Cost reduction in screening for retinopathy of prematurity in the Netherlands by comparing different screening strategies

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ORIGINAL ARTICLE

Cost reduction in screening for retinopathy of prematurity in the Netherlands by comparing different screening strategies

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Abstract

Purpose: Evaluate possibilities to reduce the number of infants screened for retinopathy of prematurity (ROP) and investigate costs and number of infants detected of current and alternative screening strategies in the Netherlands.

Methods: Prospective population-based study including clinical data from all infants born in 2017 and referred for ROP screening (NEDROP-2 study). Cost and effects of screening strategies were evaluated that differed on the criteria gestational age (GA), birth weight (BW) and presence of one or more specific risk factor(s) (RF): mechanical ventilation, sepsis, necrotizing enterocolitis, postnatal corticoids and/or hypotension treated with inotropic agents. RF obtained from the Dutch perinatal registry (Perined).

Results: Of the possible efficient strategies, the annual costs varied from €137 966 (inclusion of BW < 700, 63 infants eligible for screening, detection of 17/39 treated ROP) to €492 689 (GA < 30 weeks *and* BW < 1250 grams, together with infants with GA 30–32 and BW 1250–1500 grams with presence of one more RF, 744 infants eligible for screening, all treated infants detected). Total annual costs of the current Dutch guideline that detects all infants that need treatment for ROP amount to €552 143).

Conclusion: The current Dutch ROP guideline can be improved by implementing new screening inclusion criteria. The most effective strategy detecting all severe and treated infants, reduces the number of screened infants by 24% compared to the current guideline and the overall annual costs by €59454.

KEYWORDS
cost-effectiveness, guideline, improved vision, retinopathy of prematurity, screening

1 | INTRODUCTION

Retinopathy of prematurity (ROP) remains the most important cause of visual impairment and blindness in premature infants (Hellstrom et al., 2013). The majority of ROP cases are mild and regress spontaneously; however, timely detection and treatment of a small number of infants with progressive, sight threatening ROP is pivotal to prevent severe and permanent vision loss.

In case of severe ROP and when treatment is required, the gold standard is laser photocoagulation of the peripheral retina (Good, 2004). Alternatively, intravitreal anti-vascular endothelial growth factor (VEGF) can be considered and its use is increasing worldwide. However, the current Dutch guideline (2013) advises using anti-VEGF in ROP stage 3 in zone I and as last resort treatment only (NEDROP). Despite treatment, some infants still progress to retinal detachment, in which the corner stone of management is pars plana vitrectomy (PPV).

Developing a universal ROP screening and treatment guideline is futile, as the risk of progression depends on the overall child's health and strongly correlates with the overall neonatal health and, therefore, (regional) neonatal care (Kim et al., 2018). Therefore, it is crucial that

screening and treatment guidelines are based on circumstances of influence per individual country. Most screening programs use gestational age and/or birth weight criteria for inclusion in the screening program (Wilkinson et al., 2009; Stahl & Gopel, 2015; Fierson, 2018; Holmström et al., 2020). In addition, some of them include infants with an unstable course (Fierson, 2018; Holmström et al., 2020). Screening programs would benefit from a better defined risk-based screening profile to minimize the chance for unwarranted in- or exclusion by solely relying on expert opinion.

In the Netherlands, the first national ROP inventory was the NEDROP (2009) (van Sorge et al., 2014a). The study revealed, that many babies (1364/1688, 78%) who never developed ROP were exposed to the burden of screening (van Sorge et al., 2014b). Upon this finding, updated and risk-based screening criteria were included in the new ROP guideline (2013), predictively reducing the number of screened infants by approximately one third, while warranting detection of all infants with severe ROP (van Sorge et al., 2013; van Sorge et al., 2014a; van den Akker-van Marle et al., 2015).

Yet, since the first inventory, in the Netherlands essential changes in neonatal care were adopted that increase the risk for (severe) ROP. In 2010, the gestational age (GA) in which babies receive active neonatal treatment was lowered from 25 to 24 weeks and in 2014 higher oxygen saturation targets were implemented during the first weeks of life (Saugstad & Aune, 2014). Together with the new screening criteria, these changes called for a second national ROP inventory, resulting in the NEDROP 2, in which incidence, screening logistics, treatment and risk factors of ROP were investigated for the year 2017.

Thus, following increased survival of the most immature infants and the introduction of unfavourable neonatal factors, an increase in infants developing (severe) ROP is expected. Moreover, considering that ROP screening is uncomfortable (Mitchell et al., 2011), time-consuming and costly, the effectiveness of a screening protocol is increasingly important.

The aim of this study was to analyse if the number of infants requiring ROP screening could be reduced once more. Therefore, the effects and costs were evaluated of the current and other screening strategies.

2 | METHODS

This study was initiated and coordinated by the Leiden University Medical Center. Data collection was anonymous; therefore, approval of the medical ethical committee was not necessary. For neonatal risk factors a separate existing national register was used, called Perined, containing medical data of 97% of all neonates born in the Netherlands are reported by neonatologists and paediatricians (Perined, 2017). Data from Perined were only recorded after parental approval.

Paediatricians and neonatologists of all hospitals involved in ROP screening in the Netherlands, prospectively reported infants they considered eligible for ROP screening who were born between January 1 and December 31 of the year 2017. They used a coded dataset consisting of date of birth, four digits of the ZIP code, GA, BW and the index number in case of multiple birth (1/2, 2/2, 1/3, etc.). The latest guideline, introduced in 2013, changed inclusion criteria for screening from gestational age (GA) <32 weeks and/or birth weight (BW) <1500 g to GA < 30 weeks and/or birth weight (BW) < 1250 grams, and infants with GA 30–32 weeks and/or BW 1250–1500 grams with presence of at least one of the following risk factors: mechanical ventilation, sepsis (defined as clinically ill with positive blood cultures), postnatally administered glucocorticoids, perforated necrotizing enterocolitis and hypotension treated with inotropic agents (van Sorge et al. 2013).

Ophthalmologists provided a separate report on ophthalmological data by use of the same code, together with findings from the conducted ROP examinations: consisting of presence of plus disease, maximum zone and ROP stage per eye, reason for discontinuation of screening and, if applicable modality of treatment. ROP was classified according to the revised International Committee for the Classification of Retinopathy of Prematurity (2005). For the purpose of comparison with NEDROP 1 study, ROP was categorized into mild (stage 1–2) and severe (stage ≥3) ROP.

Data from the NEDROP 2 database and Perined were merged through the use of the earlier mentioned code (population flow chart Figure 1). For infants for which this merging failed ($n = 141$), information on the presence of risk factors was obtained using multiple imputation by predictive mean matching (van Buuren et al., 1999) using information on GA, BW, treatment, presence of ROP and when present, maximum ROP stage. In a sensitivity analysis the effect of the imputation was studied by repeating the analyses using the non-imputed data.

Based on these data, various screening strategies were evaluated, using (a combination of) the following inclusion criteria: 1. GA, 2. BW, 3. Combined GA-BW and 4. Combined GA-BW and presence of one or more risk factor (Appendix A). For each of these screening strategies the number of infants eligible for screening, the number of infants per ROP category, and the number of infants treated were assessed.

Subsequently, each strategy is compared to the other strategies that resulted in the same number of infants detected. The screening strategy that screened the lowest number of infants to detect this number of infants is a so-called efficient strategy.

2.1 | Costs

For all efficient strategies, costs were assessed from a healthcare perspective by including costs of screening and treatment during the first year after birth. Due to this short term time horizon, no discounting was applied. Costs are expressed in 2021 Euros. Cost prices of earlier years have been converted into 2021 price levels by use of the general Dutch consumer price index (Statline 19-01-2021) To obtain the screening costs, the number of examinations per infant were multiplied by the costs per screening. The mean number of screening examinations per infant per ROP category (no, mild and severe

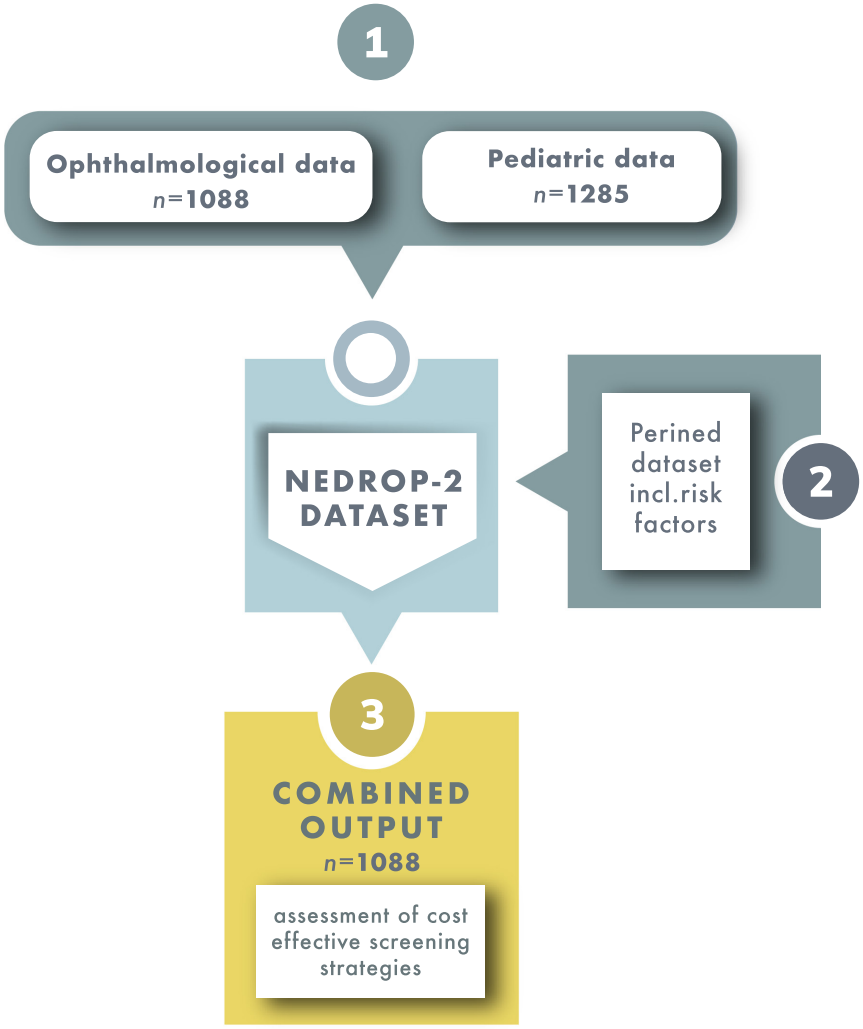

FIGURE 1 Population flow chart [Colour figure can be viewed at wileyonlinelibrary.com]

ROP), were obtained from the NEDROP 2 data and were 2.3, 4.9 and 10.2, respectively. Costs for screening consist of personnel costs of a nurse and an ophthalmologist and material costs of the eyelid speculum and eye drops amounting to €97 per screening (Table 1). Costs of bilateral ROP treatment involve transfer to the treatment centre by ambulance with obligatory escort of a resident or neonatologist (€1449) (Kanters et al., 2017) and laser treatment (€3819) for 97% of the patients or vitrectomy (€7245) for the remaining patients (Table 1). For unilateral treatment it was assumed that two-thirds of the surgery time of bilateral treatment with associated cost for surgery room and personnel, and the same material and equipment costs as for bilateral treatment was needed.

2.2 | Effects

The effects of screening are defined as improved visual acuity as a result of early laser treatment compared to no and late treatment (Good, 2004), according to the Cryotherapy for ROP (CRYO-ROP) and Early Treatment for ROP (ETROP) studies. The CRYO-ROP study compared cryotherapy versus no treatment, the ETROP study compared early laser treatment with late treatment with cryotherapy. This resulted in improved vision of 17.7% and 7.7%, respectively, using the adjusted indirect comparison method. Combined, an estimated improved vision of 25.4% was used to analyse outcomes of treatment versus no treatment.

2.3 | Cost-effectiveness

Costs and effects were combined to assess the cost-effectiveness, expressed as the average costs per infant with improved vision of a screening strategy compared to a situation without screening and treatment. Subsequently, dominant strategies were identified, that is efficient strategies for which no (combination of) other strategies exist that result in a higher number of infants with improved vision for lower costs. For these strategies the marginal costs per additional infant with improved vision were calculated, which indicates the amount that have to be paid to find an additional infant compared to the nearest dominant screening strategy that finds a lower number of infants.

3 | RESULTS

The NEDROP database included 1285 infants, of which 120 patients died before first screening. Screening was performed in 1088 babies, ROP was found in 305 babies:

TABLE 1 Costs of retinopathy of prematurity screening and treatment, 2021 euros

Cost item	Amount	Cost price (2021 €)[a]	Cost	Sources
Cost of screening				
Nurse	40 min	€35/h	€24	Personal communication; Kanters et al. 2017
Ophthalmologist	30 min	€126/h	€63	Personal communication; Kanters et al. 2017
Eyelid speculum	1	€9.92	€9.92	Tariff of manufacturer
Eyedrops		€0.58	€0.58	Price list national pharmacotherapeutic manual
Total			€97	
Cost of laser treatment				
Surgical assistants	2*2 h	€41/h	€162	Personal communication; Salary table surgical assistant[b]
Anaesthesia assistant	2 h	€41/h	€81	Personal communication; Salary table surgical assistant[b]
Anaesthetist	2 h	€126/h	€252	Personal communication; Kanters et al. 2017
Ophthalmologist	2 h	€126/h	€252	Personal communication; Kanters et al. 2017
Neonatologist	0.3 h	€126/h	€38	Personal communication; Kanters et al. 2017
Laser equipment[c]	1	€34	€34	Personal communication
Operating room	2 h	€1500	€3000	Personal communication
Total			€3819	
Cost of vitrectomy treatment				
Surgical assistants	2*3.5 h	€41/h	€284	Personal communication; Salary table surgical assistant (ref)
Anaesthesia assistant	3.5 h	€41/h	€142	Personal communication; Salary table surgical assistant (ref)
Anaesthetist	3.5 h	€126/h	€441	Personal communication; Kanters et al. 2017
Ophthalmologist	3.5 h	€126/h	€441	Personal communication; Kanters et al. 2017
Neonatologist	0.3 h	€126/h	€38	Personal communication; Kanters et al. 2017
Equipment[c] and disposables	1	€650	€650	Personal communication
Operating room	3.5 h	€1500	€5250	Personal communication
Total			€7245	
Transfer ambulance				
Ambulance (back and forth)	2	€564	€1128	Kanters et al. 2017
Escort resident or neonatologist	2 h single ride	€80/h[d]	€319	Kanters et al. 2017
Total			€1447	

[a]Cost prices of earlier years have been converted into 2021 price levels by use of the general Dutch consumer price index www.opendata.cbs.nl/statline [Accessed 19th January 2021].

[b]Salarisschalen, premies & vergoedingen, NVZ Cao Ziekenhuizen https://cao-ziekenhuizen.nl/salarisschalen-premies-vergoedingen

[c]Calculated on the basis of initial purchasing price, yearly use and depreciation, and maintenance and interest costs.

[d]Average cost per hour of resident (€34) and (€126), ref Kanters et al. 2017.

259 mild (stage 1–2) and 47 severe (stage≥3). Treatment (all retinal laser photocoagulation) was performed in 39 infants. Initial treatment was bilateral for all infants, by means of laser treatment for 97% of the infants and vitrectomy for the others. Furthermore, in 15% of the children retreatment was necessary, of which 50% with laser treatment and 25% bilateral.

In Table 2, the number of infants eligible for screening and infants treated for ROP are presented per screening strategy. The most efficient strategy detecting all infants treated for ROP, includes infants with GA < 30 weeks and BW < 1250 g *and* GA 30–32 weeks and/or BW 1250–1500 g with one or more risk factors. This would require screening of 744 children, representing a 23.8% reduction in comparison to the current screening guideline. A total of 2662 screening examinations would be performed if the strategy would apply to the NEDROP 2 population, representing a 18.7% reduction compared to the 3274 screenings that need to be carried out according to the current guideline.

In Table 3 and Figure 2 the cost-effectiveness is shown of efficient strategies in ascending number of treated infants. For comparison also the current Dutch strategy is shown.

The total annual costs (screening + treatment) of the most efficient strategies vary from €137 966 (strategy 9: BW < 700 g) detecting 17/39 of the infants treated for ROP to €492 689 (strategy 50: GA < 30 weeks and BW < 1250 grams or GA 30–32 weeks and/or BW 1250–1500 grams with at least one risk factor) detecting all 39 infants treated for ROP. Only the latter scenario detects all infants with treatment requiring ROP, while reducing annual costs by €59454 compared to the current guideline. The other strategies are more economically beneficial; however, missing children who require treatment would need to be accepted.

Detecting all 39 infants needing treatment would lead to an overall improvement of vision corresponding to an improvement of 9.9 children from no sight (0%) to full sight (100%). The Average Cost per Person with

TABLE 2 Number of infants eligible for screening and treated for ROP while using different screening inclusion criteria

	Criteria	Eligible	Treated for ROP
	GA, weeks		
1.	<26	104	21
2.	<27	208	30
3.	<28	348	35
4.	<29	535	38
5.	<30	742	38
6.	<31	885	39
7.	<32	1025	39
8.	<33	1066	39
9.			
	BW, g		
10.	<700	63	17
11.	<1000	346	33
12.	<1100	452	34
13.	<1200	602	37
14.	<1250	682	37
15.	<1300	740	37
16.	<1500	923	39
17.	<1600	984	39
18.	<1700	1022	39
19.	<1800	1047	39
20.	<1900	1069	39
21.	<2000	1074	39
	Combined, GA and BW		
22.	<29/<1200	428	37
23.	<29/<1250	452	37
24.	<29/<1500	528	38
25.	<30/<1250	545	37
26.	<30/<1500	707	38
27.	<31/<1200	542	37
28.	<31/<1250	601	37
29.	<31/<1500	805	39
30.	<32/<1200	578	37
31.	<32/<1250	643	37
32.	<32/<1500	871	39
	Combined, GA and/or BW		
33.	<29/<1200	709	38
34.	<29/<1250	765	38
35.	<29/<1500	930	39
36.	<30/<1200	847	38
37.	<30/<1250	879	38
38.	<30/<1500	958	39
39.	<31/<1200	945	39
40.	<31/<1250	966	39
41.	<31/<1500	1003	39
42.	<32/<1200	1049	39
43.	<32/<1250	1064	39
44.	<32/<1500	1077	39
	Combined GA-BW-risk factor[a]		
			Treated for ROP
45.	<30 weeks and <1250 g and at least one risk factor	402	36
46.	<32 weeks and <1500 g and at least one risk factor	564	38
	Combined GA-BW-risk factor		
			Treated for ROP
47.	<30 weeks and/or <1250 g and at least one risk factor	566	37
48.	<32 weeks and/or <1500 g and at least one risk factor	664	38
49.			
50.	<30 weeks and <1250 g & 30–32 weeks and/or 1250–1500 g and at least one risk factor	744	39
51.	NL <30 weeks and/or <1250 g & 30–32 weeks and/or 1250–1500 g and at least one risk factor	977	39
52.	escape <32 weeks and/or <1500 g	1077	39
53.	Lower limit <30 weeks and/or <1250 g	879	38

Note: The most efficient strategies for the different numbers of infants treated for ROP found are shaded.

Abbreviations: BW, birth weight; GA, gestational age; ROP, retinopathy of prematurity.

[a]Risk factors: mechanical ventilation, sepsis, perforated necrotizing enterocolitis, postnatally administered glucocorticoids and hypotension treated with inotropic agents.

Improved Vision (AC/PIV) ranges from €31951 (strategy 9: BW <700 g) to €49736 (again strategy 50). The Marginal Costs per additional PIV (MC/APIV), ranged from €32173 (strategy 9) to €250028 (strategy 50).

The sensitivity analysis using non-imputed data resulted in the same selection of efficient strategies and comparable cost-effectiveness results (Appendix B).

4 | DISCUSSION

In the Netherlands, the retinopathy of prematurity (ROP) guideline can be safely adjusted by lowering the number of infants requiring uncomfortable and time-consuming examinations by 23.8%, without missing treatment requiring ROP. The most efficient strategy detecting all patients with treatment requiring ROP, based on analyses of prospective annual national data, is the one including infants born with GA < 30 weeks *and* BW < 1250 grams, and infants with 30–32 weeks and BW 1250–1500 grams with at least one defined risk factor (mechanical ventilation, sepsis, necrotizing enterocolitis, postnatal glucocorticoids and treatment with inotropic agents). In the second NEDROP study (NEDROP-2, 2017), no new risk factors were found to be significantly correlated with development of (severe) ROP in the Dutch population (Trzcionkowska et al., Risk factors for retinopathy of prematurity in the Netherlands: a comparison of two cohorts, Neonatology, 2021). In 2009, the latter strategy also demonstrated to be the most efficient strategy to detect all patients with treatment requiring

TABLE 3 Cost-effectiveness of efficient screening strategies (shaded strategies Table 1) and current strategy, €2021 (A)PIV: additional persons with improved vision

Strategy	BW < 700	GA < 26	GA < 27	BW < 1000	BW < 1100	GA < 28	GA < 30 and BW < 1250 and ≥1 RF	GA < 29 or BW < 1200	GA < 29 or BW < 1500	GA < 30 and BW < 1250 or 30–32 and/or 1250–1500 + ≥1 RF	Current strategy
Strategy number (Table 1)	9	1	2	10	11	3	44	32	34	48	49
Infants to be treated for ROP detected	17	21	30	33	34	35	36	37	38	39	39
Number of screenings	370	584	1031	1470	1810	1503	1639	1770	2070	2662	3274
Cost of screening	35 901	56 719	100 145	142 794	175 761	146 012	159 189	171 932	201 037	258 541	317 995
Cost of treatment	91 267	112 742	161 060	177 165	182 534	187 903	193 271	198 640	204 009	209 377	209 377
Cost of retreatment	10 798	13 338	19 055	20 960	21 595	22 231	22 866	23 501	24 136	24 771	24 771
Total costs (€)	137 966	182 799	280 259	340 920	379 890	356 146	375 326	394 073	429 182	492 689*	552 143
No of PIV	4.3	5.3	7.6	8.4	8.6	8.9	9.1	9.4	9.7	9.9	9.9
AC/PIV	31 951	34 270	36 779	40 673	43 989	40 061	41 046	41 932	44 466	49 736	55 738
MC/APIV	31 951	Dominated	42 633	Dominated	Dominated	59 753	Dominated	73 806	138 225	250 028	Dominated

*Example of calculation of cost calculation for screening strategy **GA < 30 and BW < 1250 or 30–32 and/or 1250–1500 + ≥1 RF:**

Number of screenings: 47 [number of infants detected with severe ROP in this strategy] * 10.2 [mean number of screening examinations per infant with severe ROP] + 225 [number of infants detected with mild ROP in this strategy] * 4.9 [mean number of screening examinations per infant with mild ROP] + 472 [number of infants without ROP] * 2.3 [mean number of screening examinations per infant without ROP in this strategy] = **2662.**

Cost of screening: 2662 [number of screenings] * € 97 [cost of screening] = **€ 258 541.**

Cost of treatment: 39 [infants to be treated for ROP detected] * (€ 1447 [cost of transfer ambulance] + 0.97 [percentage laser] * € 3819 + 0.03 [percentage vitrectomy] * € 7245 [cost vitrectomy]) = **€ 209 377.**

Cost of retreatment: 39 [infants to be treated for ROP detected]*0.15 [percentage of infants with retreatment]*(0.5 [percentage vitrectomy]*(0.25 [percentage of infants with bilateral treatment at retreatment] * € 7245 [cost vitrectomy bilateral] + 0.75 [percentage of infants with unilateral treatment at retreatment] * € 5047 [cost vitrectomy unilateral]) + 0.5 [percentage of retreatments with laser]*(0.25 [percentage of infants with bilateral treatment at retreatment] * € 3819 [cost laser bilateral] + 0.75 [percentage of infants with unilateral treatment at retreatment] * € 2557 [cost laser unilateral])) = **€ 24 771.**

Total cost = € 258 541 [cost of screening] + € 209 377 [cost of treatment] + € 24 771 [cost of retreatment] = **€ 492 689.**

Abbreviations: AC, average costs; BW, birth weight; GA, gestational age; MC, marginal costs; PIV, person with improved vision; RF, risk factor; ROP, retinopathy of prematurity.

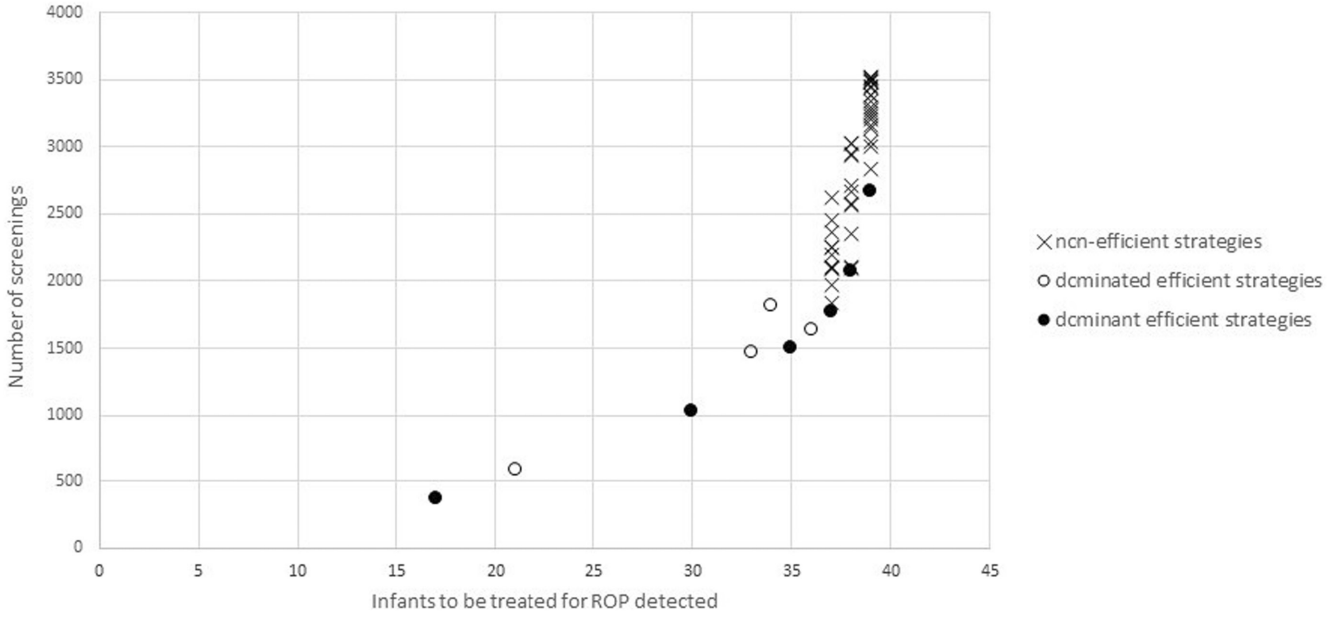

FIGURE 2 Overview of cost-effective strategies (see Table 3)

ROP. However, its implementation was approached with caution as data were based on only 1 year of ROP data (van den Akker-van Marle et al., 2015); therefore, the safer but slightly less efficient GA *and/or* BW criterion was chosen as inclusion criteria. In the present inventory all infants who required treatment were again identified by use of the new strategy which thus, can be considered safe for implementation in the upcoming new guideline.

In developed countries, severe ROP in infants born with GA over 30 weeks is uncommon (Holmström et al., 2020), therefore, subjecting more mature infants to stress evoking ROP examinations becomes debatable. However, restricting the criteria is not always possible. It is essential to adjust selection criteria in each country to the national circumstances and screening populations. Particularly in middle income countries, a combination of limited access to neonatal resources and possibly lack of ROP awareness or ophthalmological expertise play a crucial role (Erdeve et al., 2010; Romo-Aguas et al., 2019). Therefore, the risk of misdiagnosing patients who require treatment may be too high if our inclusion criteria would be adopted directly.

Nevertheless, not only in the Netherlands investigations are carried out aiming to increase efficiency of ROP screening. In Sweden it was revealed, that in the past decade no infants with GA ≥30.0 weeks were treated for ROP and only ten babies developed ROP stage ≥3, which in all ten regressed spontaneously (Holmström et al., 2020). Therefore, a modification of the inclusion criteria has been proposed from screening babies with GA < 31.0 weeks (and an additional selection of more mature infants who are referred by neonatologists based on individual risk assessment) to GA < 30.0 weeks, along with individual assessment of high-risk infants. If these criteria would apply in the Netherlands, based on GA solely, a total of 742 infants would have to be screened, two infants less compared to the most effective screening in the present study. However, in our cohort one infant with severe and treatment requiring ROP would have been missed.

If the US guideline would be used in our population (GA < 31 weeks or BW < 1500 g) (Fierson, 2018), all infants with severe and treated ROP would have been detected, but at least 60 more infants would undergo screening, resulting in unnecessary discomfort and higher costs. Use of the current UK guideline (GA < 32 weeks and/or BW < 1501 g) (Wilkinson et al., 2009) would also provide adequate detection, but would also unnecessarily increase the size of the group to be screened.

The decision whether to accept missing children with severe ROP is on the one hand ethical and on the other hand economical. We have to determine which costs per additional infant with improved vision are acceptable for society. For the efficient treatment strategies, these marginal costs range from €31951 to €250028 per additional infant with improved vision. However, we only have an indication of the willingness of the Dutch society to pay for a quality adjusted life year (QALY). In the Netherlands, the willingness to pay for a QALY varies from €20000 to €80000 depending on the burden of disease. The most likely threshold for vision loss is €20000 per QALY according to the iMTA Disease Burden Calculator (Institute for Medical Technology Assessment Calculator). Therefore, we have to translate improved vision obtained by screening and treatment into QALYs. Assuming a mean visual acuity of 0.20 in non-treated eyes and 0.48 in treated eyes (Dunbar et al., 2009), a yearly gain in utility of 0.10 can be obtained according to the formula of Sharma et al (Sharma et al., 2000). For an average life expectancy around 80 years (Statistics Netherlands 2013) and applying a discount rate of 3% over this period, this amounts to 3.3 quality adjusted life years (QALYs) for an infant with improved vision during lifetime. Relating this to the marginal costs, results in incremental cost-effectiveness ratios of €9809 to €76754 per QALY for the efficient strategies. For the screening strategy detecting all severe and treatment requiring ROP, therefore, also savings during lifetime due to treatment have to be made to be acceptable for the Dutch situation. These societal cost savings may be obtained by more self-reliance, less or no need of support

programs and lower educational costs as these infants with improved vision do not need special education, savings in home modifications and devices and costs for carers.

STRENGTHS & LIMITATIONS

This is the second study based on annual national data to study the effectiveness of ROP screening in the Netherlands. The main strength is its repeatability, which allowed consecutive demonstration of safety and benefits of significant reduction in screening. Limitations include the relative short term nature of benefit calculations. We made a rough estimation of longer term effects and costs, but future studies should elaborate on this. Implementation of our results in other countries could be limited due to varying health care costs (i.e. personnel, materials, procedures, etc.), life expectancy and epidemiology of ROP. Moreover, the relatively small annual birth number in the Netherlands, increases the importance of centralization of ROP treatment. Therefore, perhaps in other countries, transfer to another hospital for treatment might not be necessary. Our calculations and results can be used as framework, but should not be taken on without guarded adjustments.

In conclusion, two consecutive national inventories on ROP (NEDROP 1 (2009) and NEDROP 2 (2017)) both gave rise to the same preferred screening strategy. The Dutch national guideline for screening will be adjusted accordingly, resulting in fewer infants being exposed to screening examinations. This will reduce healthcare costs further by about 60 000 euro per year. Marginal costs for detecting all these infants might be acceptable for society when QALY gain and savings for society as a result of improved vision are incorporated in the decision.

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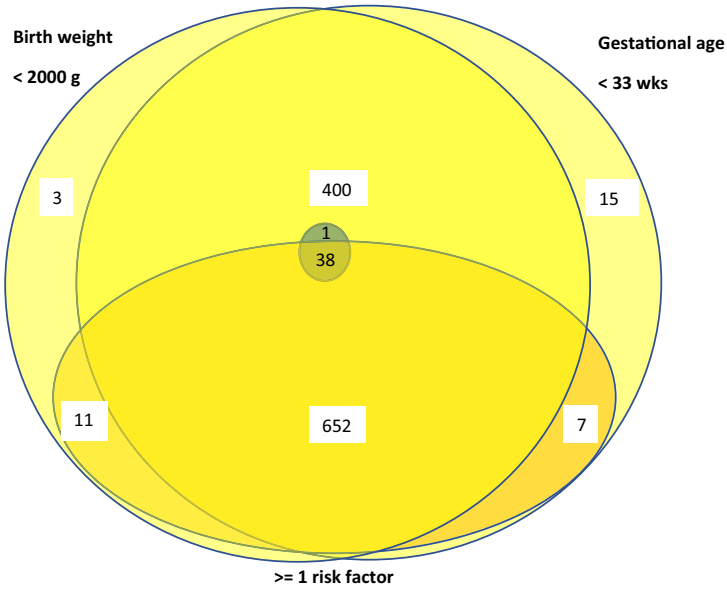
APPENDIX A

In this diagram the numbers of infants considered eligible for screening with a birth weight < 2000 g, gestational age < 33 weeks, and/or more than one risk factor are presented. In the middle, these numbers are shown for the 39 infants treated for ROP.



In this diagram the numbers of infants considered eligible for screening with a birth weight < 2000 g, gestational age < 33 weeks, and/or more than one risk factor are presented. In the middle, these numbers are shown for the 39 infants treated for ROP.

APPENDIX B

Cost-effectiveness of efficient screening strategies and current strategy based on non-imputed data, 2021 euros

Strategy	BW < 700	GA < 26	GA < 27	BW < 1000	BW < 1100	GA < 28	GA < 30 and BW < 1250 and ≥1 RF	GA < 29 or BW < 1200	GA < 29 or BW < 1500	GA < 30 and BW < 1250 or 30–32 and/or 1250–1500 + ≥1 RF	Current strategy
Infants to be treated for ROP detected	16	18	25	28	29	30	31	32	33	34	34
Number of screenings	328	498	901	1288	1592	1345	1442	1560	1838	2348	2880
Total costs (€)	128 805	157 421	239 014	294 820	330 387	312 419	327 916	345 408	378 536	434 087	485 755
No of PIV	4.1	4.6	6.4	7.1	7.4	7.6	7.9	8.1	8.4	8.6	8.6
AC/PIV	31 694	34 431	37 640	41 454	44,853	41 000	41 645	42 496	45 161	50 265	56 248
MC/APIV	31 694	Dominated	48 210	Dominated	Dominated	57 800	Dominated	64 939	130 424	218 703	Dominated

Note: (A)PIV: additional persons with improved vision.

Abbreviations: AC, average costs; MC, marginal costs.