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Brief communication (Original)

A store-and-forward telemedicine for retinopathy of prematurity screen: is it cost-effective in Thailand?

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Background: Prompt diagnosis and treatment of retinopathy of prematurity (ROP) is crucial to prevent blindness. Telemedicine for ROP diagnosis can be applied in regions that lack an expert ophthalmologist.
Objectives: To assess the value-for-money of telemedicine in screening for ROP in high-risk infants.
Methods: A cost–utility analysis of screening and diagnosis of ROP using telemedicine was compared with the current process for ROP screening (Thai Clinical Trials Registry Identification No. TCTR20130911001). We used decision analytical models to compare costs and outcomes in terms of quality-adjusted life years (QALY) to the health provider and society. We used one-way sensitivity analysis and probabilistic sensitivity analysis to consider parameter uncertainty.
Results: The total capital cost for telemedicine to the health provider was 951,000 THB per year. With the base case analysis of 400 children screened per year per RetCam, the performance of screening and diagnosis of ROP using telemedicine (100% sensitivity and 97.8% specificity) was higher compared with the current method (88.9% sensitivity and 93.4% specificity). We therefore expect that blindness can be prevented in 3 children per 400 screening cases. The incremental cost to society of telemedicine compared with the current practice was 837 THB. Preventing just one child from becoming blind can save around 146,000 THB throughout their lifetime based on savings to welfare costs for disabled people. The incremental cost–effectiveness ratio of this telemedicine was 259 THB per case of prevented blindness and 17,397 THB per QALY saved.
Conclusions: Store and forward telemedicine for ROP screening is cost-effective.

Keywords: Cost-benefit analysis, RetCam, retinopathy of prematurity, telemedicine, wide-angle digital fundus camera

Retinopathy of prematurity (ROP), a vasoproliferative retinal disorder in low birth weight premature infants, is a leading cause of avoidable childhood blindness. Globally, it is estimated that 50,000 children become blind as a result of ROP [1]. In developing countries, especially middle-income countries, survival of premature infants has increased because of advances in medical technology and better preterm labor management. The “third epidemic” of blindness as a consequence of ROP was established to highlight the increasing trend of ROP in developing middle-income countries [1]. From a national survey in Thailand (2006–2007), ROP accounted for around 67% of blindness in children, with a prevalence of blindness of 0.11% in children aged under 14 years old [2]. According to the VISION 2020 action plan, the global prevalence of blindness in children should be reduced from 0.75/1000 to 0.4/1000 by the year 2020, especially for counties where more than 10% of the causes of blindness result from ROP [3].

Timely diagnosis and early treatment can help reduce the blindness in children [4, 5]. Indirect ophthalmoscopy by experts is the criterion standard for the diagnosis of ROP. Newborns at high risk of developing ROP include those who are ≤32 weeks gestational age, ≤1500 grams birth weight, or have unstable clinical courses (the current screening criteria in Thailand), and should receive screening for ROP; ophthalmologists will determine whether these infants require further follow-up or treatment. However, because of a shortage of staff and lack of experience, newborns are often referred to tertiary hospitals where experts are present, even though this may lead to unnecessary referrals.

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Telemedicine has great potential to overcome some of the challenges regarding limited healthcare resources. The store-and-forward telemedicine can help improve travel time for ophthalmologists, logistical coordination with other healthcare staff, and accessibility to remote experts [6]. The use of the RetCam (Clarity Medical Systems, Pleasanton, CA, USA), a wide-angle digital fundus camera, in the screening of ROP to identify infants who require further treatment was warranted with 100% sensitivity and 99.8% specificity from a study conducted by the Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) telemedicine initiative [7].

In Thailand, the RetCam Shuttle—a maneuverable RetCam, also known as a mobile RetCam unit—is currently being used by the E-Sarn ROP Working Group. From May to September 2012, a trained ophthalmic technician captured images of fundi from 100 infants using a RetCam Shuttle from 6 general/regional hospitals. The images were sent to an experienced ophthalmologist for interpretation at a referral center, Srinagarind Hospital. This telemedicine program has shown benefits in several ways. First, the program alleviates the workload of the local ophthalmologists at secondary-level hospitals. Second, unnecessary referrals of infants from secondary-level hospitals to the referral center are reduced. The referral process sometimes causes harm to the infant and results in unnecessary expense. Finally, the main benefit of this program is the proper management of infants with ROP in a timely manner, thereby reducing their chance of developing unfavorable visual outcomes. From the benefits above, it would be useful to apply this telemedicine program to other regions in Thailand.

The RetCam is a relatively expensive technology with high setup costs, especially in a middle-income country like Thailand. Therefore, cost-effectiveness analysis has become increasingly important as a tool for healthcare decision-makers to allocate limited resources, especially for health technology in telemedicine [8]. The objective of this study was to demonstrate the value-for-money of telemedicine using the RetCam to capture images and have them interpreted by geographically remote experts compared with the current situation where a funduscopic examination using an indirect ophthalmoscope is conducted by local ophthalmologists. We expect that the findings from this study will be useful for decision-makers and healthcare purchasers in other regions of Thailand, and in other developing countries where infrastructure and the number of ophthalmologists are constraints.

Materials and methods

Model, design and analysis

A cost–utility analysis was conducted to compare the costs and outcomes of digital photographic ROP screening using the RetCam, an example of store-and-forward telemedicine, with interpretation by geographically remote experts with the current practice whereby general ophthalmologists determine whether a referral is needed. This study was approved by the Khon Kaen University Ethics Committee (approval Nos. HE551325 and HE57118).

The study was conducted in light of the Thai context using the viewpoint of the providers and society, with hypothetical birth cohorts. A decision tree model to compare the costs and outcomes in terms of blindness prevention and quality-adjusted life years (QALYs) of alternative ROP screenings and diagnosis was developed in Microsoft Excel software (Microsoft Office 2007). **Figure 1** illustrates the screening pathway using telemedicine compared with the current practice.

For the telemedicine method, trained technicians use RetCam to capture photographs, which are then sent digitally to expert ophthalmologists for interpretation. In these files, the capture of the fundus may or may not be interpretable depending on the child. In the case where the photo is interpretable, a positive case will be referred to experts for further care and treatment, while a negative case will not be referred. For noninterpretable cases, all newborns are referred for further investigation. The current practice—the conventional ROP screening method—requires general ophthalmologists to conduct eye examinations using an indirect ophthalmoscope to inspect the fundus of preterm infants. Referred infants are further investigated for ROP by experts in a higher-level hospital to confirm the disease and offer treatment accordingly.

A lifetime time horizon was used to estimate the long-term costs and outcomes of infants becoming blind. All future costs and outcomes were discounted at a rate of 3% per annum. For intercountry comparisons, costs were converted into international dollars ($IS) using the purchase power parity exchange rate of $IS1 = 17.659 THB (Thai baht) [9]. All costs

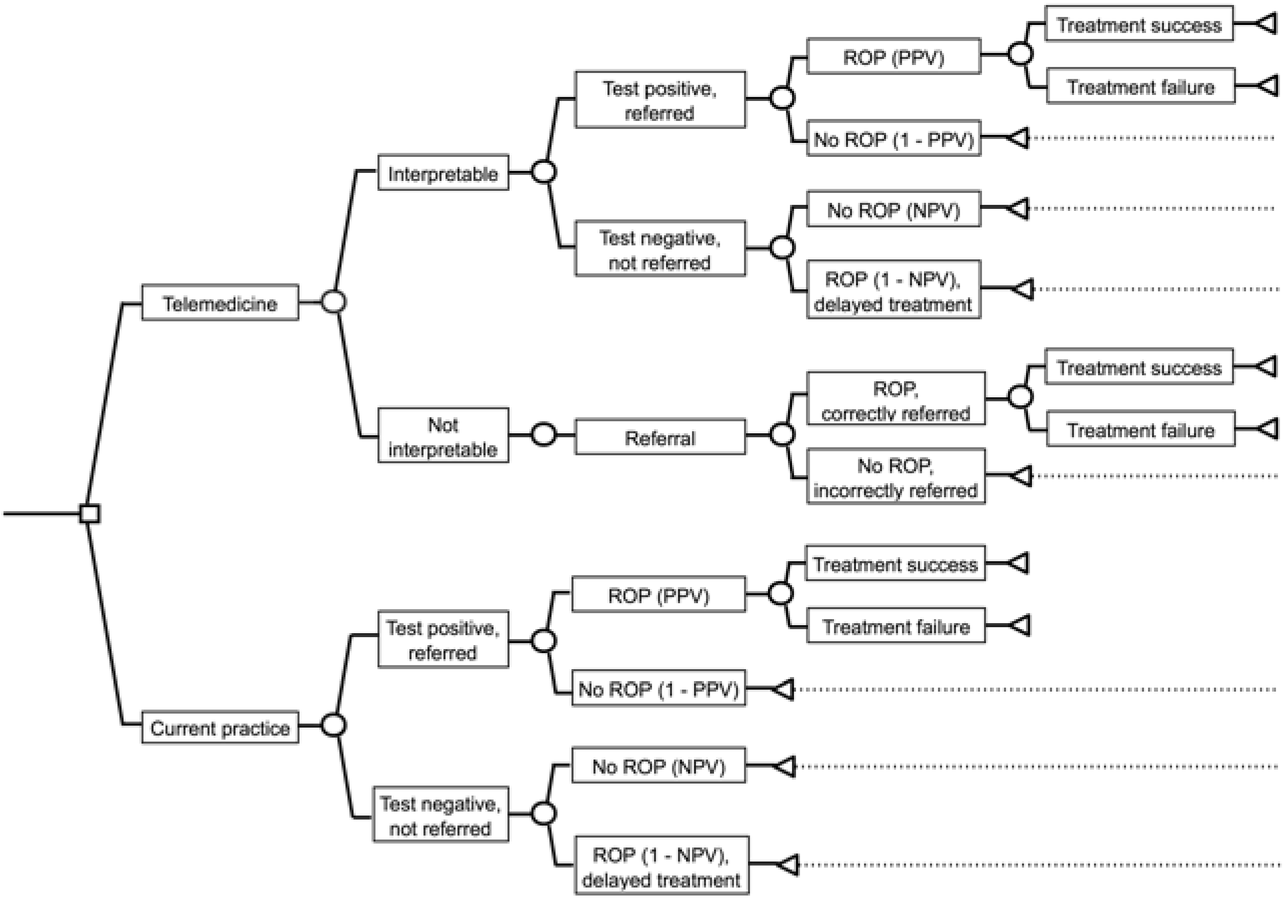

Figure 1. The decision tree for the screening of ROP in high-risk infants using telemedicine compared with the current practice.

were adjusted to 2013 values using the general consumer price index [10]. A probabilistic sensitivity analysis was conducted using a second-order Monte Carlo simulation with 1,000 repetitions, which incorporates statistical uncertainty into the model.

Model inputs

Key parameters used in the decision models are summarized in **Table 1**.

Epidemiological data and diagnostic performance

A prospective clinical trial was conducted from September to December 2013 to assess the diagnostic accuracy of RetCam in a northeast region of Thailand (Thai Clinical Trials Registry Identification No. TCTR20130911001). The mother, father, or legally authorized representative of the infant provided written informed consent for the pediatric patient participation in the study. A total of 100 infants were enrolled over the duration of 3 months. Nine of 100 infants were diagnosed with ROP requiring treatment (ROP-RT) according to the criteria set by the ETROP study [11]. Of these 9 infants, 8 had bilateral disease. The sensitivity of the RetCam in detecting ROP-RT was 1.00 (95% CI 0.70, 1.00) and specificity was 0.98 (95% CI 0.92, 0.99). The fundus images of 2 infants were not able to be interpreted because of their poor quality so they were referred to an expert ophthalmologist; this resulted in neither of the infants requiring any treatment. From interpreting the fundus images of the remaining 98 infants, 11 were categorized with ROP-RT and 87 of the 98 did not require any treatment.

The other screening method was indirect ophthalmoscopy conducted by local ophthalmologist, which showed a sensitivity of 0.89 (95% CI 0.57, 0.98) and specificity of 0.93 (95% CI 0.86, 0.97) for the detection of ROP-RT. Based on this method, 14 of the 100 infants were referred to meet expert ophthalmologists. Of the 86 remaining infants that did not require any treatment, 1 of was diagnosed at high risk for prethreshold ROP via the criterion standard for ROP diagnosis, and an assessment by an expert ophthalmologist using indirect ophthalmoscopy. This infant required laser photocoagulation treatment.

Table 1. Values and distributions and sources of parameters used in the decision analytic model

Parameters	Mean (SE)	Parameter distribution	Sources
Baseline events			
Prevalence of ROP in high-risk infants	9.0% (2.9%)	Beta	Trial
Proportion of ROP in both eyes	88.9% (9.9%)	Beta	Trial
Yearly probability of dying in general population	Age-dependent	–	[11]
Performance			
Proportion of referrals from IO by general ophthalmologists	14.0% (3.5%)	Beta	Trial
Proportion of referrals from RetCam	11.2% (3.2%)	Beta	Trial
Sensitivity of IO by general ophthalmologists	88.9% (95% CI: 57%–98%)	Beta	Trial
Specificity of IO by general ophthalmologists	93.4% (95% CI: 86%–97%)	Beta	Trial
Sensitivity of RetCam by expert ophthalmologists	100.0% (95% CI: 70%–100%)	Beta	Trial
Specificity of RetCam by expert ophthalmologists	97.8% (95% CI: 92%–99%)	Beta	Trial
Proportion of non-interpretable photo	2.0% (1.4%)	Beta	Trial
Proportion of ROP in non-interpretable photo	50.0% (28.9%)	Beta	Trial
Costs (2013, THB)			
Direct medical costs			
General ophthalmologist monthly salary	20,000 (6,000)	Gamma	Trial
Nurse monthly salary	15,000 (4,500)	Gamma	Trial
Photographer monthly salary	8,000 (2,400)	Gamma	Trial
Expert ophthalmologist monthly salary	20,000 (6,000)	Gamma	Trial
Training costs	2,500 (750)	Gamma	Trial
Follow-up and treatment costs			
Cost of follow-up per visit	291 (87)	Gamma	
Cost of retinal detachment	5,754 (1,726)	Gamma	
Cost of laser treatment	1,053 (316)	Gamma	
Resource used			
Time use for providing telemedicine (minutes)			
General ophthalmologist	10 (3)		
Nurse	60 (18)	Gamma	Trial
Expert ophthalmologist (after screening)	60 (18)		
Time use for providing telemedicine (minutes)			
Photographer	15 (5)		
Nurse	6 (2)	Gamma	Trial
Expert ophthalmologist	5 (2)		
Number of follow-ups			Assumption
For retinal detachment	6		
For laser treatment	3		
For low risk of ROP	5		
Referral costs			
Fuel	2,149 (285)	Gamma	Trial
Staff	1,791 (276)	Gamma	Trial
Direct nonmedical costs			
Parental income loss per visit	965(144)	Gamma	Trial
Travelling cost	1,794 (2,056)	Gamma	Trial
Food cost	343 (318)	Gamma	Trial
Accommodation cost	1,156 (159)	Gamma	Trial
Government subsidy per year	5,000		
Health outcomes and utility estimates			
Probability of unfavorable outcome (blind/low vision) from laser treatment	9.82% (1.62%)	Beta	[4]
Hazard ratio of death for some VI versus no VI	1.23 (95% CI: 1.16–1.31)	Log normal	[12]
Hazard ratio of death for severe VI versus no VI	1.54 (95% CI: 1.28–1.86)	Log normal	[12]
Utility for unilateral blindness	0.89 (0.0079)	Beta	[13]
Utility for bilateral blindness	0.81 (0.0098)	Beta	[13]

ROP = retinopathy of prematurity, IO = indirect ophthalmoscopy, VI = visual impairment

Costs of the program

The costs of the telemedicine program were collected from a prospective clinical trial in order to determine the diagnostic accuracy of the RetCam. Direct medical costs were identified from a database, chart reviews and expert opinions, while direct non-medical costs were collected from the clinical trial using a cost questionnaire and cost diary.

For the telemedicine program, the annual capital costs for machinery were calculated by dividing the total costs by the annuity factor, when scrap value equals to 0. The annuity factor can be calculated using the following formula:

$$\text{Annuity factor} = \left(\frac{1}{r}\right) - \left(\frac{1}{r(1+r)^n}\right),$$

where r represents the discount rate and n denotes the number of years. An annual discount rate of 3% was used. The costing guideline recommended that medical machinery should be estimated at around 8 years, with variation between 5 and 10 years. The direct medical costs of telemedicine and the current practice are shown in **Table 2**.

Health outcomes and utility estimates

Based on the natural course of ROP, when an infant does not receive any treatment within an appropriate timeframe, it has a very high probability of becoming blind. Even when an appropriate treatment such as the use of a laser is available, the probability of becoming blind is still 9.82% [4]. Blindness can cause mortality and morbidity, resulting in a lower quality of life.

In determining utility, values for monocular and binocular blindness were referenced from published literature [12]. For those with favorable outcomes, the utility is equal to 1. Subsequently, QALYs were calculated by adjusting the hazard ratio of visual impairment on mortality. The hazard ratio of monocular blindness compared with no blindness was 1.23 (95% CI 1.16, 1.31) and the hazard ratio of bilateral blindness was 1.54 (95% CI 1.28, 1.86) [13]. Data from the WHO Global Health Observatory Data Repository were used to calculate life years [14].

Model assumptions

There were several assumptions made regarding clinical practice and costs. For telemedicine, it is assumed that nurses prepare infants in a group of approximately 10 cases per week in one day. For the current method, the preparation ratio of nurses and infants is one-to-one and examinations can be conducted on any working day when a pediatrician sends a request to the ophthalmologist for ROP screening.

Table 2. Comparing direct medical costs of telemedicine with the current practice

Costs	Current practice	Telemedicine
Capital costs (per year)		
Indirect ophthalmoscope	9,972	
Lens 20/28 diopters	997	
Scleral depressor	712	
Lid speculum	142	142
RetCam Shuttle		498,597
Vehicle		142,456
Training (start-up)		2,500
Repair and maintenance costs (per year)	997	49,860
Labor (per infant screen)		
Nurse	87	9
General ophthalmologist	19	–
Technician/photographer	–	12
Expert ophthalmologist	–	10
Materials		
Medicines	4	20
Gas		650
Total fix cost (per year)	12,820	693,555
Number of infants screened	400	400
Unit cost per case screen	142	2,434

Labor costs for an expert ophthalmologist include the time they take with individual infants, including the time to wait for pupil dilatation and examination using a conventional method using indirect ophthalmoscopy. However, for ROP screening via the RetCam, the expert ophthalmologist only needs time to interpret the fundus images. Because there are no data regarding the repair and maintenance costs of the machine, we assumed that these costs account for 10 percent of the total cost.

Results

Based on the previously-mentioned assumptions and available data, including data from the prospective clinical trial and the related database, the estimated cost of diagnosis for ROP-RT by taking a digital fundus photograph and then sending the images to the expert ophthalmologist for interpretation is 27,493 baht. The cost of the conventional screening method—indirect ophthalmoscopy by local ophthalmologist is 26,657 baht. The incremental cost-effectiveness ratio (ICER) of ROP screening using the RetCam compared with the current practice was 259 baht per case of blindness prevention, 66,157 baht per life-year saved, and 17,396 baht per QALY gained. Thus, telemedicine is considered to be cost-effective given the uncertainty surrounding the parameters used in this model. The cost-effectiveness acceptability curve showed that at the threshold, telemedicine had a 75% chance of being a cost-effective intervention compared with the current practice (**Figure 2**).

When focusing on the uncertainty of each parameter by conducting a one-way sensitivity analysis, we found that two parameters affected the results of this study. The first was the sensitivity for the local ophthalmologist using indirect ophthalmoscopy to diagnose ROP-RT. When the sensitivity is higher, the RetCam will have a high ICER value, meaning that the result would become less cost-effective. The other parameter was the prevalence of ROP-RT; the higher the prevalence of ROP-RT, the more cost-effective RetCam will be (**Figure 3**). Looking at **Figure 4**, if there are 650 infants that require ROP screening via the RetCam, the ICER value is zero baht per QALY gained, meaning that the method is cost-effective.

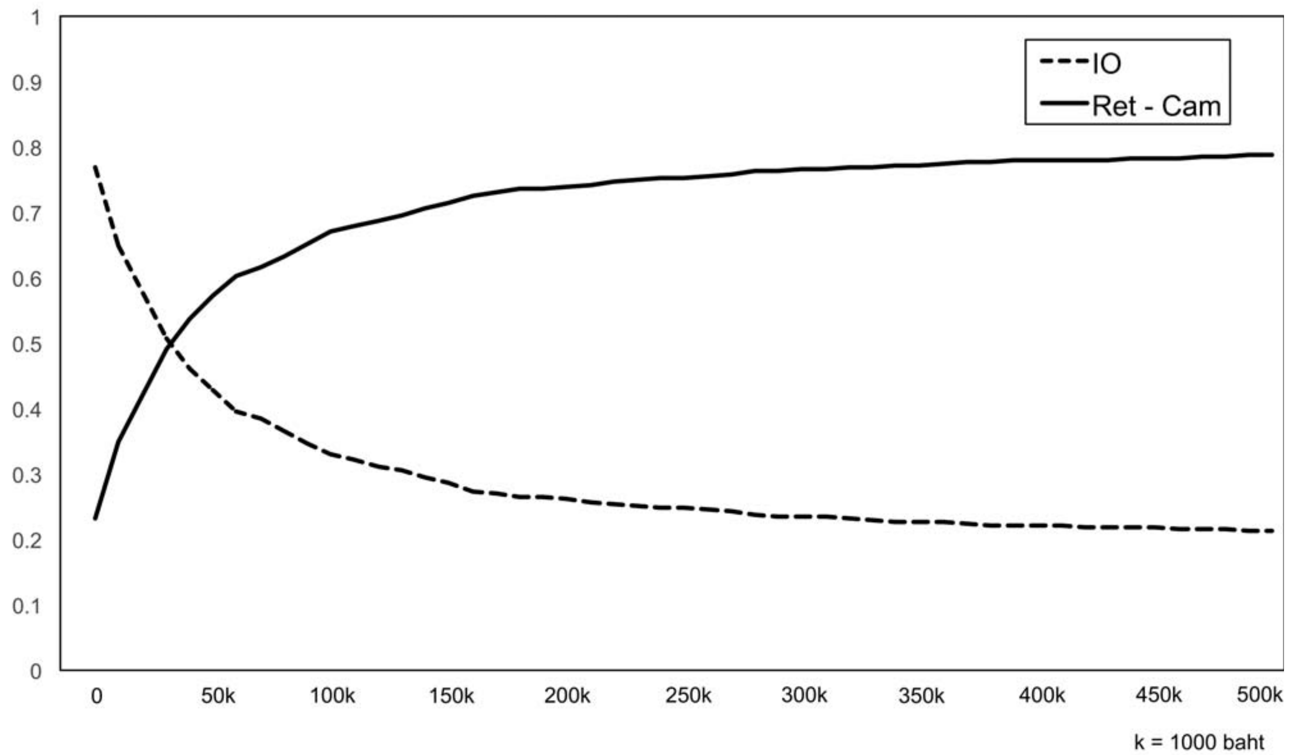

Figure 2. Cost-effectiveness acceptability curve.

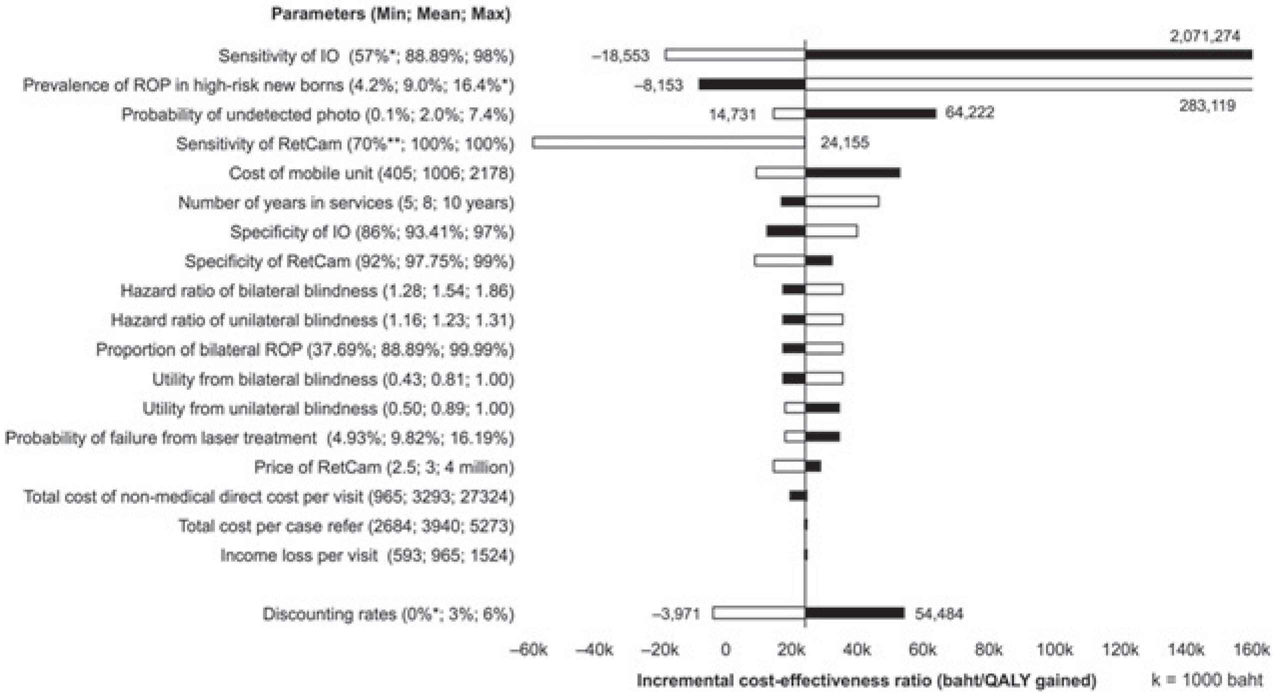

Figure 3. One-way sensitivity analysis of repair and maintenance cost of the RetCam
ROP = retinopathy of prematurity, IO = indirect ophthalmoscopy.

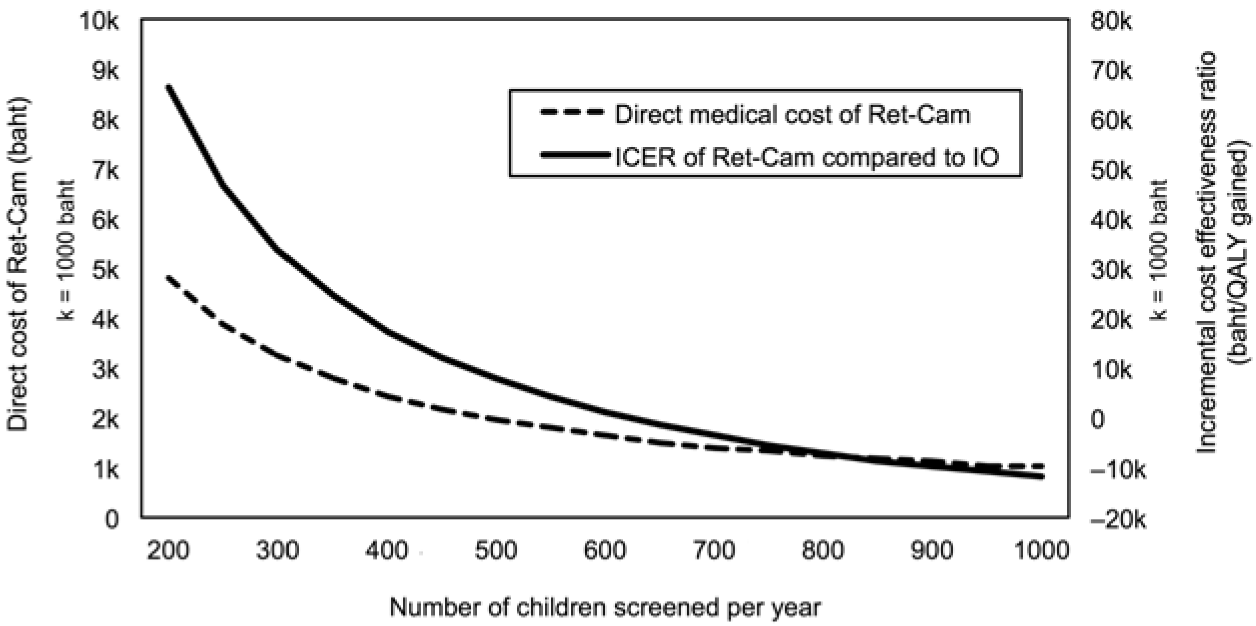

Figure 4. One-way sensitivity analysis of the number of infants who require ROP screening per year
ROP = retinopathy of prematurity, IO = indirect ophthalmoscopy, ICER = incremental cost-effectiveness ratio, QALY = quality-adjusted life years.

Discussion

Information from published literature has demonstrated the cost-effectiveness of ROP screening and treatment. Although, at the same time, ROP screening may also become burdensome work for ophthalmologists. With the further advancement of fundus camera technology, it is now widely recognized that the era of telemedicine can greatly facilitate ROP screening. Now that fundus camera technology can capture images, telemedicine can be facilitate the work of ROP screening. However, although there have been numerous reports on the accuracy of the fundus camera, only a few mention the health economics aspects. The present study shows that the ROP screening program via the RetCam is cost-effective when compared with our conventional ROP screening method. We therefore suggest that telemedicine using the RetCam to screen ROP in high-risk newborns is cost-effective as it can be a cost-saving intervention when the capacity of ROP screening increases.

ROP screening by specialist nurses trained to capture images using portable digital cameras and interpret them can be cost-effective, but the performance of ophthalmologists and the performance of a digital camera in the diagnosis of ROP was unaddressed [15]. A study of the use of a digital fundus camera for ROP screening compared with standard examinations by experienced ophthalmologists and telemedicine examinations by nonophthalmic personnel using a wide-angle imaging device and interpretation by a remote ophthalmologist showed that telemedicine is more cost-effective than standard ophthalmoscopy for ROP management [16], but the difference in accuracy of the ROP diagnosis between the two methods was not mentioned.

We came to similar conclusions as the previous studies published on the RetCam that it is more cost-effective than indirect ophthalmoscopy by ophthalmologists. However, the present study used more scientific evidence regarding the sensitivity and specificity of the two examination methods because these values are identified concurrently with economic evaluations. The outcome of ROP treatments in this study was referenced from the ETROP study [4], which is the most accepted worldwide guideline for ROP treatment. Additionally, the analysis was categorized into monocular and bilateral blindness. Finally, the life-year in this analysis has been adjusted for people with visual impairment.

A ROP examination using the RetCam can be more cost-effective if the program can examine at least 650 preterm infants or approximately 13 infants per week. At the moment, the E-Sarn ROP Working Group examines around 30 infants per week, so it is not difficult to reach that target. Another method of improving the cost-effectiveness of the RetCam in the diagnosis of ROP is to reduce the number of poor-quality fundus images by means of photography training and preparation of the infants before taking the photograph. Preparation plays a key role because the pupil of the infant should be widened sufficiently in order to obtain good quality fundus images.

A limitation of this study is the utility value used in the analysis is not the utility of Thai children who have visual impairment. This may affect the analysis because the utility of Thai children might be different from the utility of children in other countries. However, the utility values used were the most updated from the literature that used the standard gamble and time-trade-off methods to identify the utility values of parents who take care of their blind children. A second weakness is the wide sensitivity range of the RetCam in detecting ROP-RT, which may have resulted from the small sample size of our clinical trial. However, the result was still cost-effective when the sensitivity of the RetCam varies from 70% to 100%.

Conclusion

We suggested that telemedicine using the RetCam to screen ROP in high-risk newborns with remote expert interpretations is cost-effective and should be promoted in other regions of the country. However, other factors have to be considered, such as the number of children who require screening, the prevalence of ROP requiring treatment, and the sensitivity of detecting ROP requiring treatment.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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