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Cost-effectiveness of digital photographic screening for retinopathy of prematurity in the United Kingdom

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Objectives: To compare the cost-effectiveness of alternative methods of screening for retinopathy of prematurity (ROP) in the United Kingdom, including the existing method of indirect ophthalmoscopy by ophthalmologists and digital photographic screening by nurses.
Methods: A decision tree model was used to compare five screening modalities for the UK population of preterm babies, using a health service perspective. Data were taken from published sources, observation at a neonatal intensive care unit (NICU), and expert judgment.
Results: We estimated that use of standard digital cameras by nurses in NICUs would cost more than current methods (£371 compared with £321 per baby screened). However, a specialist nurse visiting units with a portable camera would be cheaper (£172 per baby). These estimates rely on nurses capturing and interpreting the images, with suitable training and supervision. Alternatively, nurses could capture the images then transmit them to a central unit for interpretation by ophthalmologists, although we estimate that this would be rather more expensive (£390 and £201, respectively, for NICU and visiting nurses). Sensitivity analysis was used to examine the robustness of estimates.

This study constitutes an initiative of the Department of Ophthalmology and the Centre for Health Management at Imperial College London. The project did not have any additional financial support. Data from a UK cohort study of babies with stage 3 ROP, conducted by the Research Division of the Royal College of Paediatrics and Child Health using cases recruited through the British Ophthalmic Surveillance Unit was used. This cohort study was a joint initiative of the Royal College of Paediatrics and Child Health, the British Association of Perinatal Medicine and Royal College of Ophthalmologists, funded by the Department of Health. We thank this initiative, since without this contribution, the study could not have been carried out.

Conclusions: It is likely that there is an opportunity to improve the efficiency of the ROP screening program. We estimate that screening by specialist nurses trained in image capture and interpretation using portable digital cameras is a cost-effective alternative to the current program of direct visualization by ophthalmologists. This option would require the development of a suitable portable machine. Direct comparative research is strongly needed to establish the accuracy of the various screening options.

Keywords: Preterm (or premature) babies, Retinopathy of prematurity, Digital photography, Screening, Cost-effectiveness analysis, Decision trees

Retinopathy of prematurity (ROP) is a leading cause of blindness in babies born prematurely (17;20;26;28). It is thought to account for approximately 6 to 18 percent of childhood blindness in industrialized countries, while severe visual impairment or blindness due to ROP ranges from zero in most African countries to 38.6 percent in Cuba (19). ROP is a vasoproliferative disorder of the eye (2), related to oxygen administration to preterm babies. However, other factors, such as genetics, ethnicity, socioeconomic status, and fertility programs, may also influence the development of the disease (31;39).

The severity of ROP is classified by five stages of disease. Stage 1 and 2 disease is referred to as "mild," as it does not require treatment and resolves without adverse effect on vision. Stage 3 disease has the potential to cause visual impairment. It can regress spontaneously, but may also progress to stage 4 or 5, where retinal detachment is present and treatment is not effective. Treatment is recommended, thus, for stage 3 ROP beyond a designated "threshold," where the risk of blindness is estimated to be approximately 50 percent (9).

Cryotherapy was the first treatment available for ROP. This treatment was shown to be effective in the Cryo-ROP study (5–14). Nowadays, however, almost all treatment is by laser. Although randomized controlled trial (RCT) evidence is limited (3;4;30), there is a consensus that laser treatment is equally or even possibly more effective and better tolerated than cryotherapy (17;18). Brown et al. (1) conducted a cost-effectiveness analysis comparing cryotherapy and laser treatment for "threshold" ROP. They took a health payer perspective, but excluded the costs of screening and follow-up. Clinical outcome data were taken from two RCTs (3;10) that reported visual acuity over a follow-up period of around five years. Brown et al. did not present an incremental cost-effectiveness ratio (ICER) between cryotherapy and laser treatment, but this can be inferred from information presented in their study as $305 per quality-adjusted life year (QALY) gained (1999 US$). This finding suggests that laser therapy is a highly cost-effective option.

Javitt and colleagues (23) conducted another economic evaluation. They evaluated various screening and cryotherapy treatment strategies from a governmental perspective, concluding that they cost between approximately $2,500 and $6,100 per QALY gained (1993 US$) compared with no screening or treatment. Thus, ROP screening seems to be a very cost-effective use of health-care funds, and indeed, most developed countries have instituted screening programs for ROP. Before 1988, because this condition could neither be prevented nor treated, screening in the United Kingdom was not widespread. In mid-1988, when the Cryo-ROP Study demonstrated that treatment significantly reduced unfavorable outcomes (9), screening became a priority, national guidelines were produced, and by 1994, it was undertaken in 96 percent of neonatal units (21). Ophthalmologists use indirect ophthalmoscopy (IO) to visualize the peripheral retina. They are given additional training for this task. Current UK guidelines recommend examination for all babies born at less than thirty-two weeks gestational age or birth weight less than 1,501 g (24). Screening for ROP commences at six to seven weeks of chronological age and is performed every two weeks until either the threshold condition is developed or vascularization is complete. Treatment is recommended by two to three days after detection of threshold disease. These norms are quite similar to those applied in the United States and other developed countries.

The organization of screening and compliance with guidelines has been a matter of concern in the United Kingdom in the past decade. In 1995, the Department of Health funded a five-year program of research into ROP screening and treatment in the United Kingdom. This research, which was undertaken by the Royal College of Ophthalmologists, the Royal College of Pediatrics and Child Health, and the British Association of Perinatal Medicine, consisted of a survey of services for the screening and treatment of ROP, including adherence to screening guidelines, and a cohort study of all babies diagnosed with stage 3 ROP over a fifteen-month period (16;21;25) Both this national study and a later regional audit (42) found that some babies at risk were not being promptly identified or treated because of noncompliance with guidelines over the timing of screening or because of poor coordination between units. There were also some problems of communication with parents. ROP screening is an infrequent activity in neonatal units and most ophthalmologists spend little time on this task. Haines et al. (21) suggested that reducing the number of identified screeners would increase skills, confidence, and the ability to recognize severe disease and facilitate the incorporation of this work into consultant work plans.

Digital photography (DP) is now being introduced in some neonatal intensive care units (NICUs). The RetCam

120 is a fiberoptic, digital colour fundus camera capable of imaging all stages and many clinical features of ROP (33;34). This technology may constitute a great opportunity to improve the organization of ROP screening. It could potentially be handled by nonophthalmic professionals with adequate training, and images could be transferred electronically for interpretation at a central unit (27). It has been suggested that the RetCam 120 allows documentation of nearly the entire retina, while the ophthalmologist's view may be limited. Electronic storage of images also offers the potential for improvements in training and quality control.

However, evidence of the accuracy of this screening technology is still scarce. In a study at the Jackson Memorial Medical Centre, University of Miami (33), 100 photographs from thirty-two patients were examined using the RetCam 120. Its sensitivity and specificity were estimated at 82.4 percent and 93.8 percent, respectively. However, these estimates are based on a comparison with IO, which does not necessarily represent a "gold standard" for diagnosis. Roth and colleagues suggested that there are technical limitations of the speculum-camera interface that prevent a satisfactory view of the periphery of the retina. Another study (34) found that remote examiners using digital photography failed to ascertain threshold ROP in eight of ten eyes. In contrast, remote examiners were highly accurate at predicting "plus" disease (95 percent)—an important indicator of active and severe ROP that might require treatment. However, the cohort examined in this latter study was very small and atypical in terms of the incidence of the ROP stages.

METHODS

Structure of the Model

The aim of this study is to evaluate the cost-effectiveness of digital photographic screening for ROP by nurse examiners in comparison with current screening methods in the United Kingdom. We used a decision tree (38) to model the expected costs and outcomes of alternative screening programs.

Five different screening strategies were included (Table 1). In addition to the current strategy of screening by IO, these included use of a RetCam 120 machine by nurses within NICUs and use of a portable version of the machine by specialist nurses visiting neonatal units. Both of these digital photographic strategies could be implemented in a "telemedicine" modality, in which nurses would take the pictures then transmit them electronically to a central unit for interpretation by specialists. Alternatively, the nurses could be responsible for both image capture and interpretation, with appropriate training and support.

The baseline assumptions used in the model are defined in Table 2 and a simplified version of the decision tree is shown in Fig. 1. The model includes specification of the relationship between the incidence of the disease and the sensitivity and specificity of the screening tests, as summarized in the receiver-operator curve (ROC) equations (35). Parameter estimates used to populate the model were based on observation at a local unit, published sources, and expert opinion. The parameter values used in the baseline model are listed in Table 3.

Sensitivity and Specificity Estimates

The UK "cohort study" (25) was used to estimate parameters relating to the current process of screening and treatment. Between December 1997 and March 1999, 235 cases of stage 3 ROP were ascertained for follow-up. These cases constitute an estimated 84 percent of the total eligible population, based on the 1994 incidence estimate of 3.4 percent very low birth weight babies (21). Observations from the cohort study yield an estimate of 90 percent for the sensitivity and 99.2 percent for the specificity of the current screening program.

Given the current lack of clear evidence over the relative accuracy of digital photographic screening compared with IO, we assumed equal sensitivity and specificity for these technologies in the baseline analysis. However, we also conducted threshold sensitivity analyses by varying the sensitivity and specificity of digital photographic screening under the telemedicine and complete nurse screening strategies.

Table 1. Alternative Strategies for Screening Considered in the Model

Option	Professional	Technology	Organisation
a)	Ophthalmologist (current practice)	Indirect ophthalmoscopy	Visiting NICUs for screening
b)	Neonatal nurse for image capture and ophthalmologist for interpretation (telemedicine modality)	Digital photography standard RetCam 120	Capture of images in NICU, transferral of images to a central server for interpretation
c)	Neonatal nurse for image capture and interpretation (complete screening)	Digital photography standard RetCam 120	Capture and interpretation of images in NICU.
d)	Specialist visitor nurse for image capture and ophthalmologist for interpretation (telemedicine Modality)	Digital photography portable RetCam 120	Capture of images in NICU, transferral of images to a central server for interpretation
e)	Specialist visitor nurse (complete screening)	Digital photography portable RetCam 120	Capture and interpretation of images in NICU.

NICU, neonatal intensive care unit.

Table 2. Baseline Clinical and Economic Assumptions

1	Screening starts after neonatal period at 27 days
2	All patients detected with threshold ROP are treated
3	Bilateral cases are treated simultaneously in both eyes, generating a saving in the treatment cost for the second eye of 70%
4	The need for a second or third treatment does not depend on the presence of bilateral/unilateral condition
5	Patients whose ROP progresses to stage 4 or 5 are not treated and are assumed to have an unfavourable outcome
6	Outcomes for the bilateral condition are assumed to be similar for both eyes
7	Babies with a false-positive diagnosis have an extra cost equivalent to one attendance by an ophthalmologist
8	For unilateral cases requiring treatment, the untreated eye is assumed to have normal visual acuity
9	The annual discount rate is 6% for costs and 1.5% for utilities
10	A RetCam 120 in a NICU will be used for other purposes 20% of the time
11	Life expectancy at birth is 78 years
12	Visual acuity attained at 10 years will remain stable for the rest of life

ROP, retinopathy of prematurity; NICU, neonatal intensive care unit.

Cost Estimates

Costs were estimated from a UK National Health Service (NHS) perspective, using 2002 prices and an annual discount rate of 6 percent. The three components of costs included in the analysis were the cost of the screening examination; the cost of treatment; and the cost of follow-up until the age of ten years.

The costs of the screening process were estimated using a microcosting methodology. (Full details of the costing methods and assumptions are available on request from the first author). We included estimates for the costs of the

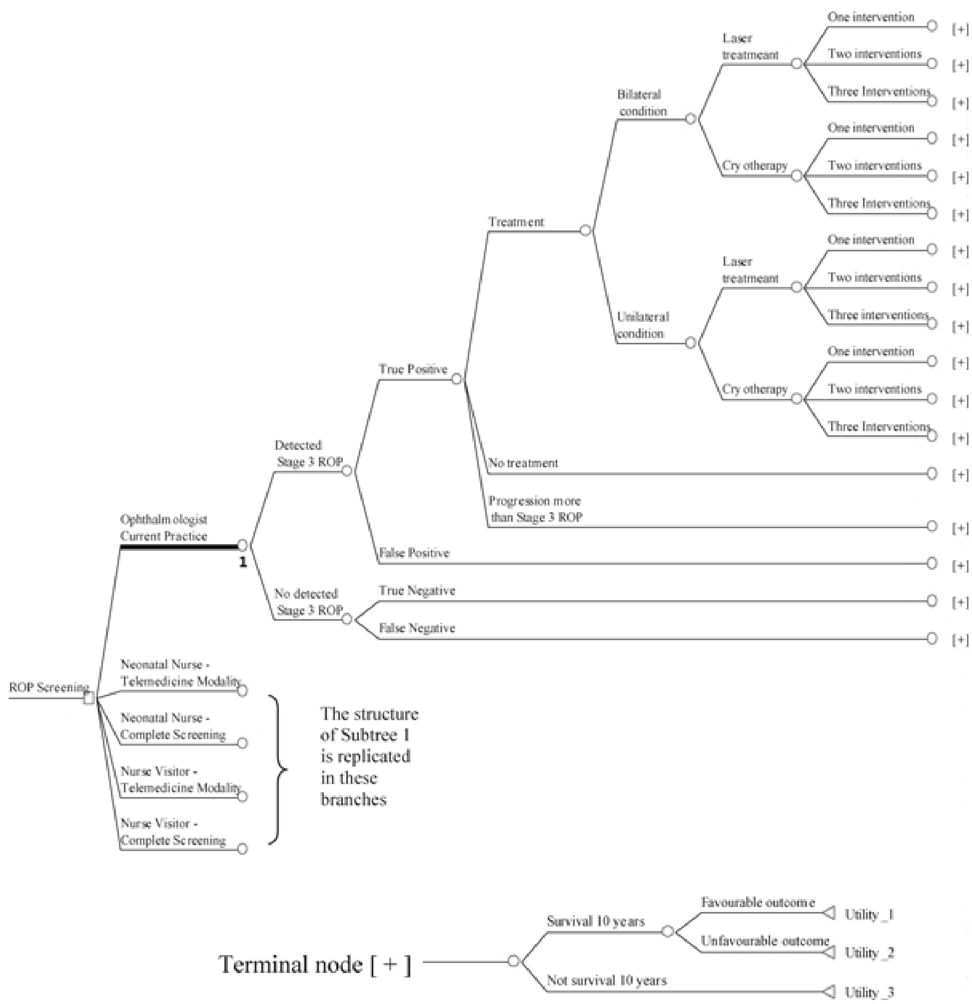

Figure 1. Simplified illustration of the decision tree.

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Table 3. Baseline Parameter Estimates

Probabilities used in the model			
Prob of reaching stage 3 ROP	.034	15 month observational study—UK the Cohort Study	Incidence rate
Prob of detecting a stage 3 ROP case	.038		
Prob of confirming a stage 3 ROP case	.8		PPV
Prob of confirming a non stage 3 ROP case	.996		NPV
Prob of detecting a stage 3 ROP in presence of the disease	.90		Sensitivity
Prob of detecting a non stage 3 ROP in absence of the disease	.992		Specificity
Prob of progressing beyond stage 3 ROP	.01		
Prob of treatment for stage 3 ROP	.59		
Prob of treatment in both eyes	.92		
Prob of treatment in one eye	.08		
Prob of one intervention	.87		
Prob of two interventions	.11		
Prob of three interventions	.02		
Prob of treatment with laser	.78		
Prob of treatment with cryotherapy	.22		
Prob of FVO after laser	.62	(Ng, E. Y. et al. 2002)	
Prob of FVO with no treatment for stage 3 ROP	.379	(Cryotherapy for Prematurity Cooperative 2001	
Prob of FVO after cryotherapy	.556		
Prob of death before 10 years	.124		
Prob of FVO without developing stage 3 ROP	.99	(Cryo-ROP, 2002)	

Screening costs per examination	Professional	Technology	Total (2002 £)
By ophthalmologist	£47	£2	£49
By neonatal nurse—telemedicine modality	£15	£46	£61
By neonatal nurse—complete examination	£11	£47	£58
By specialised nurse visitor—telemedicine modality	£20	£8	£28
By specialised nurse visitor—complete examination	£15	£8	£23

Cost of treatment	Unilateral	Bilateral
Laser Therapy	£540	£702
Cryotherapy	£339	£441

Follow-up costs until 10 years	Total cost
Patients treated for ROP	£786
Patients with stage 3 ROP not treated	£786
Patients with stage 4 or 5 ROP	£786
Any of the previous groups not surviving to 10 years	£245
False-negative patients (detected later)	£540

Utilities	QALYs	Discounted QALYs	
Utility of favourable bilateral outcome	1	45.8	Life expectancy 78 years, discount rate 1.5%.
Utility of favourable unilateral outcome	1	45.8	
Utility of unfavourable unilateral outcome	.80	36.6	For babies not surviving at 10 years, life expectancy was 2 years
Utility of unfavourable bilateral outcome	.48	22.0	
Utility for babies not surviving 10 years	.48	.9	

ROP, retinopathy of prematurity; FVO, favorable visual outcome; PPV, positive predictive value; NPV, negative predictive value; QALYs, quality-adjusted life years.

following resource items: professional time, including time for training and travel, as well as time spent screening babies and talking to parents; training provision; travel; capital equipment; and disposables. The quantities of resources used were estimated by direct observation at the Winnicott Baby Unit at St. Mary's Hospital, London, and, where necessary, by expert judgment. We assumed that five babies would need screening at each NICU each week; that ophthalmologists currently do 300 examinations per year; and that specialist nurses could visit ten NICUs per week. The unit costs of equipment and disposables were based on market prices to the NHS and the unit costs of professional staff were based on published national estimates (29). We assumed that the cost of a portable digital camera would be 10 percent higher than the current manufacturer's price for the standard version, due to additional development and manufacturing costs.

Estimates for the costs of treatment were taken from Brown et al. (1), which were converted into pounds sterling by the Purchasing Power Parity method (41) and up rated for inflation by the "Hospital and Community Health Services" inflation rate (29). We estimated that bilateral treatment would reduce costs for the second eye by 70 percent. The estimated costs of follow-up were based on assumptions about the number of follow-up visits over ten years for different groups of patients. The average cost per ophthalmology outpatient attendance was taken from national reference cost data (40).

Health Outcomes and Utilities

The probabilities of visual impairment at ten years with and without cryotherapy were taken from the Cryo-ROP Study (12;13). This was a large and methodologically robust RCT with follow-up to ten years. The effectiveness of laser treatment was estimated from another study (30), which also reported ten-year follow-up. However, this study was smaller than the Cryo-ROP study and less strong methodologically. These two studies both used the Early Treatment of Diabetic Retinopathy Study (ETDRS) logMAR visual acuity charts, which yield more precise measures than those obtained with the standard Snellen chart. However, their definitions of a "favorable outcome" were rather different. In the Cryo-ROP study, an ETDRS score above 20/200 was used to define a favorable visual outcome (FVO). In Ng et al. (30), Connolly et al. (4), favorable outcome was considered as 20/50 or better best corrected ETDRS visual acuity. It might be argued that the definition of "favorable outcome" in the Cryo-ROP study was too broad, because 20/200 represents a severe degree of vision impairment.

We used utility estimates from a published study on the "economic aspects of cataracts" (15) to convert favorable/unfavorable outcomes into QALY estimates over the whole expected lifetime of the babies. Drummond estimated that an emotionally well-adjusted blind person would have a utility of 0.48. This figure was elicited from a sample of adults, but we assume that it represents a reasonable lifetime average. We further assumed that outcomes would be similar for both eyes in bilateral cases and that the utility of an unfavorable outcome for unilateral disease was 0.8. Additionally, in the case of babies not surviving to ten years, we assumed an average life expectancy of two years with a utility equivalent to those with unfavorable outcome (0.48).

RESULTS

Under the baseline assumption of equal sensitivity and specificity for the different screening options, we need only consider their relative costs, because their expected health outcomes will be the same. The estimated costs of the five screening strategies under the baseline assumptions are given in Table 4. These finding suggest that the use of a standard RetCam 120 machine by nurses within each NICU would be more expensive than the current screening program. This is the case even if the neonatal nurses are responsible for the interpretation as well as the capture of images. However, if a portable machine could be developed for use by specialist nurses visiting NICUs, then this strategy could be cheaper than current practice, even if the pictures were transmitted to a central unit for interpretation by ophthalmologists. The cheapest alternative of all would be for the specialist visiting nurses to interpret the images themselves.

Table 4. Expected Cost Per Baby for Alternative Screening Strategies

Strategy	Cost (2002£)
c) Visitor nurse complete screening	£171.80
b) Visitor nurse telemedicine modality	£201.30
a) Screening by ophthalmologist	£321.10
e) Neonatal nurse complete screening	£370.70
d) Neonatal nurse telemedicine modality	£390.40

Sensitivity analysis was used to examine the effects of changes in various baseline parameter values on the relative costs of the screening strategies (Table 5). Although the expected costs of all strategies change with the number of babies examined each week at each NICU and with the number of examinations per baby, their relative order does not change: the visiting specialist nurse conducting complete screening always remains the cheapest option. This finding is also robust to changes in the cost per hour for the specialist nurse. This cost must almost triple (from £25 to £75 per hour) before it becomes more expensive than current screening by ophthalmologists. This rate suggests that employment of part-time specialist nurses, which would be expected to increase overall labour costs, would still be an economic method of screening. Results are also quite robust to changes in the cost of the RetCam machine. This would have to fall from the current £65,000 to below approximately £50,000 before digital photographic screening by nurses within neonatal units becomes cheaper than IO. However, in this situation, screening by specialist visiting nurses still remains the cheapest option (assuming that the cost of the portable version of the machine was to fall proportionately). The cost of the portable version of the RetCam would have to rise beyond £285,000 before IO would be cheaper than complete screening by visitor nurses.

Sensitivity analysis was also used to observe the impact of various assumptions about the accuracy of the RetCam 120 compared with IO. The accuracy of the screening program can be analyzed from different angles. For instance, the accuracy in detecting a positive case of stage 3 ROP can be attributable to the screener or to the technology used. Moreover,

Table 5. One-Way Simple Sensitivity Analysis

Variable	Baseline value	Sensitivity range		Threshold value	Impact on optimal strategy (c)
		Low	High		
Average examinations per baby	5.7	3	9	—	No change
Number of babies screened per session	5	2	8	—	No change
Cost of visitor nurse (£/hour)	£25	£20	£80	£75	Option a preferred above threshold
Cost of RetCam 120 (Standard version)	£64,750	£30,000	£70,000	—	No change
Cost of RetCam 120 (Mobile version)	£71,225	£71,225	£100,000	—	No change
Cost of maintenance for Digital Cameras	0%	0%	30%	—	No change
Sensitivity of digital photography	90.0%	30.0%	100.0%	88.2%	Option a 'cost-effective' below threshold
Specificity of digital photography	99.2%	0.0%	100.0%	—	No change
Sensitivity of nurse interpretation	90.0%	30.0%	100.0%	89.6%	Option a 'cost-effective' below threshold
Specificity of nurse interpretation	99.2%	0.0%	100.0%	41%	Option b preferred below threshold
Treatments with laser	78.0%	0.0%	100.0%	—	No change
Treatments with cryotherapy	22.0%	0.0%	100.0%	—	No change
Discount rate on costs	6.0%	0.0%	12.0%	—	No change
Discount rate on utilities	1.5%	0.0%	9.0%	—	No change

in the case of the RetCam, it can be argued that capturing the photo and its subsequent interpretation are two independent phases of accuracy.

We first tested the effect of changing the sensitivity of all four DP screening strategies simultaneously, while holding the sensitivity of IO constant at the value estimated from the cohort study (90 percent). All other parameters were held constant at their baseline values. The results of this analysis are summarized in the form of an ICER, which gives the additional cost per additional QALY gained for IO compared with the baseline strategy of complete screening by specialist visiting nurses using DP (Fig. 2). It can be seen that the

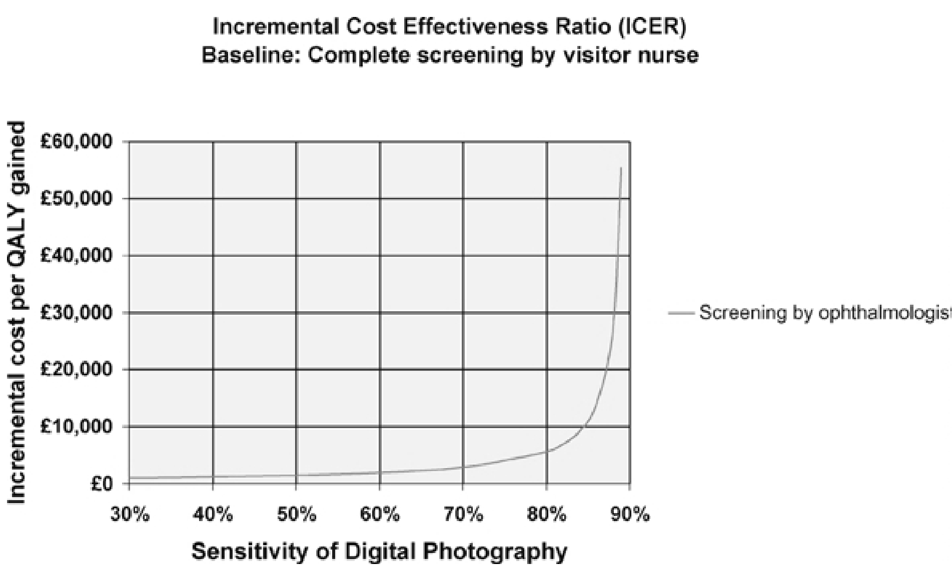

Figure 2. Threshold analysis for changes in the sensitivity of digital photographic screening.

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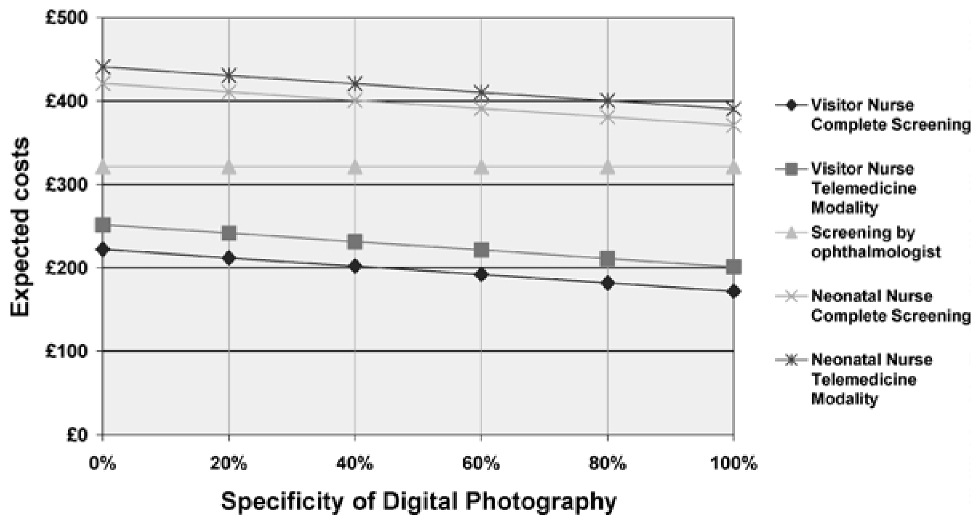

Figure 3. Threshold analysis for changes in the specificity of digital photographic screening.

incremental cost of ophthalmoscopy is estimated to be around £1,000 per additional QALY gained when the sensitivity of DP is 30 percent. This value rises exponentially as the DP sensitivity improves toward 90 percent. At 90 percent sensitivity and above, ophthalmoscopy is dominated by complete screening by visiting nurses using DP, because the former option is then less effective and more expensive than the latter. In the United Kingdom, a figure of £30,000 per QALY is commonly quoted as indicating a "cost-effective" use of health-care funds (32;37). The incremental cost of ophthalmologists compared with complete DP screening by visiting nurses is estimated to be less than £30,000 per QALY gained if the difference in the sensitivity of these two options is greater than 1.8 percentage points (88.2 percent or lower for DP compared with 90 percent for ophthalmologists). The rest of the alternatives using DP remain dominated by complete visitor nurse screening throughout the whole range of sensitivity, because they are equally effective but more expensive.

This analysis was repeated varying the specificity of the digital photographic screening options (holding all other parameters constant at their baseline values). Our model assumes that the incidence of false-positive results has no impact on clinical outcomes. Hence, the estimated QALYs for the five screening options do not vary with the specificity of DP screening. However, false-positives are assumed to have a financial cost. Figure 3 illustrates how the expected costs of the five screening options vary with DP specificity. This graph shows that the results are not altered by changes in specificity. Screening by specialist visiting nurses remains the cheapest option, reaching a maximum expected cost of £222 when the specificity of DP is zero.

Similar analyses were also conducted by varying the sensitivity then specificity of the two digital photographic screening options with interpretation of images by nurses (Figs. 4 and 5). If the sensitivity of interpretation by visiting nurses were only 30 percent, then we would expect that the additional cost of sending the images for interpretation by an ophthalmologist would be £286 per additional QALY gained (assuming 90 percent sensitivity for interpretation by ophthalmologists). This ICER value increases with the sensitivity of nurse interpretation. If the difference in sensitivity of these two options is more than 0.4 percentage points (89.6 percent or lower for nurse interpretation compared with 90 percent for the ophthalmologists), the estimated ICER is less than £30,000 per QALY gained. If telemedicine is not an option for some reason, conventional screening by ophthalmologists might possibly be more cost-effective than complete screening by visiting nurses. If the sensitivity difference for these two options is more than 0.8 percentage points (88.2 percent sensitivity for the nurses compared with 90 percent for the ophthalmologists), the ICER is less than £30,000 per QALY gained.

The estimated costs of the five screening options are shown in Fig. 5 as a function of the specificity of nurse interpretation (holding the specificity of ophthalmologist interpretation constant at 99.2 percent). As might be expected, the costs for the two options with interpretation of digital images by nurses fall as the specificity of this method increases, whereas the costs for the three options with interpretation by ophthalmologists remain constant. If the nurse specificity is greater than 41 percent, we estimate that it will be cheaper for visiting nurses to interpret the images themselves, rather than to transmit them to an ophthalmologist for interpretation.

DISCUSSION

This study has presented a cost-effectiveness analysis of digital photographic screening for premature babies at risk of developing ROP. Previous economic modelling studies have

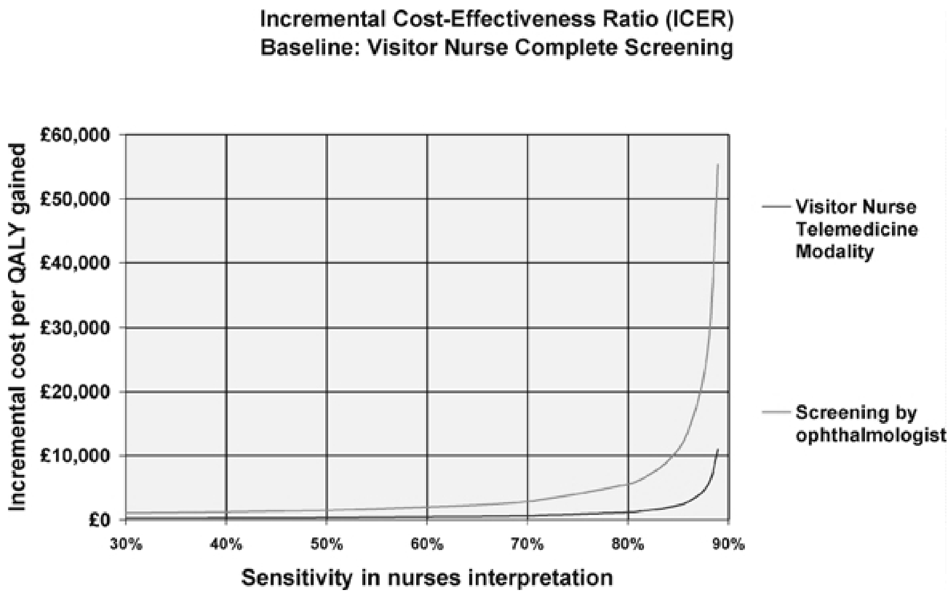

Figure 4. Threshold analysis for changes in the sensitivity of interpretation of images by nurses.

looked at the cost-effectiveness of different treatments for ROP (1) and at the cost-effectiveness of screening for this condition (23). However, to our knowledge, nobody has evaluated the cost-effectiveness of digital photographic screening compared with conventional IO.

We used a decision tree analysis informed by data from published sources, local observation, and expert opinion to compare five different screening strategies, from a UK health service perspective. A major strength of this analysis was the use of a large, national cohort study (25) to estimate the accuracy of the current screening program. Our estimates of the probability of a favorable outcome with no treatment and with cryotherapy were taken from the Cryo-ROP study (12;13), which was a well-conducted RCT with ten years of follow-up. However, the effectiveness of laser therapy was estimated from a much smaller and less robust trial (30), and the utilities used for QALY estimation (15) might also be subject to question. The lack of strong evidence over the accuracy of the different screening methods is a major problem. Consequently, we used sensitivity analysis to examine the possible implications of various assumptions about the sensitivities and specificities of different strategies. This "what-if" analysis allows us to consider which strategies are good candidates for further applied evaluation.

As with all modelling studies, our analysis may have some shortcomings based on the assumptions. For instance, equal visual outcome was assumed for bilateral cases. We also assumed that the visual acuity at ten years would remain stable over the rest of the patients' lives. In fact, the Cryo-ROP

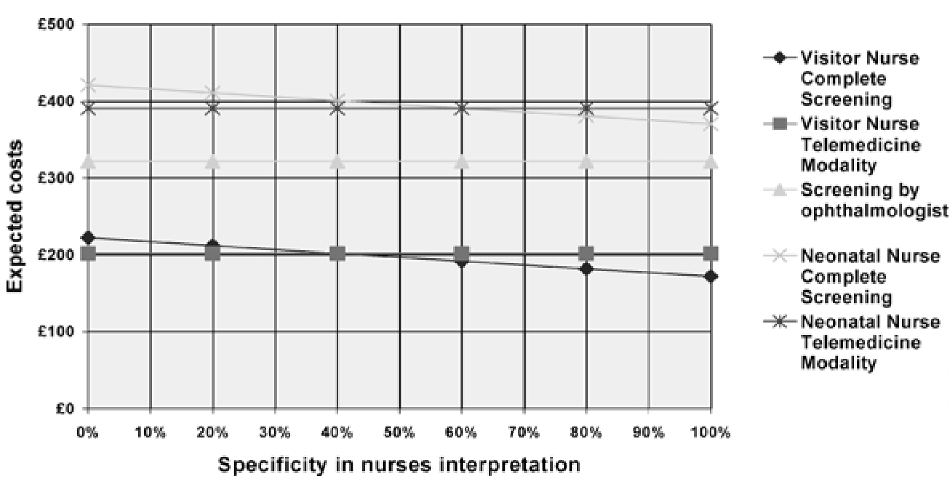

Figure 5. Threshold analysis for changes in the specificity of interpretation of images by nurses.

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study found evidence of considerable changes in visual acuity over time. Compliance with guidelines in the UK has also been a matter of concern. Therefore, we might possibly have overestimated the probability of FVO for this particular context. The effect of this overestimation in our model would be to decrease the number of QALYs gained under all screening strategies, probably with little effect on the relative ranking of the options.

We attempted to quantify the total cost of the ROP program (screening, treatment, and follow-up) under an NHS perspective. However, our estimates of treatment costs were based on those in a previous economic study (1). We did not incorporate extra costs due to complications of treatments. In the cohort study, it was observed that, in five babies, the treatment was not completed satisfactorily, thirteen babies had adverse outcomes, and one baby required three days of ventilation after treatment. An argument for omitting the costs of such complications, however, is that most of the premature babies are already hospitalized in NICUs before and after the ROP treatment. Thus, in many cases, complications would not incur significant extra health-care costs. Ideally, more accurate cost estimates for the NHS environment might have been obtained by use of a microcosting technique, including complication costs. However, this would not be expected to have had much of an impact on the ranking of the options, because the costs of screening constituted a large majority of total costs (around 90 percent).

The results of our analysis suggest that the NHS could save money on ROP screening by implementing a strategy of screening by specialist nurses, trained in the taking and interpretation of digital photographic images, visiting neonatal units with a portable camera. This proposed strategy remained the cheapest over a wide range of input parameter values. Under the most optimistic scenario, the potential savings for the NHS would be around £900 thousand per year. This estimate results from the difference in cost between screening by an ophthalmologist and complete screening by a visitor nurse (£150 per baby), multiplied by the cohort of 6,200 babies per year. In practice, however, 100 percent implementation is unlikely. One might also argue that it is unlikely that these financial savings will actually be realized, because the number of NHS ophthalmologists is hardly likely to be reduced. The gain from a more efficient ROP screening arrangement is more likely to be realized as existing ophthalmologists use their time in more productive ways, reducing waiting times for cataract operations for example.

It is important to recognize that whether this strategy constitutes a *cost-effective* use of NHS funds depends on the relative accuracy of digital photographic screening in the hands of the specialist nurses in comparison with the current methods of screening by ophthalmologists. Current evidence on this question is inconclusive. Some studies suggest that the RetCam 120 has limitations that prevent an adequate view of the periphery of the retina (33), whereas others suggest that this machine can provide a better view of the entire periphery of the retina, which is not always possible with an indirect ophthalmoscope (27). If digital photographic screening proves to be less sensitive than IO, the most cost-effective strategy might be to continue with current screening methods. We estimate that digital photographic screening cannot be "cost-effective" if its sensitivity is below 88.2 percent (assuming 90 percent sensitivity for IO and a cost-effectiveness threshold of £30,000 per QALY).

Our estimates suggest that, if digital photography were to be used, it would be cheaper to employ specialist nurses to take and interpret the images. However, this is not necessarily the most cost-effective strategy if its sensitivity is lower than when images are transmitted to a central facility for interpretation by ophthalmologists. We estimate that a "telemedicine" approach would be cost-effective if the sensitivity of nurse interpretation is less than 89.6 percent (assuming 90 percent sensitivity for interpretation of images by ophthalmologists and a cost-effectiveness threshold of £30,000 per QALY).

It may be expected that nurses would initially be overconservative in defining borderline stage 3 ROP, so as not to lose true-positive cases. Sensitivity analysis with our model suggests that the results are quite robust to the specificity of nurse screening. We found that the ranking of the five treatment strategies is not affected by changes in the overall specificity of the digital photographic options. And the specificity of nurse interpretation would have to be very low (below 41 percent for the visitor nurse option) before telemedicine would become a cheaper alternative. One of the reasons for this is that the marginal costs of false-positive results are relatively low, because all babies must be checked for a minimum period of time anyway. Additionally, the risk of overtreatment is low, because ophthalmic specialists check diagnosis before performing the treatment. Hence, we assume that false-positive results have no adverse health consequences. However, it should also be recognized that there are other "costs" of false-positive results, in terms of the discomfort of additional examinations for babies and anxiety and distress to the parents. These factors have not been considered in the above analysis.

Further research is required to determine the performance of ophthalmologists and nurse examiners in the capture and interpretation of digital photographic images. If the interpretation of photos proves to be difficult to delegate to nurses, the alternative option with a telemedicine component is still likely to be considerably cheaper than current methods and should be explored.

Even if ROP screening by nurses using digital photography is shown to be both clinically and economically acceptable, there remain significant practical challenges in the implementation of this strategy. First, the use of specialist nurses covering several NICUs depends on development of a portable version of the RetCam 120. In our analysis, the final cost of the portable machine was estimated at 110 percent of the price of the standard version. The effect of a possible underestimation of this cost was explored by means of sensitivity analysis, which indicated that, even if the cost of the portable machine was to be 50 percent higher than the standard version, it would still be cheaper than buying a machine for every NICU.

The proposed option would involve an organized program of NICU visiting over a geographic area. We assumed that a nurse could visit at least ten NICUs per week to screen at least five babies per journey using a portable machine. The practical implementation of this option may be limited by the geographic distribution of NICUs around the country, as well as the number of babies requiring screening in each unit. In London, there are 27 NICUs, based on a 1999 and 2000 census. Therefore, for a complete implementation of this option, approximately three full-time or five part-time nurses would be required. It is possible that, for geographical reasons, places in the United Kingdom located outside of the big cities may not meet the requirement of fifty babies per week for screening. However, the sensitivity analysis indicated that a minimum of thirty babies per nurse per week in this modality would still be more cost-effective than screening by ophthalmologists.

Another important precondition for the implementation of nurse screening would be their acceptance of this additional task. Although for neonatal nurses this initiative might be received with resistance, because they may see it as an additional burden on top of an already heavy workload, this program could pose a significant opportunity for specialist visiting nurses. The work could be organized into flexible schedules, as it is likely to remain an economic alternative to the current screening program, even if the nurses are employed on part-time contracts. This issue is important, given the high interest that many nurses place on flexible working arrangements, which allow them to combine family care with professional development. We have considered the deployment of nurses as being ideal for this task, because of their expertise in the care of babies, understanding of this environment, and their acknowledged ability to communicate effectively with parents. However, it could be performed also by other professionals such as medical photographers.

POLICY IMPLICATIONS

We have presented a potentially cost-effective way of incorporating digital technology in the screening for ROP in premature babies. This result poses a significant challenge to policy-makers, as the suggested approach would necessitate a change in the way that ROP screening is organized and the resources required for this process. Ophthalmologists—a relatively scarce resource for the NHS- are currently carrying out this activity. However, ROP screening using digital photography could be carried out by nurses through scheduled visits to NICUs.

The use of specialist nurses to do the screening would change the present organization of the ROP services, but new technology presents new opportunities, and the first consideration is patient care. A national audit study (21) has shown that there are currently too many ophthalmologists screening and treating far too few babies to maintain skills. The vast majority of ROP examinations are normal, and one could argue that this approach is not the best use of expensive time or expertise. Looking to the future, one can anticipate fewer ophthalmologists being involved in ROP work but becoming involved at a later stage when babies are more likely to require treatment. This is likely to enhance both the clinical quality and efficiency of care.

However, as with any service reconfiguration, careful consideration of the costs and benefits is required. Before implementation, it is essential that high-quality research is conducted to examine the effectiveness and cost-effectiveness of nurse-run digital screening under real-world conditions. The practicality of this option must also be tested. Will it be possible to recruit and train the experienced specialist nurses required? How should they be organized? And how can we ensure that the necessary support structures are in place? These logistical questions are vital to ensure that timely access to treatment is maintained.

This analysis has been undertaken at a time of rapid technological advance, both with respect to image capture and analysis. Cameras will become cheaper and more portable. It has also been shown that digitally obtained images can be semiautomatically analyzed and severe ROP differentiated from mild disease (22;36). This study might be considered a baseline or pilot for future studies. In the near future, it can be reliably predicted that simple one-shot digital screening examination paradigms will be developed with the results being automatically analyzed to determine whether an ophthalmic opinion is required.

Finally, ROP screening is becoming increasingly important for many developing countries due to increased survival of very low birth weight babies made possible by the improved technology in neonatal care. It is possible that, in the future, digital photography used by well-trained nurses could be a feasible method of extending ROP screening.

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