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Cost-effectiveness of screening for amblyopia among kindergarten children in China

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ABSTRACT

Objective: Current cost-effectiveness analyses of amblyopia screening are mainly from western countries. It remains unclear whether it is cost-effective to implement a preschool amblyopia screening programme in China. Our study aimed to evaluate the cost-effectiveness of a hypothetical kindergarten-based amblyopia screening versus non-screening among 3-year-old children.

Methods: We developed a decision tree combined with a Markov model to compare the cost and effectiveness of screening versus non-screening for 3-year-old children from a third-party payment perspective. The primary outcomes were quality-adjusted life years (QALYs) and the incremental cost-effectiveness ratio (ICER). Costs were obtained from expert opinions in different regions of China. Transition probabilities and health utilities were mainly based on published literature and open sources. Sensitivity analyses were performed to assess the impact of parameters' uncertainty on results.

Results: Base-case analysis demonstrated that the ICER of screening versus non-screening was $17,466/QALY, well below the WTP threshold ($38,223/QALY) for China. One-way sensitivity analysis showed that the prevalence of amblyopia, the transition probability per year from untreated amblyopia to healthy, and the discount rate were the top three factors. The likelihood of cost-effectiveness of screening compared with non-screening was 92.56%, according to probabilistic sensitivity analysis. Scenario analysis also indicated that ICER was lower than the WTP threshold even if the time horizon was shortened or the screening was delayed to the age of 4 or 5.

Conclusions: Amblyopia screening could be considered a cost-effective strategy compared to non-screening for 3-year-old children in China. Screening for children at the age of 4 or 5 may even yield better results.

1. Introduction

Amblyopia is a common pediatric vision deficit attributed to inadequate visual experience or abnormal binocular interaction during the sensitive period of visual development, causing abnormalities in the function and structure of the visual cortex (Birch, 2013). Amblyopia mostly manifests as reduced vision in one eye, and the risk of lifetime bilateral visual impairment (VI) is almost double for children with unilateral amblyopia because of the increased risk of damage to the healthy eye (Tailor et al., 2016). Epidemiological surveys show that the prevalence of amblyopia among preschool children is about 1.09 %–4.83 % in China (Pi et al., 2012, Li et al., 2019, Wang et al., 2022). The optimal time to treat amblyopia is during the sensitive stage of visual development, which is also the risk period for its onset. Once the optimal treatment period is missed, it will cause irreversible damage to the child's vision. Moreover, it will be difficult to completely restore visual

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function even if treated, resulting in a burden to both the individuals and society (Hsieh et al., 2022).

Due to the fact that many children with amblyopia do not exhibit strabismus, their parents often overlook the condition. Coupled with a lack of comparative visual experience, it is difficult for the children to recognize the presence of amblyopia unless they undergo screening. Early detection of amblyopia or its related risk factors is the key to amblyopia treatment (Repka et al., 2023). Thus, attention should be paid to amblyopia screening in preschool children. A previous meta-analysis also showed that amblyopia treatment outcomes were better in children aged 3–7 years than in those aged 7–13 years (Holmes et al., 2011). Moreover, it is also important to assess the cost-effectiveness of the screen programme considering the large number of affected children and the limited health resources. Current cost-effectiveness analyses of amblyopia screening are mainly from western countries, suggesting it is likely to be cost-effective compared with non-screening or standard care for children aged 3 to 5 years (König and Barry, 2004a, Rein et al., 2012, Heijnsdijk et al., 2022, König and Barry, 2004b). According to current literature, the long-term effect of amblyopia on quality of life or life outcomes may be small. In such cases, screening may not be cost-effective (Carlton et al., 2008). Meanwhile, the treatment process itself may be difficult and distressing, and the evidence regarding its utility remains limited. Hence, the current evidence on health utility due to amblyopia screening still carries uncertainty (Guimaraes et al., 2022), which may underestimate the cost-effectiveness of screening programs. On the other hand, their findings may not be generalized to the Chinese context given the substantial differences in disease profile and healthcare system between China and western countries.

At present, screening for amblyopia in Chinese children is mainly carried out in certain large and medium-sized cities, while less is done in undeveloped and rural areas. Previous studies have indicated that screening programmes for amblyopia in young children can achieve high detection and referral rates at comparatively low cost (Arnold et al., 2005, Longmuir et al., 2010). However, it remains unclear whether it is an economically attractive strategy to implement a preschool amblyopia screening programme in China. Hence, the study aims to evaluate the cost-effectiveness of a hypothetical kindergarten-based amblyopia screening programme versus non-screening among 3-year-old children to inform resource allocation decisions in health care in China.

2. Materials and methods

2.1. Study design

The United States Preventive Services Task Force (USPSTF) recommends screening all children 3 to 5 years of age at least once. Nevertheless, there is insufficient evidence on the benefit of screening for amblyopia in children younger than 3 years (Grossman et al., 2017). Experts advise routine vision screening and assessment for children between 0 and 6 years in the Chinese Expert Consensus on Prevention and Treatment of Amblyopia in Children (Wei et al., 2021). Children often begin kindergarten around 3 years old in China, and the prevalence of amblyopia increases with age, especially around 3 years old (Hu et al., 2022). As a result, the target population of our study was chosen to be 3-year-olds enrolled in kindergarten.

From a third-party payment perspective, the study compared the costs and health outcomes of screening for amblyopia versus non-screening among 3-year-old children. We assumed that amblyopia could always be identified when children visit an ophthalmologist in the non-screening group, regardless of whether they were referred (e.g., by a pediatrician). In our study, we simulated 100,000 Chinese children, with simulated individuals entering the study at age 3 and followed until death or age 78 (the average life expectancy in China) (World Health Organization, 2022). Our study was conducted and reported in accordance with the reporting guidelines of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (Husereau et al., 2022).

2.2. Model overview

A two-phase model, including a short-term decision tree and a long-term Markov survival model, was developed in TreeAge Pro 2020 (TreeAge, Williamstown, MA). The primary outcomes were quality-adjusted life-years (QALYs) and the incremental cost-effectiveness ratio (ICER). The time horizon of the model was set to start screening at age 3 until death (78 years), and a 1-year model cycle was used in the model. For costs and outcomes, we considered a half-cycle correlation and applied a 5 % annual discount rate. The willingness-to-pay (WTP) threshold was defined as $38,223 per QALY, which was estimated based on three times the per-capital gross domestic product (GDP) in 2022 ($12,741).

Unilateral visual impairment was defined as a two-line interocular difference in best corrected visual acuity (BCVA) with a value of 20/32 (logMAR 0.2) in the worse eye. Bilateral subnormal BCVA 20/50 (logMAR 0.4) was used to define bilateral visual impairment (Huang et al., 2018). The decision tree root node included all 3-year-old children in kindergartens in China (appendix A. Fig. S1). According to whether their parents or legal guardians gave consent to participate in the screening, the children would follow two pathways (screening or non-screening). In the screening strategy, the children were divided into cooperators and non-cooperators according to their level of cooperation. Subsequently, the children with and without amblyopia were further divided into two groups according to the sensitivity and specificity of the screening. All children were referred to an ophthalmologist (referral +/-) after a positive or inconclusive screening result. According to the treatment results, the children who had been diagnosed by ophthalmologists were categorized as either cured or not cured (cure +/-). The framework of non-screening was the same as that of screening after the "cooperation" node. Following the procession of the decision pathway, children ended up in one of three health states: "*Healthy*", for those who had no amblyopia or were treated successfully; "*Unilateral VI* (caused by amblyopia)", for those who had amblyopia and were not cured; and "*Untreated amblyopia*", for those whose amblyopia was present and not treated.

The three health states at the end node of the decision tree were taken as the initial health states of Markov models, and three corresponding Markov models (models A, B, and C) were thus established (Fig. 1, appendix A. Methods). Model A included six states describing the course of disease, with the initial health state "*Untreated amblyopia*". Model B included three states, with the initial health state "*Healthy*". Model C included three states, with the initial health state "*Unilateral VI* (caused by amblyopia)". Because the initial states of Models B and C were both included in Model A, the possible transitions within the two models were covered by the transitions of Model A.

2.3. Transition probabilities

According to the field study, literature, and expert opinions, the screening and transition characteristics of amblyopia were estimated (Table 1). The proportion of 3-year-old children in kindergarten was the ratio of the number of children in preschool to the total number of 3-year-olds (National Bureau of Statistics, 2020). The proportion of participation in the screening programme, the prevalence of amblyopia, the percentage of compliance with referrals to ophthalmologists after cooperative screening, the sensitivity of amblyopia screening, the specificity of amblyopia screening, and the proportion of cooperation were also gathered or estimated (Li et al., 2019, Chen et al., 2016).

The success rate of treatment (*p_eff*) for children aged 3 to 7 years was set at 50 % based on published reviews (Holmes and Clarke, 2006). The treatment of children aged 8–12 years was assumed to be 20 % less effective than treatment for those younger than 7 years (Jonas et al., 2017, Holmes and Levi, 2018, Franceschetti, 2006).

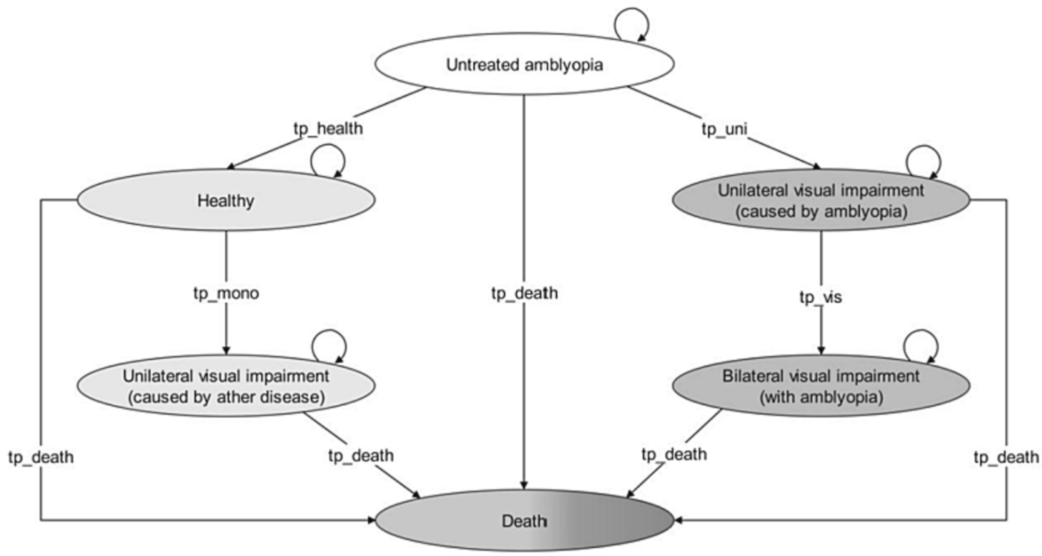

Fig. 1. Markov models. Ovals represent health states, and transition probabilities between different states are shown by arrows. The variable names of the transition probabilities for each cycle (one year) are adjacent to the arrows and are described in Table 1. Rounded arrows indicate that the health states can persist for longer than one cycle (one year).

It was also assumed that all-cause death causes the transition from any healthy state to a death state. Age- and gender-specific mortality data were obtained from the seventh national census in 2020 (appendix A. Table S1) (National Bureau of Statistics, 2020). The mortality rates for men and women were defined as R_m and R_f, respectively. The annual probabilities of the transition (*tp_death*) from other states to the death state were derived by using the formula.

$tp\_death = 1 - e^{-Rt}$(t, length of cycle).

To estimate the age-specific transition probabilities from untreated amblyopia to healthy, we assumed that a child with untreated amblyopia could be definitively diagnosed and has a chance to be cured if she or he was treated by an ophthalmologist for any cause. Based on previous data, the probability of a visit (*op_visit*) to an ophthalmologist was estimated at 0.3. For children up to 13 years, the probability of transitioning to a unilateral VI (caused by amblyopia) state from untreated amblyopia (*tp_uni*) was obtained by multiplying (*op_visit*) and the failure rate of treatment (1-*p_eff*). After 13 years, the transition probability was assumed to be 1-*tp_death*.

For the annual transition probability from healthy to unilateral VI (caused by other diseases) and from unilateral impairment (caused by amblyopia) to bilateral impairment, we referred to the estimated values reported in a German amblyopia screening study (König and Barry, 2004b).

2.4. Costs

Our study only considered direct medical costs, which are screening costs, including equipment costs and labor costs for medical staff, and treatment costs based on a review of 12 ophthalmologists from eastern, central, and western regions of China and a field study in Suzhou.

In the screening cohort, all children would undergo examinations for distance visual acuity (HOTV logMAR VA chart, Good-Lite, Elgin, Illinois, USA). The children with abnormal results would be further exanimated with topical 1.0 % cyclopentolate (Cyclogyl, Puurs, Alcon, Belgium). The average screening cost per person was \$10.3 (appendix A. Methods). The treatment costs of amblyopia were estimated based on expert opinion since no public cost data was available. The mean number of items and services for up to 10 years was estimated, and the aggregated cost of treatment per person is shown in Table 1.

All costs were inflated to 2022 values, according to China's consumer price index (National Bureau of Statistics, 2022). We have expressed the costs in US dollars according to the average exchange rate in 2022 (Central People's Government of the People's Republic of China, 2023).

2.5. Health utilities

Quality-adjusted life years (QALYs) gains generated from the two strategies were computed by multiplying the duration in each health state with the corresponding health utility values (HUV) for the state. To estimate the impact of amblyopia on QALYs for the entire life cycle, we defined the HUVs for each possible health state during the progression of amblyopia. HUV of 0.985 was assumed for a health state without any visual impairments (Yao et al., 2021), and 0 for death. Few studies have been conducted in China on the HUV of unilateral and bilateral vision impairments. Following results from Graaf and König et al (van de Graaf et al., 2016, König and Barry, 2004a), the HUVs of myopes with unilateral and bilateral VI were assumed to be 0.925 and 0.780, respectively. According to their standard deviations, their ranges were assumed to be 0.882–0.968 and 0.710–0.850, respectively. The HUV of untreated amblyopia, unilateral VI (caused by amblyopia), and unilateral VI (caused by other diseases) was assumed to be the same because they exhibited the same symptoms.

2.6. Sensitivity analysis

One-way sensitivity analysis and probabilistic sensitivity analysis (PSA) were carried out to investigate the robustness of the model. In the one-way sensitivity analysis, we obtained the parameter ranges from the published 95 % confidence interval or by assuming $\pm$ 20 % of the base case values. The most influential parameters were presented as bars in a tornado diagram. The PSA was conducted by running 10,000 Monte Carlo simulations with different parameters randomly picked from their statistical distributions. Among them, the β distribution was used for the utility values and probability, and the γ distribution was adopted for the cost parameters (Table 1). The results of PSA were illustrated with cost-effective acceptability curves and a scatter chart to evaluate the potential of amblyopia screening for 3-year-old children in kindergartens to be cost-effective at different WTP thresholds. Finally, we also conducted a scenario analysis to explore the impact of varying the time horizon (i.e., 9 years, 18 years, 30 years, 45 years, and 60 years) and screening initiation ages (i.e., 4 and 5 years old) on the results. For the latter, we calculated the proportion in kindergarten for 4 and 5-year-old children

Table 1
Input parameters for Decision tree and Markov model.

Variables	Base-case value	Range	Distribution	Reference
Probabilities				
Screening population				
Proportion of 3-year-old in kindergarten	74.03 %	55.52 %-92.53 %	β	(National Bureau of Statistics, 2020)
Proportion of 4-year-old in kindergarten	84.20 %	67.36 %-100.00 %	β	(National Bureau of Statistics, 2020)
Proportion of 5-year-old in kindergarten	100.00 %	74.03 %-100.00 %	β	(National Bureau of Statistics, 2020)
Proportion of participation in screening program	78.65 %	76.98 %-80.32 %	β	(Expert opinion)
Prevalence of amblyopia	3.36 %	1.07 %-5.65 %	β	(Chen et al., 2016, Li et al., 2019)
Compliance with referral to ophthalmologists				
After cooperative screening	92.00 %	75.04 %-97.78 %	β	(Expert opinion)
After non-cooperative screening	60.00 %	20.00 %-100.00 %	β	(Mao et al., 2016, Zhou et al., 2007)
Test characteristics of amblyopia screening				
Sensitivity	89.29 %	72.82 %-96.29 %	β	(Expert opinion)
Specificity	96.76 %	95.80 %-97.50 %	β	(Expert opinion)
Proportion of cooperation	93.65 %	92.43 %-94.68 %	β	(Expert opinion)
The success rate of treatment				
Age of 3 to 7	50 %	10 %-60 %	β	(Jonas et al., 2017, Holmes and Levi, 2018, Franceschetti, 2006)
Age of 8 to 12	20 %			
All-cause mortality by age and gender	see Table S1	NA	NA	(National Bureau of Statistics, 2020)
Probability of visit to ophthalmologist	0.3	0.1–0.5	β	(König and Barry, 2004a)
Transition probability per year from untreated amblyopia to healthy, by age	tp_health= op_visit* p_eff If age > 13: tp_health = 0	NA	β	(König and Barry, 2004a)
Transition probability per year from untreated amblyopia to unilateral visual impairment (caused by amblyopia), by age	tp_uni = op_visit* (1-p_eff) If age > 13: tp_uni = 1-tp_death	NA	β	(König and Barry, 2004a)
Transition probability per year from healthy to Unilateral visual impairment (caused by other disease), by age				
49–51	0.00278	0.00020–0.01117	β	(König and Barry, 2004a)
52–59	0.00040			
60–69	0.00387			
70–80	0.00746			
Transition probability per year from unilateral impairment (caused by amblyopia) to bilateral impairment, by age				
49–51	0.00106	0.00008–0.00429	β	(König and Barry, 2004a)
52–59	0.00016			
60–69	0.00146			
70–80	0.00286			
Utilities				
Healthy	0.985	0.970–1.000	β	(Yao et al., 2021)
Unilateral visual impairment	0.925	0.882–0.968	β	(van de Graaf et al., 2016)
Bilateral visual impairment	0.780	0.710–0.850	β	(König and Barry, 2004a)
Death	0	NA	NA	(Yao et al., 2021)
Costs ($)				
Costs of amblyopia screening examination	10.3	12.38–8.25	γ	(Huang et al., 2018)
Costs of treatment, by age at beginning of treatment		165–446	γ	(Expert opinion)
3 years	206			
4 years	209			
5 years	217			
6 years	228			
7 years	236			
8 years	236			
9 years	310			
10 years	315			
11 years	437			
12 years	437			
Discounting rate				
Cost/Utility	0.05	0–0.08	β	(China Guidelines for Pharmacoeconomic Evaluations, 2020)

based on publicly available data (National Bureau of Statistics, 2020). We also adjusted treatment costs while keeping other variables consistent with those set at the age of 3.

2.7. Ethic compliance

This study met the institution's guidelines for protection of human subjects concerning their safety and privacy and was approved by the Institutional Review Board of Soochow University.

3. Results

3.1. Base case results

The results of the base-case analysis are shown in Table 2. In the absence of screening, 1,008 children would visit an ophthalmologist for

Table 2
Base case results of amblyopia screening compared with non-screening. All results are presented per 100,000 children.

	Screening group	Non-screening group	Incremental
Participate in screening	58,225	–	58,225
Referrals/Visit ophthalmologists	5715	1008	4707
Cases detected by screening	1636	–	1636
Persistent amblyopia (Treatment failed or undetected)	2360	2856	496
Total Cost ($)	5851323.739	4039815.717	1811508.023
QALYs gained	1946685.654	1946581.938	103.716
ICER	17,466		

Abbreviations: QALY, Quality-Adjusted Life Years; ICER, incremental cost-effectiveness ratio.

a diagnostic evaluation, and 2,851 would have persistent amblyopia (treatment failure or undetected cases) among these 100,000 children. In the screening group, a total of 58,225 children participated in the screening program, and 1,636 cases of amblyopia were detected through screening. Compared to the non-screening group, 4,707 more referrals were made, and 496 cases of persistent amblyopia were prevented. For each child with untreated unilateral amblyopia, the total cost of the screening group was $58.513 and yielded 19.4669 QALYs, compared with $40.398 and 19.4658 QALYs in the non-screening group based on a 76-year time horizon. The ICER of amblyopia screening versus non-screening was thus $17,466 /QALY, well below the WTP threshold ($38,223/QALY).

3.2. Sensitivity analysis

The results of one-way sensitivity analysis are demonstrated in Fig. 2. The prevalence of amblyopia was the most influential factor, with the ICER value ranging from $12,028/QALY to $46,180/QALY. The transition probability per year from untreated amblyopia to healthy was ranked as the second influencing factor, with the ICERs between $2,265/QALY and $21338/QALY. Other important parameters included the discount rate and the probability of a visit to an ophthalmologist. Fig. 3 illustrates the results of PSA: 92.56 % of the scatter points were placed below the line when WTP was set at $38,223/QALY, indicating the probability that amblyopia screening in kindergarten was very likely to be cost-effective. Scenario analyses for different time horizons and screening onset ages are shown in appendix A. Table S2. Although shortening the time horizon to 60 years, 45 years, and 30 years or less resulted in higher ICERs for screening, screening consistently generated higher QALY gains than non-screening. At the same time, if we delay the screening to 4 and 5 years of age, the ICERs are $15446/QALY and $13304/QALY, respectively, which are lower than the WTP threshold.

4. Discussion

Our results showed that the screening strategy generated an incremental effect of 0.0011 QALYs per child, and the associated ICER was $17,466/QALY compared to non-screening. Hence, the amblyopia screening programme was a cost-effective strategy in comparison with non-screening for 3-year-old children in kindergartens in China, which was further supported by various sensitivity and scenario analyses. The finding was also consistent with prior results (König and Barry, 2004a, Rein et al., 2012, Heijnsdijk et al., 2022, König and Barry, 2004b). A previous meta-analysis also demonstrated that amblyopia treatment was more effective in children aged 3–7 years than in those aged 7–13 years (Holmes et al., 2011).

One-way sensitivity analysis showed that the prevalence of amblyopia, the transition probability per year from untreated amblyopia to healthy, and the discount rate were the top three factors that had a great impact on ICER. If the prevalence reaches 1 % (baseline value: 3.36 %), the amblyopia screening program would very likely not be cost-

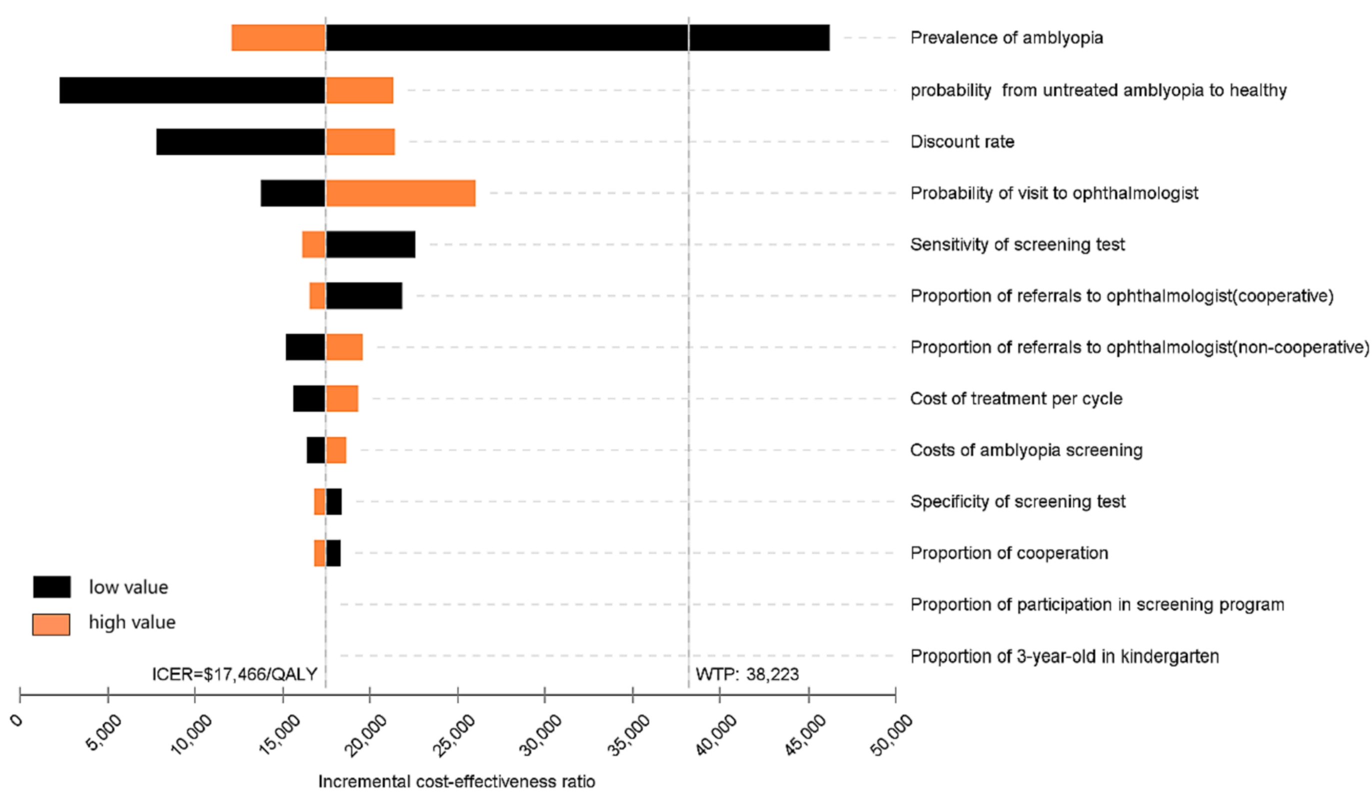

Fig. 2. Tornado diagram of one-way sensitivity analysis. The dashed lines where the two colors intersect indicate the ICER values of the base case results. ICER, incremental cost-effectiveness ratio; QALY, quality adjustment life year; WTP, willingness-to-pay.

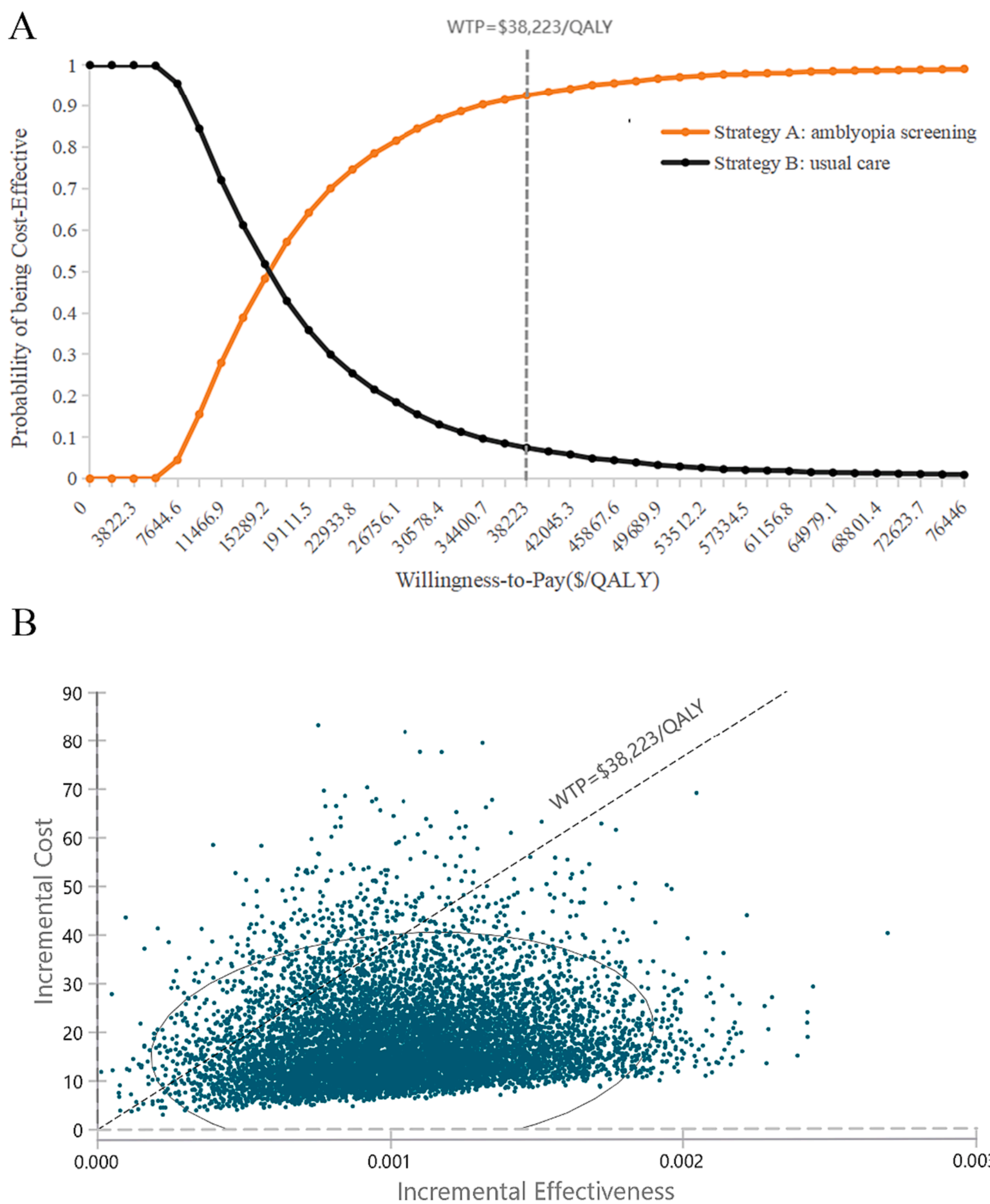

Fig. 3. Probabilistic sensitivity analysis. (A) Cost-effectiveness acceptability curves of two regimens at willingness to pay thresholds. (B) Scatter plot with lines stands for the threshold of willingness to pay in the 3 times per capita GDP of China. QALY, quality-adjusted life year; GDP, gross domestic product; WTP, willingness-to-pay.

effective. Our study used prevalence data from eastern and southern China as the base value, as there is no national population data. The differences in socioeconomic levels between regions may lead to differences in eye health awareness and access to eye health care. Nevertheless, the prevalence is relatively high in the south and east relative to other parts of China (Li et al., 2019, Chen et al., 2016). Hence, our results may overestimate the cost-effectiveness of the screening programme. Future studies investigating the national prevalence of amblyopia are thus warranted. Treatment success decreases as children age, and amblyopic vision loss can be irreversible if not treated early. Thus, we assumed that after 13 years, the transition probability per year from untreated amblyopia to healthy was 0. The level of the probability may affect the proportion of children in the cohort who are in a unilateral amblyopia state. The prevalence of amblyopia (König and Barry, 2004a) and discount rate (Neubauer and Neubauer, 2005) were also important factors of ICER in previous studies. It was worth noting that the long-term effect of unilateral vision loss was the greatest potential factor in Rein et al.'s study (Rein et al., 2012), which conservatively assumed a utility loss for amblyopia ranging from 0 to 0.03. This resulted in little difference in utility gain between children who participate in screening and non-screening/standard care groups, leading to a large ICER value. Our study drew on the HUSs (van de Graaf et al., 2016) and assumed a unilateral amblyopia utility loss in the range of 0.03–0.22, which may lead to a larger utility gap between the two groups of strategies, and thus, a smaller ICER. But compared with other factors in our study, the effect of unilateral utility loss on ICER may be less significant. We also conducted scenario analysis to explore the impact of varying the time horizon on the results, which remained consistent with the baseline results.

It should be noted that a recent study published in Canada considered the choice of the optimal strategy in both screening models based on amblyopia and amblyopia risk factors (ARFs) in children. The results showed that universal screening for amblyopia and ARFs in children aged 3–5 years was not cost-effective (Asare et al., 2023). Screening for ARFs allows for earlier identification of potential amblyopias and timely referral for intervention, improving amblyopia cure rates. The American

Academy of Ophthalmology and the American Association for Pediatric Ophthalmology and Strabismus have incorporated screening based on ARFs into their clinical guidelines (Arnold et al., 2022, American Academy of Ophthalmology, 2022). However, screening based on ARFs may prolong the observation period, leading to higher referral rates and false positive, and subsequently increased treatment costs (Horwood et al., 2023). Therefore, it is crucial to establish more stringent referral thresholds (Lowry and de Alba Campomanes, 2015). There is currently no unified diagnostic reference standard for identifying ARFs in China, and the screening model of ARFs has not been included in our study due to the lack of relevant data. Therefore, it is necessary to incorporate ARFs into future cost-utility analysis (CUA) of the screening in China.

Our study offers several strengths that should be highlighted. First, it is the first CUA study focusing on an Asian population and provides updated economic evaluation evidence based on the latest clinical evidence. Although Wang et al. explored the cost-effectiveness of implementing different vision screening models among children aged 4–5 years in rural China, the outcome measure was the number of true cases of failed vision screening detected (Wang et al., 2019). The metric is only an intermediate endpoint for clinical diagnosis, making it difficult to track costs and effectiveness across the entire life cycle. It is necessary to simulate the whole chain of health outcomes throughout the remaining lifetime by including the Markov process in decision analyses. A systematic review identified 13 studies on the cost-effectiveness of amblyopia screening published before 2019 (Asare et al., 2022). Only three of them used the Markov model to consider the complexity of possible amblyopia progression in the remaining life years (Rein et al., 2012, König and Barry, 2004a, König and Barry, 2004b), while the others were one-time decision analyses. Furthermore, most children's vision can only be reliably assessed when they turn 3 years old (Chou et al., 2011). Our study also confirms the economic value of screening for amblyopia starting at age 3 years in the kindergarten population, which is consistent with the USPSTF recommended age of onset of screening. Additionally, evidence has indicated that the the testability of 3-year-old children is lower than that of those aged 4–5, requiring a higher level of professionalism from testers during the screening process. As a result, delaying screening by 1–2 years may reduce repeated testing, unnecessary referrals, and thus improve the results of sensitivity and cost-effectiveness (Heijnsdijk et al., 2022, Schmidt et al., 2006, Telleman et al., 2019). Our scenario analysis of screening at 4 and 5 years old confirmed the assumption. It also implies that our study fills the gap in exploring the optimal age of amblyopia screening initiation in China.

This study also has some limitations. First, the six health states used in the Markov model are relatively simple, but the occurrence and process of diseases in reality are more complex. Second, unlikely events, such as the transition from unilateral VI to a healthy state, were not considered in the model because the transition probabilities were considered low (Bavelier et al., 2010). With respect to parameter values, the quality of the assumption and input data may be limited. For example, the success rate of treatment may be affected by compliance, frequency, and other factors (König and Barry, 2004b). Third, therapeutic criteria are defined differently in diagnostic studies. For example, different methods are used for visual acuity examinations, refractive status examinations, and other fundus examinations depending on age (National Health Commission of the People's Republic of China, 2021). It was difficult to obtain appropriate parameter values through meta-analysis. Additionally, due to the lack of data on the annual transition probability from healthy to unilateral VI (caused by other diseases) and from unilateral impairment (caused by amblyopia) to bilateral impairment in either China or Asia, the existing literature only allowed us to develop a model based on data from other countries, which has impaired the generalizability of our findings. However, we analyzed the effect of different parameter values within a certain range on the results in the sensitivity analysis.

The global increase in amblyopia over the next 20 years will mainly come from Asia. China, the second most populous country, will have a large number of cases by 2040 (Fu et al., 2020). Vision screening may be the only timely method to identify amblyopia. Only a few children have access to vision screening due to national circumstances such as the uneven distribution of medical resources. China also does not have an officially recognized national screening program for amblyopia in children. Hence, there is an urgent need for low-cost yet effective early detection strategies. In the future, studies could explore the cost-effectiveness of different combinations of starting ages and screening frequencies in conjunction with ARFs screening modalities in a wider range of target populations.

5. Conclusions

From a third-party payment perspective, amblyopia screening could be considered a cost-effective strategy compared to non-screening for 3-year-old children in kindergartens in China. Screening for children at other ages (i.e., 4 or 5 years old) may even yield better results.

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CRediT authorship contribution statement

Yu-Ting Gu: Writing – original draft, Software, Methodology, Conceptualization. **Bing Shi:** Writing – original draft, Resources, Data curation. **Dan-Lin Li:** Visualization, Validation. **Tian-Tian Zhang:** Methodology, Investigation. **Pei Wang:** Writing – review & editing, Supervision, Methodology. **Jie Jiang:** Writing – review & editing, Visualization. **Chen-Wei Pan:** Writing – review & editing, Funding acquisition, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2024.102662.

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