensitive to the broad range of parameter values that we set in the model, and the ICURs were consistently within one time the per capita GDP for rural and urban settings. The tornado diagram shows the 5 parameters that had the greatest impact on the results. In our study, the cost and utility of early and advanced stages, transition from early stage to advanced stage, and specificity of different screening strategies were common parameters in most scenarios (Figure 1).

The probabilistic sensitivity analysis showed that the base-case ICURs were robust to randomly distributed parameters in both rural and urban environments. Under the current WTP threshold, both screening strategies were cost-effective in more than 90% of the simulations (Figure 2).

By taking 10,000 random draws, we got the cost-effectiveness acceptability curves (Figure 3). It meant that when both traditional screening and telescreening were available, telemedicine screening was the dominant strategy in 71.2% of simulations in urban areas ($36,000) and 65.6% of simulations in rural areas ($21,000) under the current WTP threshold.

We also evaluated the related economic indicators for different screening intervals to recommend the most cost-effective screening strategy for Chinese policy

| Costs per person, $ | QALYs per person | Years of blindness avoided per 100,000 people screened, $ | Years of blindness per person | ICURs (95% CI), $ | ICERs (95% CI), $ |
|---------------------|------------------|----------------------------------------------------------|--------------------------------|------------------|------------------|
| Rural setting       |                  |                                                          |                                |                  |                  |
| No screening        | 869.59           | 16.06952                                                 | 0.17269                        | 191 (95% CI: 66 to 239) |
| Traditional screening | 877.67         | 16.11751                                                | 1.023176                       | 199 (95% CI: -12 to 217) |
| Telemedicine screening | 878.12        | 16.1233                                                 | 1.033326                       | 201 (95% CI: -12 to 217) |
| Urban setting       |                  |                                                          |                                |                  |                  |
| No screening        | 1,514.18         | 15.70452                                                | 0.17269                        | 191 (95% CI: -12 to 217) |
| Traditional screening | 1,501.76       | 15.70994                                                | -1,242,326                     | Dominating       |                  |
| Telemedicine screening | 1,500.87     | 15.73984                                                | -1,331,737                     | Dominating       |                  |

Table 2: Base-case cost-utility and cost-effectiveness results from AMD and DR combined screening programs.

AMD=age-related macular degeneration. DR=diabetic retinopathy. QALY=quality-adjusted life-year. ICUR=incremental cost-utility ratio. ICER=incremental cost-effectiveness ratio. CI=confidence interval. Costs, QALYs, and years of blindness are defined as lifetime values per person, whereas incremental costs, incremental QALYs, ICURs, ICERs, and years of blindness avoided are defined as values per 100,000 people screened. Negative ICURs and ICERs are regarded as dominating.
Figure 1. Deterministic 1-way sensitivity analysis. Costs are given in US dollars. The top 5 parameters that caused the greatest impact on ICURs are shown in above figures. We did 1-way sensitivity analyses for rural (a-b) and urban (c-d) settings respectively, and for traditional (a and c) and telemedicine (b and d) screening respectively. The intervention was defined as cost-effective if it cost less than $21,000 in rural areas (per-capita GDP $7,000) and less than $36,000 in urban areas (per-capita GDP $12,000). GDP=gross domestic product. ICUR=incremental cost-utility ratio. QALY=quality-adjusted life-years. STDR=sight-threatening diabetic retinopathy. AMD=age related degeneration. GA=geographic atrophy. NVAMD=neovascular AMD. DME=diabetic macular edema.
Figure 2. Probabilistic sensitivity analysis of the incremental costs and incremental QALYs. Costs are given in US dollars. Incremental benefits are defined as incremental QALYs. We did probabilistic sensitivity analyses for rural (a-b) and urban (c-d) settings respectively, and for traditional (a and c) and telemedicine (b and d) screening respectively. Dashed and solid lines represent one-time and three-times GDP, respectively. QALY= quality-adjusted life-year. GDP= gross domestic product.
makers. In rural settings, all of these acceptable strategies (from every 1 to 5 years) were likely to be cost-effective, since ICERs were between $8,099 and $10,097 for traditional screening and between $8,124 and $10,060 for telemedicine screening. All screening intervals were highly cost-effective in urban settings, and ICERs were between $2,629 and $4,355 for traditional screening and between $2,415 and $5,055 for telemedicine screening. As screening intervals became more intensive, the cost increased, but the number of years of blindness decreased, which meant annual screening was the best scenario in both rural and urban areas (735 and 773 years of blindness were avoided for 100,000 participants for traditional and telemedicine screening in rural settings separately; 1,039 and 1,057 years of blindness were avoided for 100,000 participants for traditional and telemedicine screening in urban settings separately) (Table 3).

To determine the optimal screening strategies, we also evaluated the costs and benefits of telemedicine screening versus traditional screening. For all acceptable screening intervals, telemedicine screening resulted in greater decreases in the number of years of blindness, and annual telescreening avoided the most years of blindness per 100,000 people screened than traditional screening (119 and 270 years in rural and urban settings, respectively). Since the ICERs were always less than three times the per capita GDP in rural areas (between $2,559 and $8,809) and one time the per capita GDP in urban areas (less than $5,564), annual telescreening was the best screening strategy in both rural and urban China (Appendix Table 12).

Discussion

The results of our study show that population-based combined AMD and DR screening using either a traditional or telemedicine approach was highly cost-effective in rural and urban China, and annual screening avoided the most years of blindness. Since telescreening yielded the most effectiveness compared with traditional screening, it was the best option under the current WTP threshold. In broad sensitivity analyses, our results were robust and insensitive to a wide range of changes in parameters.

Although there has been a great increase of economic studies on eye diseases screening in ophthalmology, most of them were cost-effectiveness analyses of DR screening. Previous studies have shown that systematic DR screening, especially telemedicine screening, was a cost-effective strategy for diabetic population in both high- and low-income countries. A recent economic study in China also confirmed that DR screening for patients with newly diagnosed type 2 DM was cost-effective at an ICER of $7,312 per QALY. However, it is difficult to determine whether screening for AMD would be cost-effective.
| Screening Interval | Costs per person, $ | Years of blindness per person | Years of blindness avoided per 100,000 people screened | ICERs, $ | Costs per person, $ | Years of blindness per person | Years of blindness avoided per 100,000 people screened | ICERs, $ |
|--------------------|---------------------|-------------------------------|-----------------------------------------------|---------|---------------------|-------------------------------|-----------------------------------------------|---------|
|                     | Rural               |                               |                                               |         | Urban               |                               |                                               |         |
|                     | 877.67              | 0.16938                       |                                               |         | 9,141               | 1,501.76                      | 0.23                                           |         |
| Every 5 years       | 907.47              | 0.16612                       | 326                                           | 9,141   | 1,526.07            | 0.22389                       | 611                                           | 3,979   |
| Every 4 years       | 916.86              | 0.16519                       | 93                                            | 10,097  | 1,532.77            | 0.22204                       | 185                                           | 3,622   |
| Every 3 years       | 929.09              | 0.16368                       | 151                                           | 8,099   | 1,540.29            | 0.21918                       | 286                                           | 2,629   |
| Every 2 years       | 954.57              | 0.16082                       | 286                                           | 8,909   | 1,556.31            | 0.21424                       | 494                                           | 3,243   |
| Every 1 year        | 1,023.69            | 0.15347                       | 735                                           | 9,404   | 1,601.56            | 0.20385                       | 1,039                                         | 4,355   |
| Telemedicine screening | 878.12             | 0.1692                        |                                               |         | 1,500.87            | 0.22866                       |                                               |         |
| Every 5 years       | 910.15              | 0.16568                       | 352                                           | 9,099   | 1,531.31            | 0.22188                       | 678                                           | 4,490   |
| Every 4 years       | 920.21              | 0.16468                       | 100                                           | 10,060  | 1,535.97            | 0.21995                       | 193                                           | 2,415   |
| Every 3 years       | 933.29              | 0.16307                       | 161                                           | 8,124   | 1,544.58            | 0.2169                        | 305                                           | 2,823   |
| Every 2 years       | 960.49              | 0.16002                       | 305                                           | 8,918   | 1,563.15            | 0.21172                       | 518                                           | 3,585   |
| Every 1 year        | 1,034.14            | 0.15229                       | 773                                           | 9,528   | 1,616.58            | 0.20115                       | 1,057                                         | 5,055   |

Table 3: Cost-effectiveness of different screening intervals in rural and urban settings.
ICER=incremental cost-effectiveness ratio. Costs are given in US dollars. Costs and years of blindness are defined as lifetime values per person, whereas years of blindness avoided and ICERs are defined as values per 100,000 people. ICERs are calculated per 100,000 people screened against the previous screening interval scenario.
Kingdom, South Korea and Hong Kong have concluded that AMD screening was cost-effective. But one study in Japan pointed that although AMD screening was highly effective in reducing the total number of patients with blindness, and early screening programs were more effective than complementary therapy, AMD screening was still not cost-effective because the ICER exceeded the WTP threshold in Japan. In addition, few studies have explored the cost-effectiveness of AMD screening or combined screening for different eye diseases in mainland China.

Our study found that combined screening for AMD and DR might be very cost-effective in rural and urban China for several possible reasons. First, China’s national conditions are different from those of other countries. Due to the aging of the population and changes in lifestyle, uneven allocation of medical resources between urban and rural areas, and insufficient attention paid to blindness-causing eye diseases, each additional screening had the potential to detect more patients with early stage AMD, DR, or both. Secondly, due to the low detection rate and high blindness rate of AMD and DR, early detection and timely treatment can delay the development of the disease to the severe stage and reduce the economic burden on the government and individuals. Third, although foreign studies generally believe that early AMD screening is not cost-effective, combined AMD and DR screening does not add additional costs, which means that combined screening may be cost-effective in China. Forth, combined screening might be cheaper in China, largely because China’s labor costs are lower than those of high-income countries.

In terms of screening intervals, annual screening for people aged 50 years old or older was the optimal choice in our study. It could not only detect the early stages of blindness-causing diseases and slow their progression with treatment but also offered additional benefits, such as allowing glaucoma, cataracts and other blindness-causing diseases to receive earlier medical attention. The guidelines of many countries recommend annual ophthalmic examinations for patients with DM. Many developed countries, such as the United Kingdom, found that annual screening or more frequent screening for those with background DR could save up to 50% of the potential sight years lost. In contrast, a recent study in mainland China demonstrated that screening every 4 years produced the greatest increase in QALYs, while the marginal cost resulted in ICERs of annual screening exceeding the WTP threshold. Similarly, another cost-effectiveness analysis of DR screening in the United States suggested that the marginal benefit offered by annual screening for the entire United States population was so small that annual screening may be overzealous and unnecessary. Considering the current situation, Wu et al. and Vijan et al. recommended that screening strategies should be adjusted according to the patient’s risk factors, such as the age at DM diagnosis and glycemic control. When patients were diagnosed with DM at an age <40 years, screening every 3 years was cost-effective. When they were diagnosed over the age of 60 years, a strategy of screening every 6 years or more could be applied.

In view of the differences in epidemiology and economics between rural areas and cities, we made economic analysis of different screening strategies in rural and urban settings respectively. The results showed that tele-screening was more cost-effective. When considering different screening intervals, the ICER of tele-screening in rural areas was always less than three times the per capita GDP, and that in urban areas was less than one time the per capita GDP. The reasons why telemedicine-based screening was cost-effective are as follows. On the one hand, tele-screening has the potential to make nationwide screening a reality because of China’s vast territory, large population, inconvenient transportation and insufficient medical resources in remote areas, and large workforce of manpower for traditional screening. On the other hand, tele-screening can reduce transportation costs and time-related wage losses, thus reducing the individuals’ out-of-pocket costs. In China, urban residents pay more attention to general eye health and are more willing to receive regular ophthalmic examination. Although urban residents can access to tertiary settings for eye check-ups without referral through primary settings, the long waiting time and fast-paced work often prevent them from going to the hospitals regularly. The convenient and time-saving characteristics of tele-screening enable it to meet the high-quality requirements of residents for general eye health.

With the rapid advances in digital technology, artificial intelligence (AI) and 5G wireless systems, telemedicine has been introduced in ophthalmology, and the COVID-2019 pandemic has accelerated the development and adoption of these technologies. For instance, real-time video consultations between hospital-based ophthalmologists and emergency physicians or other specialists can help emergency patients get timely evaluations and referrals, improving diagnostic accuracy. What’s more, the development of self-screening and home monitoring based on smartphones is a convenient and real-time tele-screening mode that can improve patient compliance and achieve regular monitoring of disease progression. In recent years, China has gradually implemented some DR screening programs. For example, the telemedicine-based “China Diabetic Retinopathy Screening and Prevention Project”, organized by the National Committee for the Prevention of Blindness and the Chinese Society of Microcirculation, has covered 577 hospitals in 29 provinces and screened more than 800,000 diabetes patients. Actually, the Chinese government not only pays attention to eye disease screening, but also strives...
to build a complete chronic eye disease management system. Chronic eye disease management is a patient-centered chronic disease management system that follows timely, coordinated, continuous, safe and effective mode. However, there are still many deficiencies in the management of chronic eye diseases in China. One the one hand, the working mechanism of chronic eye disease prevention and control led by the government and participated of the whole society has not been completely established. On the other hand, the implementation of the national basic medical insurance policy in different provinces is not equal. In the future, it is necessary to establish a complete telemedicine-based chronic eye diseases diagnosis and treatment system that includes screening, referral, treatment and follow-up, and promote equitable distribution of health resources. We referred to the relevant literature and proposed a process for telemedicine-based chronic eye disease management system in the future.17,18 (Appendix Figure 14).

In order to successfully implement telescreening programs in China, the government must step up publicity efforts. First, it is important to educate the public on the importance of early screening and treatment for blindness causing eye diseases through the Internet, radio broadcasts and lectures. Second, the government needs to deepen residents’ understanding and acceptance of telescreening through various means. The acceptance of telescreening increased only when residents became aware of the additional benefits caused by this novel screening mode, such as time and “out-of-pocket” money savings. Third, the increasing attention to information security and personal privacy and clinicians’ fear of malpractice liability or resistance to change are also important reasons to hamper the adoption of telemedicine.14 Therefore, the government needs to constantly improve network security protection system and related policies to ensure residents’ information security well protected.

This study has various strengths. First, to the best of our knowledge, this is the first study to analyze the costs and effectiveness of AMD and DR combined screening programs and compare the cost-effectiveness of traditional face-to-face community screening and telemedicine screening using a Markov model. Second, all of the parameters used in the models were from reliable real-world studies. As such, our findings provide practical recommendations for governments and policy makers in China and might also be applicable to other low- and middle-income countries where blindness-causing eye diseases are prevalent and regular screening programs are lacking. Third, considering the uneven distribution of the population and medical resources in China and the different incidences of diseases in rural and urban areas, we developed models and analyzed the cost-effectiveness for rural and urban settings separately. Fourth, due to the rapid aging of the population and changes in people’s living habits, metabolic and age-related eye diseases are gradually becoming the main source of eye disease burden in China. Therefore, we extended the target population to all Chinese residents over 50 years old, not just those with DM, with the aim of detecting not only eye diseases but also improving the timely diagnosis and treatment of metabolic diseases.

Nonetheless, our study has several limitations. First, we assumed that AMD and DR would not be present in one person at the same time because there is no absolute evidence that the progression of AMD and DR affect each other. If a patient presents both AMD and DR at the same time, the utility, transition and costs of hospital examination and subsequent treatment might be different from the status quo.10 Second, to better describe the disease progression more clearly, we simplified the national disease grading system according to the actual situation. Third, the additional benefits of combined screening, such as detection and treatment of other common blindness-causing diseases, were not considered in our study. Fourth, due to gaps in the existing literature, we used some parameters from non-Chinese studies or expert advice from the National Committee for the Prevention of Blindness. However, extensive sensitivity analyses showed that our results were robust and insensitive to wide range fluctuation of parameters.

We believe that combined screening for multiple blindness-causing eye diseases might be more cost-effective and ideal for clinical application, and it has the potential to become the main trend of eye disease screening programs in the future. Therefore, health economic studies should be conducted to evaluate the cost-effectiveness of multimodal screening for common blindness-causing eye diseases (i.e., glaucoma, DR, AMD, retinal detachment and other retinal diseases), which could provide adequate evidence for health care providers and policymakers. In addition, the impact of gender, age groups, economic and medical level in different regions on cost-effectiveness should also be taken into consideration.

Conclusion

In conclusion, combined population-based screening for AMD and DR in rural and urban Chinese populations aged 50 years or older might be highly cost-effective, and telemedicine screening could be the best strategy in China. Our research provides a reference for the government and policy makers to use to support the implementation of large-scale eye disease screening programs in the future.

Contributors

Conception and design: Hanruo Liu, Ningli Wang, Jianjun Tang.
Acquisition or interpretation of data: Ruyue Li, Ziwei Yang, Yue Zhang, Weiling Bai. Runzhou Sun, Yifan Du.

Drafting of the manuscript: Ruyue Li.

Critical revision of the manuscript for important intellectual content: Hanruo Liu, Ningli Wang, Jianjun Tang.

Statistical analysis: Ruyue Li, Ziwei Yang.

Obtained funding: Hanruo Liu.

Supervision: Hanruo Liu, Ningli Wang, and Jianjun Tang had accessed and verified data. Hanruo Liu, Ningli Wang, and Jianjun Tang were responsible for the decision to submit the manuscript.

Data sharing statement
The parameters that we used in our model (text, tables, figures, models, and appendices) are available on reasonable request from the corresponding author (Hanruo Liu: hanruo.liu@hotmail.com) under certain conditions (with the consent of all participating centers and with a signed data access agreement).

Financial support
National Natural Science Foundation of China, NSFC (82171051); the Major Innovation Platform of Public Health & Disease Control and Prevention, Renmin University of China and Beijing Nova program (Z19110001119072).

Declaration of interests
The authors declare no conflicts of interest.

Acknowledgements
No.

Supplementary materials
Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2022.100435.

References
1. GRB 2019 Blindness and Vision Impairment Collaborators; Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the global burden of disease study. Lancet Glob Health. 2021;9:e144-e160.
2. Chan CK, Gangwani RA, McGhee SM, et al. Cost-effectiveness of screening for intermediate age-related macular degeneration during diabetic retinopathy screening. Ophthalmology. 2015;122:2278-2285.
3. Thomas RL, Winfield TG, Prettyjohns M, et al. Cost-effectiveness of biennial screening for diabetes related retinopathy in people with type 1 and type 2 diabetes compared to annual screening. Eur J Health Econ. 2020;21:993-1002.
4. Rachapalle S, Legood R, Alavy Y, et al. The cost-utility of telemedicine to screen for diabetic retinopathy in India. Ophthalmology. 2013;120:566-573.
5. Song P, Du Y, Chan KY, et al. The national and subnational prevalence and burden of age-related macular degeneration in Japan. J Glob Health. 2017;7:020703.
6. Wang L, Gao P, Zhang M, et al. Prevalence and ethnic pattern of diabetes and prediabetes in China in 2015. JAMA. 2017;317:2351-2359.
7. Xu T, Wang B, Liu H, et al. Prevalence and causes of vision loss in China from 1990 to 2019: findings from the global burden of disease study 2019. Lancet Public Health. 2020;5:e682-e693.
8. Wu B, Li J, Wu H. Strategies to screen for diabetic retinopathy in Chinese patients with newly diagnosed type 2 diabetes: a cost-effectiveness analysis. Med (Baltim). 2015;9:e1989.
9. Ra H, Song LD, Choi JA, et al. The cost-effectiveness of systematic screening for age-related macular degeneration in South Korea. PLoS One. 2018;13:e0206590.
10. Tamura H, Goto R, Akune Y, et al. The clinical effectiveness and cost-effectiveness of screening for age-related macular degeneration in Japan: a markov modeling study. PLoS One. 2015;10:e0135628.
11. Ting DSW, Cheung CY, Lim G, et al. Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. JAMA. 2021;325:2141-2152.
12. Tang J, Jiang Y, O’Neill C, et al. Cost-effectiveness and cost-utility of population-based glaucoma screening in China: a decision-analytic Markov model. Lancet Glob Health. 2019;7:e698-e708.
13. Klein R, Davis MD, Magli YL, et al. The Wisconsin age-related maculopathy grading study. Ophthalmology. 1991;98:1128-1134.
14. Bird AC, Bressler NM, Bressler SB, et al. An international classification and grading system for age-related maculopathy and age-related macular degeneration. The international Airm epidemiological study group. Surv Ophthalmol. 1995;39:367-374.
15. Seddon JM, Sharma S, Adelman RA. Evaluation of the clinical age-related maculopathy staging system. Ophthalmology. 2006;113:260-266.
16. Harding S, Greenwood R, Aldington S, et al. Grading and disease management in national screening for diabetic retinopathy in England and Wales. Diabet Med. 2002;19:965-971.
17. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol. 2001;119:1417-1436.
18. Tah V, Orlins HO, Hyer J, et al. Anti-VEGF therapy and the retina: an update. J Ophthalmol. 2015;2015:627674.
19. Wong TY, Sun J, Kawasaki R, et al. Guidelines on diabetic eye care: the international copharmacology recommendations for screening, follow-up, referral, and treatment based on resource settings. Ophthalmology. 2018;125:1608-1622.
20. Ullah W, Pathan SR, Panchal A, et al. Cost-effectiveness and diagnostic accuracy of telemedicine in macular disease and diabetic retinopathy: A systematic review and meta-analysis. Med (Baltim). 2020;99:e20306.
21. Jin G, Ding X, Xiao W, et al. Prevalence of age-related macular degeneration in rural southern China: the Yangxi Eye Study. Br J Ophthalmol. 2018;102:623-630.
22. Ye H, Zhang Q, Liu X, et al. Prevalence of age-related macular degeneration in an elderly urban Chinese population in China: the jiangning eye study. Invest Ophthalmol Vis Sci. 2014;55:6174-6180.
23. Jin G, Xiao W, Ding X, et al. Prevalence of and risk factors for diabetic retinopathy in a rural Chinese population: the Yangxi eye study. Invest Ophthalmol Vis Sci. 2018;59:5067-5073.
24. Zhang W, Wei M. The evaluation of the mortality and life expectancy of Chinese population. Popul J. 2016;38:13-28.
25. Huthuesy R, Chisholm D, Edejer TT. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. Cost Eff Resour Alloc. 2003;1:8.
26. Ben AJ, Neyeloff JL, de Souza CJ, et al. Cost-utility analysis of opportunistic and systematic diabetic retinopathy screening strategies from the perspective of the Brazilian public healthcare system. Appl Health Econ Health Policy. 2020;18:57-68.
27. Romero-Aroca P, de la Riva-Fernandez N, Valls-Mateu A, et al. Cost of diabetic retinopathy and macular oedema in a population, an eight year follow up. BMC Ophthalmol. 2016;16:35.
28 Nguyen HV, Tan GS, Tapp RJ, et al. Cost-effectiveness of a national telemedicine diabetic retinopathy screening program in Singapore. *Ophthalmology*. 2016;123:1271–1282.

29 Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. *JAMA*. 2000;283:889–896. https://doi.org/10.1001/jama.283.7.889.

30 Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet*. 2010;376:124–136.

31 Corcóstegui B, Durán S, González-Albarrán MO, et al. Update on diagnosis and treatment of diabetic retinopathy: a consensus guideline of the working group of ocular health (Spanish society of diabetes and Spanish vitreous and retina society). *J Ophthalmol*. 2017;2017:841486.

32 Davies R, Roderick P, Canning C, et al. The evaluation of screening policies for diabetic retinopathy using simulation. *Diabet Med*. 2002;19:762–770.

33 Lian JX, Gangwani RA, McGhee SM, et al. Systematic screening for diabetic retinopathy (DR) in Hong Kong: prevalence of DR and visual impairment among diabetic population. *Br J Ophthalmol*. 2016;100:151–155.

34 Lian J, McGhee SM, Gangwani RA, et al. Awareness of diabetic retinopathy and its association with attendance for systematic screening at the public primary care setting: a cross-sectional study in Hong Kong. *BMJ Open*. 2018;8:e019989.

35 Maa AY, Medert CM, Lu X, et al. Diagnostic accuracy of technology-based eye care services: the technology-based eye care services compare trial part I. *Ophthalmology*. 2020;127:88–44.

36 Wilson JM, Janguey YG. *Principios y Métodos del Examen Colectivo Para Identificar Enfermedades [Principles and Practice of Mass Screening for Disease]*. 65. Bol Oficina Sanit Panam; 1968:281–393.

37 Chen H, Pan Y, Yang J, et al. Application of 4G technology to conduct real-time telesurgical laser photoagulation for the treatment of diabetic retinopathy. *JAMA Ophthalmol*. 2021;139(3):375–382.

38 Li JO, Liu H, Ting DSJ, et al. Digital technology, tele-medicine and artificial intelligence in ophthalmology: a global perspective. *Prog Retin Eye Res*. 2021;82:100980.

39 Age-Related Eye Disease Study Research Group. The age-related eye disease study system for classifying age-related macular degeneration from stereoscopic color fundus photographs: the age-related eye disease study report number 6. *Am J Ophthalmol*. 2001;132(4):668–681.

40 UK National Screening Committee. *Essential Elements in Developing a Diabetic Retinopathy Screening Programme*. National Screening Programme for Diabetic Retinopathy. Workbook 4.3. England: National Health Service; 2009.

41 Rothman KJ. *Epidemiology: An Introduction*. 2nd ed. New York, NY: Oxford University Press; 2012.

42 Peng J, Zou H, Wang W, et al. Implementation and first-year screening results of an ocular telehealth system for diabetic retinopathy in China. *BMC Health Serv Res*. 2011;11:250.

43 Thomas S., Hodge W., Malvankar-Mehta M. The cost-effectiveness analysis of teleglaucoma screening device. *PLoS One*. 2011;6(9):e2137913.

44 Walsh L, Hong SC, Chalakkal RJ, et al. A systematic review of current teleophthalmology services in New Zealand compared to the four comparable countries of the United Kingdom, Australia, United States of America (USA) and Canada. *Clin Ophthalmol*. 2021;15:4015–4027.

45 Lai KFW, Lee RPW, Yiu EPF. Ultrawide-field retinal selfie by smartphone, high-definition television, and a novel clip-on lens. *Ophthalmology*. 2018;125(7):1027.

46 Briggs AH. Handling uncertainty in cost-effectiveness models. *PharmacoEconomics*. 2000;17(6):579–590.

47 Hopley C, Salkeld G, Wang JJ, et al. Cost utility of screening and treatment for early age related macular degeneration with zinc and antioxidants. *Br J Ophthalmol*. 2004;88(4):450–454.